Modern Predictors of Mortality in Patients Undergoing Emergency Laparotomy

Shahab Hajibandeh, MBChB, FRCS

Submitted to Swansea University in fulfilment of the requirements for the Degree of Doctor of Philosophy (PhD) by Published Works

Swansea University

2025

SUMMARY (ABSTRACT)

This thesis investigates the modern predictors of 30-day mortality in patients with non-traumatic acute abdominal pathology undergoing emergency laparotomy through 12 studies (six cohort studies and six meta-analyses) published in peer-reviewed medical journals.

The design and reporting of the cohort studies followed either the Strengthening the Reporting of Cohort Studies in Surgery (STROCSS) or the Transparent Reporting of a multivariable prediction model for Individual Prognosis or Diagnosis (TRIPOD). The design and reporting of the meta-analyses followed the Cochrane Handbook for Systematic Reviews and the Preferred Reporting Items for Systematic reviews and Meta-Analyses (PRISMA) statement standards.

The potential predictors of mortality related to the physical status of the patients, severity of the underlying abdominal pathology, healthcare setting, and socioeconomic status of the patients were evaluated. The variables related to physical status of the patients included age 80 or over (≥ 80), the American Society of Anaesthesiologists (ASA) status, sarcopenia, and clinical frailty scale (CFS). The variables related to the severity of the underlying abdominal pathology included the intraperitoneal contamination index (Hajibandeh Index), the presence of intraperitoneal contamination, and the need for bowel resection. The variables related to healthcare setting included the surgeon's seniority, the surgeon's subspeciality of interest, the weekend effect (operation during weekend), the application of enhanced recovery after surgery (ERAS) protocols in emergency surgery.

The aforementioned potential predictors were evaluated in individual studies and then, based on the knowledge obtained regarding the predictive significance of each potential predictor, a predictive model was developed and validated taking into account all important potential predictors. After a very strict multivariable analysis, Hajibandeh Index, ASA status and sarcopenia remained as final independent predictors of mortality after emergency laparotomy. The final model was called HAS which demonstrated excellent discrimination, calibration, and classification.

Word count: 288

DECLARATIONS AND STATEMENTS

This work has not previously been accepted in substance for any degree and is not being concurrently submitted in candidature for any degree.

Signed: ..[redacted]. (Shahab Hajibandeh) Date......02/11/2025...

This thesis is the result of my own investigations, except where otherwise stated. Other sources are acknowledged by footnotes giving explicit references. A bibliography is appended.

Signed: ...[redacted].. (Shahab Hajibandeh) Date......02/11/2025...

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The University's ethical procedures have been followed and, where appropriate, that ethical approval has been granted.

Signed: ...[redacted]..... (Shahab Hajibandeh) Date......02/11/2025...

CONTENTS PAGE

ACKNOWLEDGEMENTS

Firstly, I would like to thank my lovely wife, Niloo, for continuous support throughout my clinical and academic career which allowed successful completion and publication of several research projects. Secondly, I would like to thank my beautiful dog, Nancy, who was my daughter and had been faithfully sitting on my legs while I was writing my articles over the last 14 years. Although she passed away in November 2024, I am sure she is very proud of me. Then, I would like to thank my parents and my grandparents for supporting me to grow up in a peaceful environment and to progress successfully from primary school to graduation from medical school. Finally, I would like to thank Professor Venkat Kanamarlapudi and Professor Bilal Al-Sarireh for their invaluable support during enrolment process for the PhD by Published Work programme and in completion of this thesis.

LIST OF PUBLISHED WORKS WITH CONTRIBUTION STATEMENT

Article 1. Meta-analysis of mortality risk in octogenarians undergoing emergency general surgery operations

Citation: **Hajibandeh S**, Hajibandeh S, Antoniou GA, Antoniou SA. Meta-analysis of mortality risk in octogenarians undergoing emergency general surgery operations. Surgery. 2021 Jun;169(6):1407-1416. doi: 10.1016/j.surg.2020.11.027.

This serves to confirm that Shahab Hajibandeh was the first, lead, and corresponding author of the above article and he contributed to conception, design, data collection, data analysis, write up, and critical revision of the article.

Author 2:	Shahin Hajibandeh	**Date:**	20/04/2025	[redacted]
Author 3:	George A. Antoniou	**Date:**	20/04/2025	[redacted]
Author 4:	Stavros A. Antoniou	**Date:**	20/04/2025	[redacted]

Article 2. The risk and predictors of mortality in octogenarians undergoing emergency laparotomy: a multicentre retrospective cohort study

Citation: **Hajibandeh S**, Hajibandeh S, Shah J, Martin J, Abdelkarim M, Murali S, Maw A, Mansour M, Satyadas T. The risk and predictors of mortality in octogenarians undergoing emergency laparotomy: a multicentre retrospective cohort study. Langenbecks Arch Surg. 2021 Sep;406(6):2037-2044. doi: 10.1007/s00423-021-02168-y.

This serves to confirm that Shahab Hajibandeh was the first, lead, and corresponding author of the above article and he contributed to conception, design, data collection, data analysis, write up, and critical revision of the article.

Author 2:	Shahin Hajibandeh	**Date:**	25/05/2025	[redacted]
Author 3:	Jigar Shah	**Date:**	25/05/2025	[redacted]

Author 4:	Julia Martin	**Date:**	25/05/2025	[redacted]
Author 5:	Mostafa Abdelkarim	**Date:**	25/05/2025	[redacted]
Author 6:	Sreedutt Murali	**Date:**	25/05/2025	[redacted]
Author 7:	Andrew Maw	**Date:**	25/05/2025	[redacted]
Author 8:	Moustafa Mansour	**Date:**	25/05/2025	[redacted]
Author 9:	Thomas Satyadas	**Date:**	25/05/2025	[redacted]

Article 3. Sarcopenia versus clinical frailty scale in predicting the risk of postoperative mortality after emergency laparotomy: a retrospective cohort study

Citation: **Hajibandeh S,** Hajibandeh S, Brown C, Harper ER, Saji AP, Hughes I, Mitra K, Rashwany H, Clayton A, Patel N, Abdelrahman T, Foliaki A, Kumar N. Sarcopenia versus clinical frailty scale in predicting the risk of postoperative mortality after emergency laparotomy: a retrospective cohort study. Langenbecks Arch Surg. 2024 Feb 14;409(1):59. doi: 10.1007/s00423-024-03252-9.

This serves to confirm that Shahab Hajibandeh was the first, lead, and corresponding author of the above article and he contributed to conception, design, data collection, data analysis, write up, and critical revision of the article.

Author 2:	Shahin Hajibandeh	**Date:**	25/05/2025	[redacted]
Author 3:	Christopher Brown	**Date:**	25/05/2025	[redacted]
Author 4:	Elizabeth Ryan Harper	**Date:**	25/05/2025	[redacted]
Author 5:	Alwin Puthiyakunnel Saji	**Date:**	25/05/2025	[redacted]
Author 6:	Ioan Hughes	**Date:**	25/05/2025	[redacted]
Author 7:	Kalyan Mitra	**Date:**	25/05/2025	[redacted]

Author 8:	Hind Rashwany	**Date:**	25/05/2025	[redacted]
Author 9:	Amy Clayton	**Date:**	25/05/2025	[redacted]
Author 10:	Neil Patel	**Date:**	25/05/2025	[redacted]
Author 11:	Tarig Abdelrahman	**Date:**	25/05/2025	[redacted]
Author 12:	Antonio Foliaki	**Date:**	25/05/2025	[redacted]
Author 13:	Nagappan Kumar	**Date:**	25/05/2025	[redacted]

Article 4. Synergistic effect of sarcopenia and ASA status in predicting mortality after emergency laparotomy: a systematic review and meta-analysis with meta-regression

Citation: Al-Sarireh A, Al-Sarireh H, Ambler O, Hajibandeh S, **Hajibandeh S**. Synergistic effect of sarcopenia and ASA status in predicting mortality after emergency laparotomy: a systematic review and meta-analysis with meta-regression. Updates Surg. 2025 Apr;77(2):591-603. doi: 10.1007/s13304-025-02105-4.

This serves to confirm that Shahab Hajibandeh was the lead and corresponding author of the above article and he contributed to conception, design, data collection, data analysis, write up, and critical revision of the article.

Author 1:	Ahmad Al-Sarireh	**Date:**	13/04/2025	[redacted]
Author 2:	Hashim Al-Sarireh	**Date:**	13/04/2025	[redacted]
Author 3:	Olivia Ambler	**Date:**	13/04/2025	[redacted]
Author 4:	Shahin Hajibandeh	**Date:**	13/04/2025	[redacted]

Article 5. Intraperitoneal contamination index (Hajibandeh index) predicts nature of peritoneal contamination and risk of postoperative mortality in patients with acute abdominal pathology: a prospective multicentre cohort study

Citation: **Hajibandeh S,** Shah J, Hajibandeh S, Murali S, Stephanos M, Ibrahim S, Asqalan A, Mithany R, Wickramasekara N, Mansour M. Intraperitoneal contamination index (Hajibandeh index) predicts nature of peritoneal contamination and risk of postoperative mortality in patients with acute abdominal pathology: a prospective multicentre cohort study. Int J Colorectal Dis. 2021 May;36(5):1023-1031. doi: 10.1007/s00384-020-03822-5.

This serves to confirm that Shahab Hajibandeh was the first, lead, and corresponding author of the above article and he contributed to conception, design, data collection, data analysis, write up, and critical revision of the article.

Author 2:	Jigar Shah	**Date:**	25/05/2025	[redacted]
Author 3:	Shahin Hajibandeh	**Date:**	25/05/2025	[redacted]
Author 4:	Sreedutt Murali	**Date:**	25/05/2025	[redacted]
Author 5:	Mina Stephanos	**Date:**	25/05/2025	[redacted]
Author 6:	Sherif Ibrahim	**Date:**	25/05/2025	[redacted]
Author 7:	Ahmad Asqalan	**Date:**	25/05/2025	[redacted]
Author 8:	Reda Mithany	**Date:**	25/05/2025	[redacted]
Author 9:	Nuwan Wickramasekara	**Date:**	25/05/2025	[redacted]
Author 10:	Moustafa Mansour	**Date:**	25/05/2025	[redacted]

Article 6. Hajibandeh Index versus NELA score in predicting mortality following emergency laparotomy: A retrospective Cohort Study

Citation: **Hajibandeh S,** Hajibandeh S, Waterman J, Miller B, Johnson B, Higgi A, Hale J, Pearce D, Evans L, Satyadas T, Mansour M, Havard T, Maw A. Hajibandeh

Index versus NELA score in predicting mortality following emergency laparotomy: A retrospective Cohort Study. Int J Surg. 2022 Jun;102:106645. doi: 10.1016/j.ijsu.2022.106645.

This serves to confirm that Shahab Hajibandeh was the first, lead, and corresponding author of the above article and he contributed to conception, design, data collection, data analysis, write up, and critical revision of the article.

Author 2:	Shahin Hajibandeh	**Date:**	25/05/2025	[redacted]
Author 3:	Jennifer Waterman	**Date:**	25/05/2025	[redacted]
Author 4:	Bethany Miller	**Date:**	25/05/2025	[redacted]
Author 5:	Bethan Johnson	**Date:**	25/05/2025	[redacted]
Author 6:	Adnan Higgi	**Date:**	25/05/2025	[redacted]
Author 7:	Jay Hale	**Date:**	25/05/2025	[redacted]
Author 8:	Dafydd Pearce	**Date:**	25/05/2025	[redacted]
Author 9:	Louis Evans	**Date:**	25/05/2025	[redacted]
Author 10:	Thomas Satyadas	**Date:**	25/05/2025	[redacted]
Author 11:	Moustafa Mansour	**Date:**	25/05/2025	[redacted]
Author 12:	Tim Havard	**Date:**	25/05/2025	[redacted]
Author 13:	Andrew Maw	**Date:**	25/05/2025	[redacted]

Article 7. Prognostic significance of socioeconomic deprivation in patients undergoing emergency laparotomy: A retrospective cohort study

Citation: **Hajibandeh S,** Efstathiou A, Hajibandeh S, Al-Sarireh A, Al-Sarireh H, Duffaydar H, Stechman M, Egan RJ, Lewis WG. Prognostic significance of socioeconomic deprivation in patients undergoing emergency laparotomy: A retrospective cohort study. World J Surg. 2024 Oct;48(10):2433-2442. doi: 10.1002/wjs.12332.

This serves to confirm that Shahab Hajibandeh was the first, lead, and corresponding author of the above article and he contributed to conception, design, data collection, data analysis, write up, and critical revision of the article.

Author 2:	Anastasia Efstathiou	**Date:**	13/05/2025	[redacted]
Author 3:	Shahin Hajibandeh	**Date:**	13/05/2025	[redacted]
Author 4:	Ahmad Al-Sarireh	**Date:**	13/05/2025	[redacted]
Author 5:	Hashim Al-Sarireh	**Date:**	13/05/2025	[redacted]
Author 6:	Hamza Duffaydar	**Date:**	13/05/2025	[redacted]
Author 7:	Michael Stechman	**Date:**	13/05/2025	[redacted]
Author 8:	Richard John Egan	**Date:**	13/05/2025	[redacted]
Author 9:	Wyn G. Lewis	**Date:**	13/05/2025	[redacted]

Article 8. Socioeconomic Deprivation and Risk of Operative Mortality After Emergency Laparotomy: A Systematic Review and Meta-Analysis

Citation: Ambler O, Hajibandeh S, **Hajibandeh S**. Socioeconomic Deprivation and Risk of Operative Mortality After Emergency Laparotomy: A Systematic Review and Meta-Analysis. Am Surg. 2025 Apr;91(4):644-652. doi: 10.1177/00031348251314151.

This serves to confirm that Shahab Hajibandeh was the lead and corresponding author of the above article and he contributed to conception, design, data collection, data analysis, write up, and critical revision of the article.

Author 1:	Olivia Ambler	**Date:**	31/05/2025	[redacted]
Author 2:	Shahin Hajibandeh	**Date:**	31/05/2025	[redacted]

Article 9. Meta-analysis of Enhanced Recovery After Surgery (ERAS) Protocols in Emergency Abdominal Surgery

Citation: <u>Hajibandeh S</u>, Hajibandeh S, Bill V, Satyadas T. Meta-analysis of Enhanced Recovery After Surgery (ERAS) Protocols in Emergency Abdominal Surgery. World J Surg. 2020 May;44(5):1336-1348. doi: 10.1007/s00268-019-05357-5.

This serves to confirm that Shahab Hajibandeh was the first, lead, and corresponding author of the above article and he contributed to conception, design, data collection, data analysis, write up, and critical revision of the article.

Author 2: Shahin Hajibandeh **Date:** 10/05/2025 [redacted]

Author 3: Victor Bill **Date:** 10/05/2025 [redacted]

Author 4: Thomas Satyadas **Date:** 10/05/2025 [redacted]

Article 10. Impact of weekend effect on postoperative mortality in patients undergoing emergency General surgery procedures: Meta-analysis of prospectively maintained national databases across the world

Citation: <u>Hajibandeh S</u>, Hajibandeh S, Satyadas T. Impact of weekend effect on postoperative mortality in patients undergoing emergency General surgery procedures: Meta-analysis of prospectively maintained national databases across the world. Surgeon. 2020 Aug;18(4):231-240. doi: 10.1016/j.surge.2019.09.006.

This serves to confirm that Shahab Hajibandeh was the first, lead, and corresponding author of the above article and he contributed to conception, design, data collection, data analysis, write up, and critical revision of the article.

Author 2: Shahin Hajibandeh **Date:** 10/05/2025 [redacted]

Author 3: Thomas Satyadas **Date:** 10/05/2025 [redacted]

Article 11. Effect of surgeon's seniority and subspeciality interest on mortality after emergency laparotomy: A systematic review and meta-analysis

Citation: Al-Sarireh H, Al-Sarireh A, Mann K, Hajibandeh S, **Hajibandeh S**. Effect of surgeon's seniority and subspeciality interest on mortality after emergency laparotomy: A systematic review and meta-analysis. Colorectal Dis. 2024 Aug;26(8):1495-1504. doi: 10.1111/codi.17079.

This serves to confirm that Shahab Hajibandeh was the lead and corresponding author of the above article and he contributed to conception, design, data collection, data analysis, write up, and critical revision of the article.

Author 1:	Ahmad Al-Sarireh	**Date:**	13/05/2025	[redacted]
Author 2:	Hashim Al-Sarireh	**Date:**	13/05/2025	[redacted]
Author 3:	Karan Mann	**Date:**	13/05/2025	[redacted]
Author 4:	Shahin Hajibandeh	**Date:**	13/05/2025	[redacted]

Article 12. Development and Validation of HAS (Hajibandeh Index, ASA Status, Sarcopenia) - A Novel Model for Predicting Mortality After Emergency Laparotomy

Citation: **Hajibandeh S,** Hajibandeh S, Hughes I, Mitra K, Puthiyakunnel Saji A, Clayton A, Alessandri G, Duncan T, Cornish J, Morris C, O'Reilly D, Kumar N. Development and Validation of HAS (Hajibandeh Index, ASA Status, Sarcopenia) - A Novel Model for Predicting Mortality After Emergency Laparotomy. Ann Surg. 2024 Mar 1;279(3):501-509. doi: 10.1097/SLA.0000000000005897.

This serves to confirm that Shahab Hajibandeh was the first, lead, and corresponding author of the above article and he contributed to conception, design, data collection, data analysis, write up, and critical revision of the article.

Author 2:	Shahin Hajibandeh	**Date:**	02/05/2025	[redacted]
Author 3:	Ioan Hughes	**Date:**	02/05/2025	[redacted]
Author 4:	Alwin Puthiyakunnel Saji	**Date:**	02/05/2025	[redacted]
Author 5:	Kalyan Mitra	**Date:**	02/05/2025	[redacted]
Author 6:	Amy Clayton	**Date:**	02/05/2025	[redacted]
Author 7:	Giorgio Alessandri	**Date:**	02/05/2025	[redacted]
Author 8:	Trish Duncan	**Date:**	02/05/2025	[redacted]
Author 9:	Julie Cornish	**Date:**	02/05/2025	[redacted]
Author 10:	Chris Morris	**Date:**	02/05/2025	[redacted]
Author 11:	David O'Reilly	**Date:**	02/05/2025	[redacted]
Author 12:	Nagappan Kumar	**Date:**	02/05/2025	[redacted]

FULL TEXTS OF PUBLISHED WORKS

Full text 1

Article 1. Meta-analysis of mortality risk in octogenarians undergoing emergency general surgery operations

Citation: **Hajibandeh S**, Hajibandeh S, Antoniou GA, Antoniou SA. Meta-analysis of mortality risk in octogenarians undergoing emergency general surgery operations. Surgery. 2021 Jun;169(6):1407-1416. doi: 10.1016/j.surg.2020.11.027.

Contribution: Conception, design, data collection, data analysis, write up, and critical revision

Surgery 169 (2021) 1407–1416

Contents lists available at ScienceDirect

Surgery

journal homepage: www.elsevier.com/locate/surg

Intestine

Meta-analysis of mortality risk in octogenarians undergoing emergency general surgery operations

Shahab Hajibandeh, MD, MRCS[a,*], Shahin Hajibandeh, MD, MRCS[b], George A. Antoniou, MD, PhD, MSc, FEBVS[c,d], Stavros A. Antoniou, MD, PhD, MPH, FEBS, FACS[e,f]

[a] *Department of General Surgery, Glan Clwyd Hospital, the Betsi Cadwaladr University Health Board, Rhyl, United Kingdom*
[b] *Department of General Surgery, Hereford County Hospital, Wye Valley NHS Trust, United Kingdom*
[c] *Department of Vascular & Endovascular Surgery, The Royal Oldham Hospital, Pennine Acute Hospitals NHS Trust, Northern Care Alliance NHS Group, Manchester, United Kingdom*
[d] *Division of Cardiovascular Sciences, School of Medical Sciences, The University of Manchester, United Kingdom*
[e] *Surgical Service, Mediterranean Hospital of Cyprus, Limassol, Cyprus*
[f] *Medical School, European University Cyprus, Nicosia, Cyprus*

A R T I C L E I N F O

Article history:
Accepted 16 November 2020
Available online 4 January 2021

A B S T R A C T

Background: This study aimed to quantify the risk of perioperative mortality in octogenarians undergoing emergency general surgical operations and to compare such risk between octogenarians and nonoctogenarians.
Methods: A systematic review was performed in accordance with the Preferred Reporting Items for Systematic Reviews and Meta-Analyses standards to identify studies reporting the mortality risk in patients aged over 80 years undergoing emergency general surgery operations. The primary outcome measure was 30-day mortality, which was stratified based on American Society of Anesthesiologists (ASA) status and procedure type. The certainty of evidence was assessed using the Grading of Recommendations, Assessment, Development, and Evaluation system. Random-effects models were applied to calculate pooled outcome data.
Results: Analysis of 66,701 octogenarians from 22 studies showed that the risk of 30-day mortality was 26% (95% confidence interval 18%–34%) for all operations: 29% (95% confidence interval 25%–33%) for emergency laparotomy; 9% (95% confidence interval 1%–23%) for nonlaparotomy emergency operations; 21% (95% confidence interval 13%–30%) for colon resection; 17% (95% confidence interval 11%–25%) for small bowel resection; 9% (95% confidence interval 7%–11%) for adhesiolysis; 6% (95% confidence interval 5.9%–6.8%) for perforated ulcer repair; 3% (95% confidence interval 2.6%–4%) for appendicectomy; 3% (95% confidence interval 2.8%–3.3%) for cholecystectomy; and 5% (95% confidence interval 0.2%–14%) for hernia repair. When stratified based on the patient's ASA status, the risk was 11% (95% confidence interval 4%–20%) for ASA 2 status, 22% (95% confidence interval 10%–36%) for ASA 3 status, 39% (95% confidence interval 29%–48%) for ASA 4 status, and 94% (95% confidence interval 77%–100%) for ASA 5 status. The risk was higher in octogenarians compared with nonoctogenarians (odds ratio: 4.07, 95% confidence interval 2.40–6.89), patients aged 70 to 79 (odds ratio: 1.21, 95% confidence interval 1.13–1.31), and patients aged 50 to 79 (odds ratio: 2.03, 95% confidence interval 1.68–2.45).
Conclusion: The risk of perioperative mortality in octogenarians undergoing emergency general surgical operations is high. The risk of perioperative death in this group is higher than in younger patients. Laparotomy, bowel resection, and ASA status above 3 carry the highest risk.

Introduction

Emergency general surgery operations, in particular emergency laparotomies, are associated with significant morbidity, mortality, and reduced quality of life.[1] The risk is even higher in elderly patients owing to underlying frailty, age-related loss of skeletal

* Reprint requests: Shahab Hajibandeh, Department of General Surgery, Glan Clwyd Hospital, the Betsi Cadwaladr University Health Board, Rhyl, UK.
E-mail address: [redacted] (S. Hajibandeh).

https://doi.org/10.1016/j.surg.2020.11.027
0039-6060/

muscle mass, comorbidity, and reduced physiological reserve.[2–4] Considering the increased life-expectancy and rapid expansion of the aging population, the number of emergency general surgery operations being performed on elderly patients is increasing.[5] Therefore, appropriate preoperative risk assessment and prognostication of postoperative outcomes are crucial in elderly patients.

The number of individuals aged over 80 is expected to double within the next 2 decades[6]; nevertheless, the prognostic outcomes of emergency general surgical operations in this population are poorly understood. Knowledge about the risk of postoperative mortality in individuals aged over 80 is crucial for accurate risk assessment and stratification, decision-making, and allocation of resources, and for identifying the patients who are likely or unlikely to benefit from a high-risk major operation.

We aimed to perform a systematic review and meta-analysis to quantify the risk of perioperative mortality in octogenarians undergoing emergency general surgery operations and to compare such risk between octogenarians and nonoctogenarians.

Methods

This study was reported according to Preferred Reporting Items for Systematic reviews and Meta-Analyses standards.[7] The study protocol was prospectively registered with the International Prospective Register of Systematic Reviews (Registration number: CRD42020191894)

Objectives

This study has the following objectives: (1) to quantify the stratified risk of postoperative mortality in octogenarians undergoing emergency general surgery operations using proportion meta-analysis model and (2) to compare the risk of postoperative mortality between octogenarians and nonoctogenarians using a direct comparison meta-analysis model

Eligibility criteria

Considering that being an octogenarian is a characteristic rather than an intervention, conducting a randomized controlled trial on the topic of the current review is not possible. Consequently, all observational studies (cohort studies, case-control studies, and case series) reporting the risk of perioperative mortality in patients aged over 80 undergoing emergency general surgery operations were considered eligible. Emergency general surgery operations included laparotomy, small bowel resection, segmental or total colectomy, lysis of peritoneal adhesions, operative management of perforated viscus, cholecystectomy, appendicectomy, and emergency abdominal wall hernia repair. For the first objective of this study, being over 80 years old was considered the prognostic factor of interest. For the second objective of this study, being over 80 years old was considered as prognostic factor of interest and being under 80 years old was considered as the comparator of interest.

Outcome measure

The outcome of this study was 30-day postoperative mortality. It was defined as death owing to any cause occurring within 30 days after emergency operation. The 30-day postoperative mortality was stratified and reported based on a patient's American Society of Anesthesiologists (ASA) status and the type of emergency general surgery operation.

Search methods

A comprehensive search strategy was developed using appropriate keywords, thesaurus headings, search limits, and operators (Appendix I). The developed strategy was applied and adopted by 2 independent authors with experience in evidence synthesis on the following electronic databases: the Cochrane Central Register of Controlled Trials; the Excerpta Medica database; the Medical Literature Analysis and Retrieval System Online; and the Cumulative Index to Nursing and Allied Health Literature.

The search strategy had no language restrictions and was last applied on 10 May 2020. In order to identify potentially eligible unpublished or ongoing studies, the following sources were explored: the European Association for Grey Literature Exploitation; the System for Information on Grey Literature; the World Health Organization International Clinical Trials Registry; the International Standard Randomised Controlled Trial Number Registry; and ClinicalTrials.gov.

Reference lists of relevant reviews and articles were screened to identify potentially eligible studies that had not been identified by the above strategies.

Selection of studies

To select eligible studies, the articles identified after application of the above search strategy were screened against the eligibility criteria by 2 authors independently (SH, SH). The process of screening involved reading the titles and abstracts of the identified articles followed by full-text retrieval and selection of potentially eligible studies. Disagreements between the first 2 authors were resolved by a separate third author (GA).

Data extraction and management

Random pilot-testing technique was used to develop an online data extraction sheet consistent with Cochrane's data collection form. Two authors (SH, SH) independently extracted the following data from the included studies: first author, country of origin, year and journal of the published study, study design, sample size, clinical condition of the study participants, age, sex, ASA status, type of operation, and 30-day mortality. When required, the disagreements between the first 2 authors were resolved by a separate third author (S.A.).

Assessment of risk of bias in included studies

The methodological quality of studies included in the proportion meta-analysis model was assessed using the Joanna Briggs Institute Critical Appraisal tool for case series.[8] The Joanna Briggs Institute tool evaluates the methodological quality in terms of eligibility criteria, measurement of condition/exposure/factor of interest, consecutiveness and completion of recruitment process, demographics and clinical characteristics of the included population, outcome measures, and statistical analyses. The methodological quality of studies included in the direct comparison meta-analysis model was assessed using the Quality In Prognosis Studies tool.[9] The Quality In Prognosis Studies tool evaluates the risk of bias in studies of prognostic factors in terms of study participation, study attrition, prognostic factor measurement, outcome measurement, study confounding, and statistical analysis and reporting. This step was conducted by 2 authors independently (S.H., S.H.). Disagreements between the first 2 authors were resolved by a separate third author (S.A.).

Data analysis

To quantify the risk of 30-day mortality using proportion meta-analysis, we integrated the quantitative incidence of 30-day mortality from individual studies and calculated a numerical estimate of the overall effect as described by Petrie et al.[10] We used the Freeman-Tukey double arcsine transformation to calculate the weighted summary proportion under the random effects modelling. To compare the risk of 30-day mortality between octogenarians and nonoctogenarians using direct comparison meta-analysis, we calculated the odds ratio (OR) as the summary measure using random effects modelling. The unit of analysis was an individual patient. The heterogeneity was quantified and reported as I^2 using Cochran Q test (χ^2). I^2 was interpreted as follows: 0% to 50% suggests low heterogeneity; 50% to 75% suggests moderate heterogeneity; and 75% to 100% suggests high heterogeneity.

Publication bias was assessed for outcomes reported by at least 10 studies. For studies entered into proportion meta-analysis models, publication bias was assessed based on LFK index and the symmetry of Doi plot. In terms of interpretation of LFK index, an index of −1 to 1 would indicate no asymmetry, an index of 1 to 2 or −1 to −2 would indicate minor asymmetry, and an index of >2 or <−2 would indicate major asymmetry. For studies entered into direct comparison meta-analysis models, publication bias was assessed visually based on the symmetry of funnel plots. Direct comparison meta-analysis was conducted using the Review Manager 5.4 software and proportion meta-analysis was conducted using the MetaXL (www.epigear.com) plug-in for Microsoft Excel (Microsoft, Redmond, WA).

Sensitivity analyses

We modelled additional analyses for outcomes reported by at least 5 studies. The sensitivity analyses included independent calculation of risk ratio and risk difference, elimination of 1 study at a time followed by repeating the analyses, and separate analyses for studies judged to be low overall risk of bias

Subgroup analyses

Depending on the availability of data, we planned to perform subgroup analyses for the following subgroups: type of procedure (emergency laparotomy, nonlaparotomy emergency operation, colon resection, small bowel resection, adhesiolysis, repair of perforated ulcer, appendicectomy, cholecystectomy, and hernia repair); ASA status; octogenarians versus patients aged 70 to 79; and octogenarians versus patients aged 50 to 79.

Summary of findings table

The Grading of Recommendation, Assessment, Development and Evaluation system was used to grade the quality and certainty of available evidence for each outcome. The quality and certainty of available evidence was considered as very low, low, moderate, or high based on the following domains: across studies risk of bias, directness of evidence, heterogeneity, precision of effects estimates, and risk of publication bias.

We compiled and summarized the best evidence on the most important and clinically relevant outcomes thought to be essential for clinical decision-making. The results were presented in a "Summary of findings" table.

Deviations from the registered protocol

The reported methodology is consistent with planned methodology in the registered protocol with no deviations from the protocol.

Results

Results of the search

After applying the search strategy in the above databases, 8,877 articles were identified. Among these, 8,849 articles were excluded as they were not relevant to the topic of this study. After assessing the full texts of the remaining articles, 6 more articles were excluded because they did not provide postoperative mortality data. Therefore, 22 observational studies[11–32] including 66,701 octogenarians qualified for inclusion (Supplementary Fig 1). Table I outlines the characteristics of the included studies.

Risk of bias in included studies

The outcomes of methodological quality assessment of the studies included in proportion meta-analysis, and those included in the direct comparison meta-analysis are presented in the Supplementary Fig 2 and Supplementary Fig 3, respectively. In summary, the studies included in the proportion meta-analysis model were judged to be at low risk of bias in terms of eligibility criteria, measurement of condition/exposure/factor of interest, consecutiveness and completion of recruitment process, clinical characteristics of the included population, outcome measures, and statistical analyses, but the risk of bias associated with demographics of the included population was judged to be unclear in 15 out of 22 studies. The studies included in the proportion meta-analysis model were judged to be at low risk of bias in terms of study participation, study attrition, prognostic factor measurement, outcome measurement, and statistical analysis and reporting, but the risk of bias associated with study confounding was judged to be unclear.

Outcome synthesis

Procedure-adjusted 30-day mortality (Fig 1)

All operations. Analysis of 66,701 octogenarians from 22 studies[11–32] showed that the pooled risk of 30-day mortality after all emergency general surgery operations was 26% (95% confidence interval [CI] 18%–34%) (Fig 2, *A*). The between-study heterogeneity was high ($I^2 = 99\%$, $P < .0001$), and Doi plot suggested major asymmetry (LFK index: 9.94) (Supplementary Fig 4, *A*). The certainty of the evidence was judged to be moderate (Supplementary Table 1).

Emergency laparotomy. Analysis of 19,084 octogenarians from 22 studies[11–32] showed that the pooled risk of 30-day mortality following emergency laparotomy was 29% (95% CI 25%–33%) (Fig 2, *B*). The between-study heterogeneity was high ($I^2 = 95\%$, $P < .0001$) and the Doi plot suggested major asymmetry (LFK index: 6.70) (Supplementary Fig 4, *B*). The certainty of the evidence was judged to be moderate (Supplementary Table 1).

Non-laparotomy emergency operations. Analysis of 47,617 octogenarians from 6 studies[13,16,17,22,27,31] showed that the pooled risk of 30-day mortality after nonlaparotomy emergency operations was 9% (95% CI 1%–23%) (Fig 2, *C*). The between-study heterogeneity was high ($I^2 = 98\%$, $P < .0001$). The certainty of the evidence was judged to be low (Supplementary Table 1).

Table I
Baseline characteristics of the included studies

Study	Year	Country	Journal	Included population	Design	Sample size
Cihoric 2020	2020	Denmark	*Perioper Med*	Patients aged over 80 undergoing emergency laparotomy	Retrospective cohort	277
Aakre 2020	2020	Norway	*Acta Anaesthesiol Scand*	Patients aged over 80 undergoing emergency laparotomy	Retrospective cohort	106
Narueponjirakul 2020	2020	United States	*J Trauma Acute Care Surg*	Patients aged over 80 undergoing emergency laparotomy	Retrospective cohort	385
van Beekum 2019	2019	Germany	*Med Klin Intensivmed Notfmed*	Patients aged over 80 undergoing emergency laparotomy	Retrospective cohort	34
Eugene 2018	2018	United Kingdom	*Br J Anaesth*	Patients aged over 80 undergoing emergency laparotomy	Retrospective cohort	7,840
Ho 2018	2018	United States	*J Am Geriatr Soc*	Patients aged over 80 undergoing emergency general surgery	Retrospective cohort	49,045
Bolger 2018	2018	Ireland	*Geriatr Gerontol Int*	Patients aged over 80 undergoing emergency general surgery	Retrospective cohort	128
Peacock 2018	2018	United Kingdom	*Br J Surg*	Patients aged over 80 undergoing emergency laparotomy	Retrospective cohort	2,568
Tengberg 2017	2017	Denmark	*Anaesthesia*	Patients aged over 80 undergoing emergency laparotomy	Retrospective cohort	292
Simpson 2017	2017	United Kingdom	*Eur J Trauma Emerg Surg*	Patients aged over 80 undergoing emergency laparotomy	Retrospective cohort	136
Stevens 2017	2017	Australia	*World J Surg*	Patients aged over 80 undergoing emergency laparotomy	Retrospective cohort	4,679
Khan-Kheil 2016	2016	United Kingdom	*Ann R Coll Surg Engl*	Patients aged over 80 undergoing emergency general surgery	Retrospective cohort	63
Howes 2015	2015	United Kingdom	*Anaesthesia*	Patients aged over 80 undergoing emergency laparotomy	Prospective cohort	30
Watt 2014	2014	United Kingdom	*Eur J Trauma Emerg Surg*	Patients aged over 80 undergoing emergency laparotomy	Retrospective cohort	70
Wilson 2014	2014	United Kingdom	*Int J Surg*	Patients aged over 80 undergoing emergency laparotomy	Retrospective cohort	73
Green 2013	2013	United Kingdom	*World J Gastrointest Surg*	Patients aged over 80 undergoing emergency laparotomy	Retrospective cohort	100
Vaughan-Shaw 2012	2012	United Kingdom	*Int J Surg*	Patients aged over 80 undergoing emergency general surgery	Retrospective cohort	88
Saunders 2012	2012	United Kingdom	*Br J Anaesth*	Patients aged over 80 undergoing emergency laparotomy	Retrospective cohort	342
Clarke 2011	2011	United Kingdom	*Eur J Anaesthesiol*	Patients aged over 80 undergoing emergency laparotomy	Prospective cohort	26
Zerbib 2005	2005	France	*World J Surg*	Patients aged over 85 undergoing emergency laparotomy	Retrospective cohort	45
Arenal 2003	2003	Spain	*Can J Surg*	Patients aged over 80 undergoing emergency general surgery	Retrospective cohort	346
Cook 1998	1998	United Kingdom	*Br J Anaesth*	Patients aged over 85 undergoing emergency laparotomy	Retrospective cohort	28

Colon resection. Analysis of 8,474 octogenarians from 6 studies[13,16,17,22,30] showed that the pooled risk of 30-day mortality after emergency colon resection was 21% (95% CI 13%–30%) (Fig 2, *D*). The between-study heterogeneity was moderate ($I^2 = 75\%$, $P = .003$). The certainty of the evidence was judged to be moderate (Supplementary Table 1).

Small bowel resection. Analysis of 6,498 octogenarians from 4 studies[13,16,22,30] showed that the pooled risk of 30-day mortality after emergency small bowel resection was 17% (95% CI 11%–25%) (Fig 2, *E*). The between-study heterogeneity was moderate ($I^2 = 62\%$, $P = .05$). The certainty of the evidence was judged to be moderate (Supplementary Table 1).

Adhesiolysis. Analysis of 10,843 octogenarians from 4 studies[13,16,17,30] showed that the pooled risk of 30-day mortality after emergency adhesiolysis was 9% (95% CI 7%–11%) (Fig 2, *F*). The between-study heterogeneity was low ($I^2 = 7\%$, $P = .36$). The certainty of the evidence was judged to be high (Supplementary Table 1).

Repair of perforated ulcer. Analysis of 13,397 octogenarians from 2 studies[16,30] showed that the pooled risk of 30-day mortality after repair of perforated ulcer was 6% (95% CI 5.9%–6.8%) (Fig 2, *G*). The between-study heterogeneity was low ($I^2 = 0\%$, $P = .87$). The certainty of the evidence was judged to be moderate (Supplementary Table 1).

Appendicectomy. Analysis of 2,143 octogenarians from 4 studies[13,16,17,27] showed that the pooled risk of 30-day mortality after emergency appendicectomy was 3% (95% CI 2.6%–4%) (Fig 2, *H*). The between-study heterogeneity was low ($I^2 = 0\%$, $P = .46$). The certainty of the evidence was judged to be high (Supplementary Table 1).

Cholecystectomy. Analysis of 13,883 octogenarians from 4 studies[13,16,17,30] showed that the pooled risk of 30-day mortality after emergency cholecystectomy was 3% (95% CI 2.8%–3.3%) (Fig 2, *I*). The between-study heterogeneity was low ($I^2 = 0\%$, $P = .56$). The certainty of the evidence was judged to be high (Supplementary Table 1).

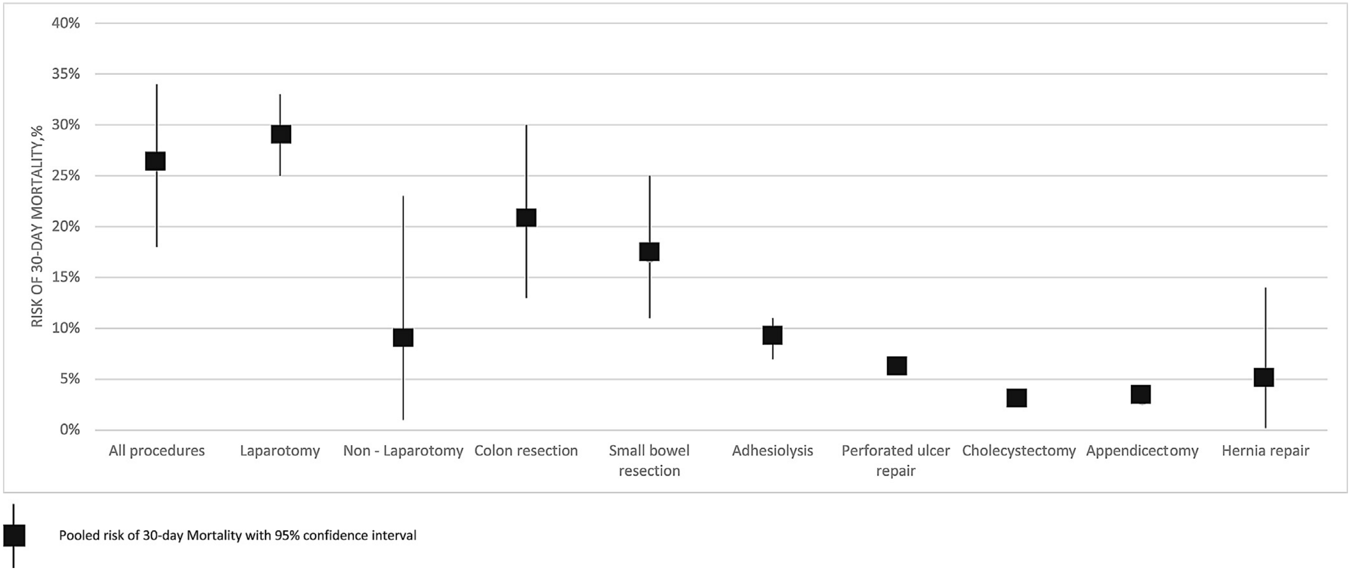


Fig 1. Pooled risk of 30-d mortality stratified based on type of operation.

Hernia repair. Analysis of 82 octogenarians from 4 studies[13,17,22,27] showed that the pooled risk of 30-day mortality after emergency hernia repair was 5% (95% CI 0.2%–14%) (Fig 2, *J*). The between-study heterogeneity was low ($I^2 = 44\%$, $P = .15$). The certainty of the evidence was judged to be moderate (Supplementary Table 1).

ASA-Adjusted 30-day mortality

Figure 3 demonstrates the ASA-adjusted 30-day mortality. The risk of 30-day mortality was 11% (95% CI 4%–20%; $I^2 = 44\%$, $P = .15$) in octogenarians with ASA 2 status; 22% (95% CI 10%–36%; $I^2 = 81\%$, $P = .001$) in octogenarians with ASA 3 status; 39% (95% CI 29%–48%; $I^2 = 26\%$, $P = .26$) in octogenarians with ASA 4 status; and 94% (95% CI 77%–100%; $I^2 = 0\%$, $P = .90$) in octogenarians with ASA 5 status.

Comparisons

Octogenarians versus nonoctogenarians. Analysis of 85,911 patients from 11 studies[11,14–16,18,19,21,23,24,28,32] showed that the risk of 30-day mortality was significantly higher in octogenarians compared with nonoctogenarians (OR: 4.07, 95% CI 2.40–6.89; $P < .00001$) (Fig 4, *A*). The between-study heterogeneity was high ($I^2 = 99\%$, $P < .00001$), and the certainty of the evidence was judged to be moderate (Supplementary Table 2). The funnel plot suggested possibility of publication bias (Supplementary Fig 4, *C*).

The results remained consistent for populations from the United Kingdom (OR: 3.02, 95% CI 2.21–4.14; $P < .00001$), from the United States (OR: 1.84, 95% CI 1.65–2.06; $P < .00001$), from Europe (OR: 3.21, 95% CI 2.58–4.00; $P < .00001$), and from Australia (OR: 21.05, 95% CI 17.93–24.73; $P < .00001$).

Octogenarians versus patients aged 50 to 79. Analysis of 64,476 patients from 9 studies[11,14–16,18,19,21,28,32] showed that the risk of 30-day mortality was significantly higher in octogenarians compared with patients aged 50 to 79 (OR: 2.03, 95% CI 1.68–2.45; $P < .00001$) (Fig 4, *B*). The between-study heterogeneity was high ($I^2 = 89\%$, $P < .00001$), and the certainty of the evidence was judged to be moderate (Supplementary Table 2).

The results remained consistent for populations from the United Kingdom (OR: 2.31, 95% CI 1.43–3.74; $P = .0006$), from the United States (OR: 1.84, 95% CI 1.65–2.06; $P < .00001$), from Europe (OR: 2.00, 95% CI 1.32–3.03; $P = .001$), and from Australia (OR: 1.81, 95% CI 1.63–2.01; $P < .00001$).

Octogenarians versus patients aged 70 to 79. Analysis of 19,407 patients from 4 studies[11,15,19,28] showed that the risk of 30-day mortality was significantly higher in octogenarians compared with patients aged 70 to 79 (OR: 1.21, 95% CI 1.13–1.31; $P < .00001$) (Fig 4, *C*). The between-study heterogeneity was low ($I^2 = 0\%$, $P = .65$), and the certainty of the evidence was judged to be high (Supplementary Table 2).

The results remained consistent for populations from the United Kingdom (OR: 1.20, 95% CI 1.11–1.29; $P < .00001$) and from Europe (OR: 1.44, 95% CI 1.08–1.92; $P = .01$).

Sensitivity analyses (Supplementary Table 3)

The sensitivity analyses showed that the results remained consistent after separate calculation of risk ratios and risk differences, after eliminating 1 study at a time, and when separate analyses of studies with low possibility of bias were performed.

Discussion

We performed a systematic review and meta-analysis to quantify the risk of perioperative mortality in octogenarians undergoing emergency general surgery operations and to compare such risk between octogenarians and nonoctogenarians. Analysis of 66,701 octogenarians from 22 studies[11–32] showed that the pooled risk of 30-day mortality in octogenarians undergoing emergency general surgery operations was 26% (95% CI 18, 34). The analyses suggested that the risk of 30-day mortality was higher among octogenarians undergoing emergency laparotomy and bowel resection and in patients with ASA status 3 or above. The risk of 30-day mortality was found to be significantly higher in octogenarians compared with nonoctogenarians. The quality and certainty of available evidence were moderate.

To the best of our knowledge, this is the first meta-analysis investigating the perioperative mortality risk in octogenarians undergoing emergency general surgery operations. The relatively high risk of 30-day mortality in this population can be explained by various factors. Octogenarians are likely to have more comorbidities and higher baseline ASA status compared with non-octogenarians. It has been previously demonstrated that the comorbid burden and ASA status are strong predictors of postoperative mortality and morbidity.[33] In addition, age-related loss of

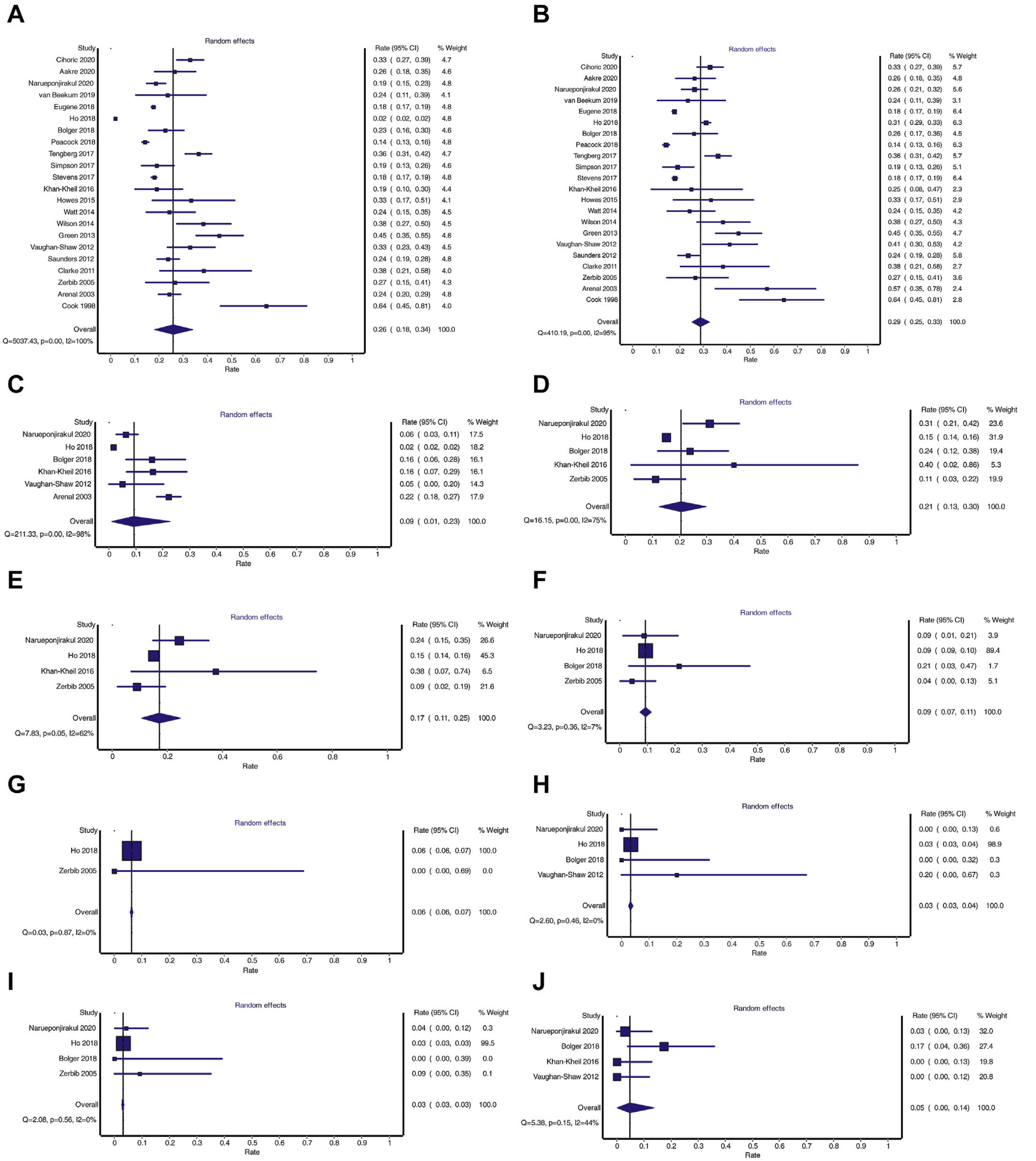


Fig 2. Forest plots of 30-d mortality for (*A*) all procedures; (*B*) emergency laparotomy; (*C*) nonlaparotomy emergency operation; (*D*) colon resection; (*E*) small bowel resection; (*F*) adhesiolysis; (*G*) repair of perforated ulcer; (*H*) appendicectomy; (*I*) cholecystectomy; and (*J*) hernia repair. (Color version of figure is available online.) *CI*, confidence interval.

skeletal muscle mass, known as sarcopenia, is expected to be more prevalent in octogenarians. We have previously shown that sarcopenia is a strong predictor of mortality in emergency general surgery and other settings.[3,4] Such factors, along with a reduced physiological reserve and the effect of acute abdominal pathology warranting an emergency operation, would explain the high risk of postoperative mortality in this group of patients.

The pooled estimate of 30-day mortality was higher in octogenarians undergoing emergency laparotomy than those undergoing nonlaparotomy emergency operations. Emergency laparotomy is known to be a major cause of mortality and morbidity.[34] The underlying pathology is likely to be associated with higher risks of intraperitoneal contamination, need for bowel resection, larger abdominal incision, longer operative time, more postoperative

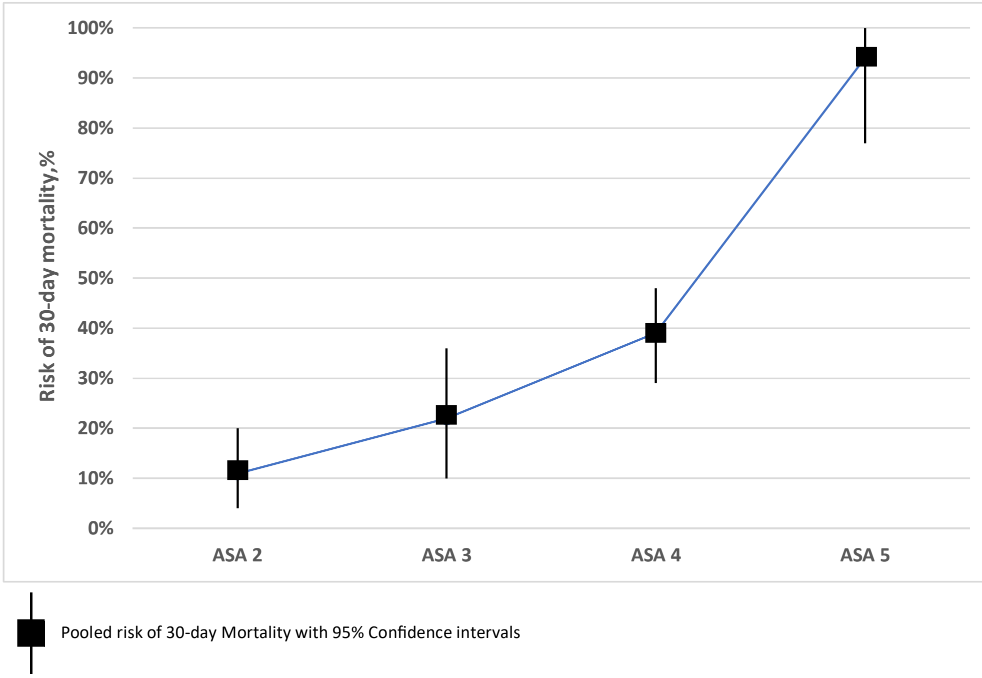


Fig 3. Pooled risk of 30-d mortality stratified based on patient's American Society of Anesthesiologists (ASA) status. (Color version of figure is available online.)

complications, and a greater need for postoperative supportive care in comparison to pathologies that do not require emergency laparotomy (appendicitis, cholecystitis, incarcerated hernia, etc). Intraperitoneal contamination has been shown to be associated with higher risks of postoperative complications and mortality.[35] On the other hand, as shown in this study, bowel resection in an emergency setting carries a relatively higher risk of mortality. All of these factors would explain the high perioperative mortality rates in this study.

There have been many efforts made to improve outcomes in patients undergoing emergency laparotomy, including accurate preoperative mortality and morbidity risk assessment and stratification, prediction of the need for perioperative supportive treatment in a high dependency or intensive care unit, and application of enhanced recovery after emergency surgery.[36,37] In this context, it is paramount to identify the patients who are likely or unlikely to benefit from emergency operation. The most commonly used preoperative mortality risk assessment tools do not take into account important predictors including frailty, sarcopenia, or need for bowel resection. Moreover, advanced age, and specifically being an octogenarian, has not been incorporated in risk prediction models. The findings of our study highlights that an emergency laparotomy in a patient older than 80 with ASA status more than 3 who is likely to need bowel resection carries a high mortality risk, and such a risk may not be accurately reflected by current risk predictive tools.

Although current risk prediction tools, including the National Emergency Laparotomy Audit tool,[38] are useful and help decision-making in emergency settings, there is a need to incorporate modern prognostic factors such as frailty, sarcopenia, need for bowel resection, and being an octogenarian, into mortality predictive tools. This would allow a more accurate risk assessment and objective identification of patients who may not benefit from emergency operation owing to high risk of mortality. Among the available risk prediction tools, the American College of Surgeons National Surgical Quality Improvement Program Surgical Risk Calculator takes most of the relevant preoperative factors including demographics, comorbidities, and type of procedure into account to predict the risk of postoperative morbidity and mortality. We believe that incorporating modern prognostic factors into American College of Surgeons National Surgical Quality Improvement Program Surgical Risk Calculator may potentially make it the most comprehensive and even most accurate risk prediction tool.[39]

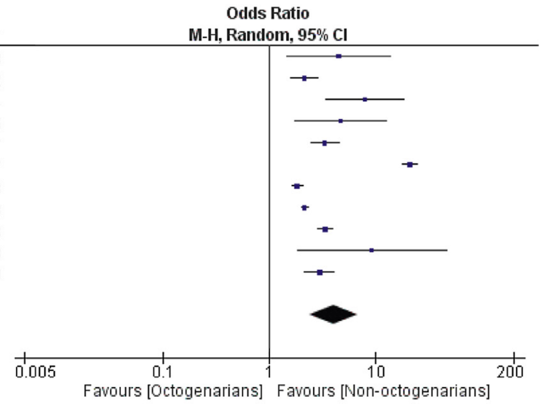
The results of current study further highlight the need for dedicated geriatric surgery pathways to improve perioperative outcomes in octogenarians undergoing emergency general surgery operations. Such pathways should follow an evidence-based multidisciplinary model of care comprising comprehensive preoperative multidomain (medical, functional, psychological, and social) geriatric assessment and optimization of these vulnerable high-risk patients.[40–42] These include assessment of the patient's cognitive ability and capacity, identifying risk factors for developing postoperative delirium and pulmonary complications, performing preoperative cardiac evaluation, determining the patient's baseline frailty, functional and nutritional status, determining the patient's treatment goals and expectations, determining the patient's family and social support system, and optimization across all domains in order to modify perioperative risk.[40–42] The postoperative management of the patients should be based on shared clinical working and decision-making by a consultant geriatrician and surgeon focusing on proactive recognition of postoperative medical complications and functional decline, standardized management of medical complications, establishment of appropriate ceilings of care, and promoting timely discharge planning.[40–42]

The findings of the current study may also have implications in terms of clinical governance, education, and training. In fact, the high risk of mortality in octogenarians undergoing emergency general surgery operations highlights the need for holding joint geriatric and surgical clinical governance and audit meetings and encourages development of joint integrated guidelines, pathways, and patient safety initiatives. Moreover, a preoperative and perioperative surgical curriculum for the management of older surgical patients should be developed across various specialties including

A

Study or Subgroup	Octogenarians Events	Octogenarians Total	Non-octogenarians Events	Non-octogenarians Total	Weight	Odds Ratio M-H, Random, 95% CI	Year
Cook 1998	18	28	8	28	7.1%	4.50 [1.46, 13.89]	1998
Saunders 2012	81	342	190	1503	10.1%	2.14 [1.60, 2.87]	2012
Watt 2014	17	70	10	256	8.3%	7.89 [3.42, 18.20]	2014
Howes 2015	10	30	11	114	7.7%	4.68 [1.76, 12.49]	2015
Tengberg 2017	106	292	124	847	10.1%	3.32 [2.45, 4.51]	2017
Stevens 2017	845	4679	191	18436	10.3%	21.05 [17.93, 24.73]	2017
Ho 2018	625	2005	1435	7280	10.4%	1.84 [1.65, 2.06]	2018
Eugene 2018	1391	7840	2826	30990	10.4%	2.15 [2.00, 2.30]	2018
Peacock 2018	368	2568	354	7423	10.3%	3.34 [2.86, 3.89]	2018
van Beekum 2019	8	34	2	62	5.3%	9.23 [1.83, 46.48]	2019
Cihoric 2020	91	277	114	807	10.1%	2.97 [2.16, 4.09]	2020
Total (95% CI)		**18165**		**67746**	**100.0%**	**4.07 [2.40, 6.89]**	
Total events	3560		5265				

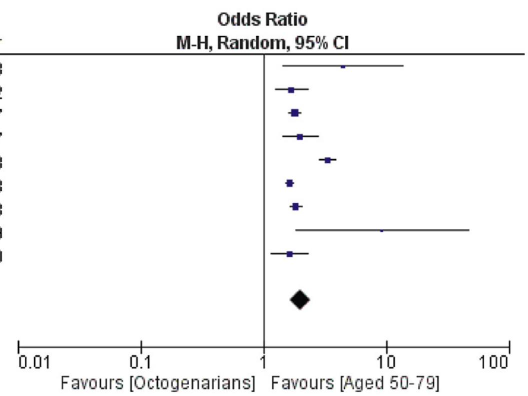
Heterogeneity: Tau² = 0.69; Chi² = 737.81, df = 10 (P < 0.00001); I² = 99%
Test for overall effect: Z = 5.22 (P < 0.00001)



B

Study or Subgroup	Octogenarians Events	Octogenarians Total	Aged 50-79 Events	Aged 50-79 Total	Weight	Odds Ratio M-H, Random, 95% CI	Year
Cook 1998	18	28	8	28	2.4%	4.50 [1.46, 13.89]	1998
Saunders 2012	81	342	172	1122	11.7%	1.71 [1.27, 2.31]	2012
Stevens 2017	845	4679	769	7078	15.8%	1.81 [1.63, 2.01]	2017
Tengberg 2017	106	292	94	422	11.0%	1.99 [1.43, 2.77]	2017
Peacock 2018	368	2568	354	7423	15.0%	3.34 [2.86, 3.89]	2018
Eugene 2018	1391	7840	2616	22577	16.3%	1.65 [1.53, 1.77]	2018
Ho 2018	625	2005	1435	7280	15.8%	1.84 [1.65, 2.06]	2018
van Beekum 2019	8	34	2	62	1.2%	9.23 [1.83, 46.48]	2019
Cihoric 2020	91	277	96	419	10.8%	1.65 [1.17, 2.31]	2020
Total (95% CI)		**18065**		**46411**	**100.0%**	**2.03 [1.68, 2.45]**	
Total events	3533		5546				

Heterogeneity: Tau² = 0.05; Chi² = 74.62, df = 8 (P < 0.00001); I² = 89%
Test for overall effect: Z = 7.40 (P < 0.00001)



C

Study or Subgroup	Octogenarians Events	Octogenarians Total	Aged 70-79 Events	Aged 70-79 Total	Weight	Odds Ratio M-H, Random, 95% CI	Year
Saunders 2012	81	342	92	466	4.9%	1.26 [0.90, 1.77]	2012
Tengberg 2017	106	292	38	135	2.8%	1.45 [0.93, 2.27]	2017
Eugene 2018	1391	7840	1499	9795	88.2%	1.19 [1.10, 1.29]	2018
Cihoric 2020	91	277	66	260	4.0%	1.44 [0.99, 2.09]	2020
Total (95% CI)		**8751**		**10656**	**100.0%**	**1.21 [1.13, 1.31]**	
Total events	1669		1695				

Heterogeneity: Tau² = 0.00; Chi² = 1.64, df = 3 (P = 0.65); I² = 0%
Test for overall effect: Z = 5.04 (P < 0.00001)

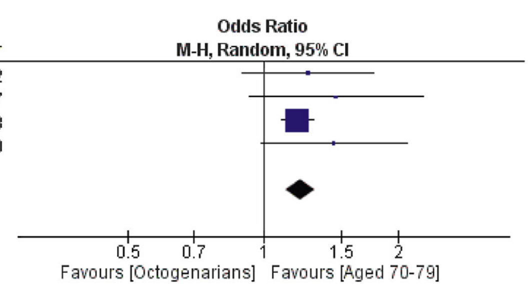


Fig 4. Forest plots of 30-d mortality for the following comparisons: (*A*) octogenarians versus nonoctogenarians; (*B*) octogenarians versus patients aged 50–79; and (*C*) octogenarians versus patients aged 70–79. (Color version of figure is available online.)

anesthetics, surgery, and medicine in order to improve knowledge and skills required for achieving better perioperative outcomes.[40,42]

In the current study, an objective, transparent methodology was used to analyze and report a summary of the best available evidence and to examine the possibility of bias in the included studies. The 30-day mortality was stratified and reported based on type of emergency operation and ASA status. The results were unaffected through additional analyses corroborating the review findings. Inherent limitations in this review need to be acknowledged. Most of the included studies were retrospective; therefore, results of studies comparing surgery in octogenarians versus younger patients may be subject to selection bias. The potential effect of confounders could not be accounted for, because none of the studies reported on confounder-adjusted analyses. Nevertheless, considering that being an octogenarian is a characteristic rather than an intervention, performing a randomized controlled trial on the topic is not possible. Although it is well recognized that physiological status plays a significant role in determining the perioperative outcomes, the available data from the included studies was not adequate to perform subgroup analyses or stratify the analyses based on baseline physiological status of included patients. Moreover, although stratification of data based on disease severity would have more implications in terms of outcomes and would allow comparing the outcomes among different diseases based on their severity, it was not possible to perform subgroup analysis based on disease severity using well-recognized scoring systems such as the American Association for the Surgery of Trauma system. Moreover, comparison of mortality based on ASA status between octogenarians and nonoctogenarians was not possible owing to the limited available data. All of these may subject the results of the current study to potential confounding bias. As expected, the between-study heterogeneity was high; however, analyses for type of surgery and ASA status showed reduced or even negligible heterogeneity. In order to address high heterogeneity, we used random-effects modelling and downgraded the certainty of evidence owing to inconsistency.

In conclusion, the risk of postoperative mortality in octogenarians varies among different general surgery operations and is higher than the risk in nonoctogenarians. An emergency laparotomy requiring bowel resection in patients aged over 80 with ASA status above 3 carries a high perioperative risk. Such patients must be carefully selected, and risks must be balanced against potential benefits.

Funding/Support

This research received no specific grant from any funding agency in the public, commercial, or not-for-profit sectors.

Conflict of interest/Disclosure

None declared.

Supplementary Materials

Supplementary material associated with this article can be found, in the online version, at [https://doi.org/10.1016/j.surg.2020.11.027].

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Full text 2

Article 2. The risk and predictors of mortality in octogenarians undergoing emergency laparotomy: a multicentre retrospective cohort study

Citation: **Hajibandeh S**, Hajibandeh S, Shah J, Martin J, Abdelkarim M, Murali S, Maw A, Mansour M, Satyadas T. The risk and predictors of mortality in octogenarians undergoing emergency laparotomy: a multicentre retrospective cohort study. Langenbecks Arch Surg. 2021 Sep;406(6):2037-2044. doi: 10.1007/s00423-021-02168-y.

Contribution: Conception, design, data collection, data analysis, write up, and critical revision

Langenbeck's Archives of Surgery (2021) 406:2037–2044
https://doi.org/10.1007/s00423-021-02168-y

ORIGINAL ARTICLE

The risk and predictors of mortality in octogenarians undergoing emergency laparotomy: a multicentre retrospective cohort study

Shahab Hajibandeh[1,2] · Shahin Hajibandeh[3,4] · Jigar Shah[5] · Julia Martin[6] · Mostafa Abdelkarim[2] · Sreedutt Murali[2] · Andrew Maw[2] · Moustafa Mansour[5] · Thomas Satyadas[6]

Received: 19 November 2020 / Accepted: 31 March 2021 / Published online: 7 April 2021

Abstract

Objectives This study aims to evaluate the risk of postoperative mortality in octogenarians undergoing emergency laparotomy.

Methods In compliance with STROCSS guideline for observational studies, we conducted a multicentre retrospective cohort study. All consecutive patients aged over 80 with acute abdominal pathology requiring emergency laparotomy between April 2014 and August 2019 were considered eligible for inclusion. The primary outcome measure was 30-day postoperative mortality, and the secondary outcome measures were in-hospital mortality and 1-year mortality. Statistical analyses included simple descriptive statistics, binary logistic regression analyses, and Kaplan–Meier survival statistics.

Results A total of 523 octogenarians were eligible for inclusion. Emergency laparotomy in octogenarians was associated with 21.8% (95% CI 18.3–25.6%) 30-day postoperative mortality, 22.6% (95% CI 19.0–26.4%) in-hospital mortality, and 40.2% (95% CI 35.9–44.5%) 1-year mortality. Binary logistic regression analysis identified ASA status (OR, 2.49; 95% CI 1.82–3.38, $P < 0.0001$) and peritoneal contamination (OR, 2.00; 95% CI 1.30–3.08, $P = 0.002$) as predictors of 30-day postoperative mortality. The ASA status (OR, 1.92; 95% CI 1.50–2.46, $P < 0.0001$), peritoneal contamination (OR, 1.57; 95% CI 1.07–2.48, $P = 0.020$), and presence of malignancy (OR, 2.06; 95% CI 1.36–3.10, $P = 0.001$) were predictors of 1-year mortality. Log-rank test showed significant difference in postoperative survival rates among patients with different ASA status ($P < 0.0001$) and between patients with and without peritoneal contamination ($P = 0.0011$).

Conclusions Emergency laparotomies in patients older than 80 years with ASA status more than 3 in the presence of peritoneal contamination carry a high risk of immediate postoperative and 1-year mortality. This should be taken into account in communications with patients and their relatives, consent process, and multidisciplinary decision-making process for operative or non-operative management of such patients.

Keywords Emergency surgery · Laparotomy · Mortality · Octogenarians

Shahab Hajibandeh and Shahin Hajibandeh contributed equally to this work and joined first authorship is proposed.

✉ Shahab Hajibandeh
[redacted]

1 Department of General Surgery, Wrexham Maelor Hospital, Betsi Cadwaladr University Health Board, Wrexham, UK

2 Department of General Surgery, Glan Clwyd Hospital, Betsi Cadwaladr University Health Board, Rhyl, UK

3 Department of General Surgery, Hereford County Hospital, Wye Valley NHS Trust, Hereford, UK

4 Department of General Surgery, Sandwell and West Birmingham Hospitals NHS Trust, Birmingham, UK

5 Department of General Surgery, North Manchester General Hospital, North Manchester Care Organisation, Manchester, UK

6 Department of Hepatobiliary and Pancreatic Surgery, Manchester Royal Infirmary Hospital, Manchester, UK

Introduction

Emergency laparotomies in elderly patients are associated with significant reduced quality of life, morbidity, and mortality due to age-related loss of skeletal muscle mass, underlying frailty, reduced physiological reserve, and comorbidity.[1–4] The increased life expectancy and rapid expansion of the ageing population resulted in a significant increase in the number of emergency laparotomies being performed on elderly patients.[5] This highlights the importance of appropriate preoperative risk assessment and prognostication of postoperative outcomes in elderly patients.

It is expected that the number of individuals aged over 80 will double over the next two decades[6]; nevertheless, the prognostic outcomes of emergency laparotomies in this population are poorly understood. Knowledge about the risk of postoperative mortality in individuals aged over 80 is crucial for accurate risk assessment and stratification, decision-making, and allocation of resources, and for identifying the patients who are likely or unlikely to benefit from a high-risk major operation. In view of this, we aimed to conduct a multicentre cohort study to evaluate the risk of postoperative mortality in octogenarians undergoing emergency laparotomy.

Methods

This multicentre retrospective cohort study was conducted and presented in compliance with the strengthening the reporting of cohort studies in surgery (STROCSS) guideline for observational studies[7] and followed an agreed predefined protocol. Considering the nature of this study, patient consent and approval by research ethics committees were not required; however, the study was conducted in accordance with institutions' policies and internal arrangements approved by the local clinical governance units.

Study design and patient selection

We conducted a multicentre retrospective cohort study involving four emergency general surgery centres located in the UK (one centre in the North Wales; two centres in the North West England; one centre in the West Midlands). The study period was between April 2014 and August 2019. All consecutive patients aged over 80 who underwent an emergency laparotomy due to an acute abdominal pathology were considered eligible for inclusion. The indications for emergency laparotomy included intestinal ischaemia, visceral perforation, large bowel obstruction, small bowel obstruction, intraabdominal sepsis of any source, intraabdominal bleeding, and intraabdominal abscess. We excluded the patients who underwent trauma-related laparotomy.

Outcome measures

The primary outcome of this study was 30-day postoperative mortality which was defined as death due to any cause occurring within 30 days after emergency laparotomy. The secondary outcome measures were in-hospital mortality and 1-year mortality.

Data collection

Data collection was performed by two independent authors, and an independent third author was consulted in the event of disagreement. An electronic data collection pro forma was developed which included data on the following parameters: patients' demographic data (age and sex), the American Society of Anaesthesiologists (ASA) score, background of cognitive impairment (defined as formal diagnosis of Alzheimer's disease, vascular dementia, Lewy body dementia, frontotemporal dementia, or any other type of dementia), indication for emergency laparotomy (intestinal ischaemia, visceral perforation, large bowel obstruction, small bowel obstruction, intraabdominal sepsis of any source, intraabdominal bleeding, and intraabdominal abscess), performed procedure, colon resection, small bowel resection, presence of intraabdominal malignancy, type and extent of intraperitoneal contamination, postoperative admission to the intensive care unit (ICU), length of ICU stay, length of hospital stay, 30-day mortality, in-hospital mortality, and 1-year mortality. In order to obtain data regarding 30-day and 1-year mortality, patients' medical records including primary care (community) and secondary care (hospital) records were explored to confirm whether the patient has survived or not.

Data synthesis and statistical analyses

The statistical analyses were performed using MedCalc 13.0 software. Simple descriptive statistics were used to present the baseline characteristics and outcome data. Data were summarised with mean ± standard deviation (SD) for continuous variables and frequencies or percentages for categorical variables. Binary logistic regression models were constructed to investigate predictors of postoperative mortality. Postoperative mortality was considered as dependent variable, and the patient's sex, baseline ASA score, cognitive impairment, colon resection, small bowel resection, type and extent of intraperitoneal contamination, and presence of intraabdominal malignancy were considered as independent variables. All statistical tests were two-tailed, and statistical significance was assumed at $P < 0.05$. Postoperative survival was illustrated with Kaplan–Meier survival statistics stratified according to the predictors identified in regression models, and the log-rank test was used to identify significant differences. Moreover, in order to further evaluate the association between the identified variables and postoperative mortality, Cox proportional-hazards regression was conducted using stepwise approach allowing variables with $P < 0.05$ to enter the model.

Results

Baseline patient characteristics

A total of 531 patients were identified; 8 patients were excluded as they underwent emergency laparotomy due to abdominal trauma. Therefore, 523 patients were eligible for inclusion. The mean age of the included patients was 84.3 (95% CI 84.0–84.6), and 236 out of 523 (45%) were male. In terms of ASA status, 3 out of 523 (0.6%) patients were classified as ASA 1; 97 out of 523 (18.5%) as ASA 2; 249 out of 523 (47.6%) as ASA 3; 163 out of 523 (31.2%) as ASA 4; and 11 out of 523 (2.1%) as ASA 5. A total of 20 out of 523 (3.8%) patients had cognitive impairment. Colon resection was required in 182 out of 523 (34.8%) patients, and small bowel resection was required in 130 out of 523 (24.9%) patients. Peritoneal contamination was present in 157 out of 523 (30%) patients of which 42 (26.8%) were classed as feculent, 51 (32.5%) as purulent, and 64 (40.7%) as gastrointestinal content. The extent of contamination was classed as localised in 74 out of 157 (47%) patients and as generalised in 83 out of 157 (53%) patients. Abdominal malignancy was present in 121 out of 523 patients (23.1%). Postoperative ICU admission was required in 396 out of 523 (75.7%) patients, and the mean length of ICU stay was 4.8 days (95% CI 4.0–5.6). The mean length of hospital stay was 25.7 days (95% CI 22.9–28.5). The follow-up data was available for all the included patients. The study flow chart and the baseline characteristics of the included population are demonstrated in Fig. 1 and Table 1, respectively. The indications for emergency laparotomy are provided in Table 2.

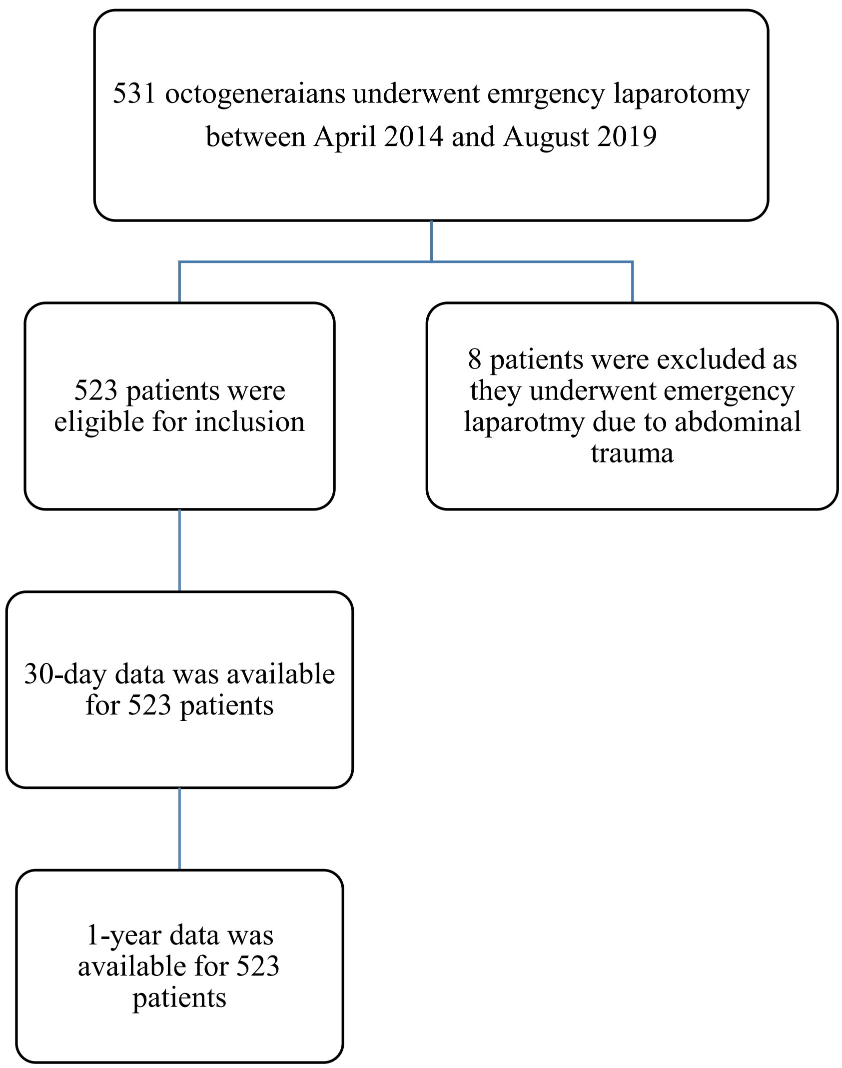

Fig. 1 The study flow chart

Table 1 Baseline characteristics of the included population

Number of patients	523
Mean age, years (95% CI)	84.3 (84.0–84.6)
Male	236 out of 523 (45%)
Female	287 out of 523 (55%)
ASA status	
1	3 out of 523 (0.6%)
2	97 out of 523 (18.5%)
3	249 out of 523 (47.6%)
4	163 out of 523 (31.2%)
5	11 out of 523 (2.1%)
Cognitive impairment	20 out of 523 (3.8%)
Colon resection	182 out of 523 (34.8%)
Small bowel resection	130 out of 523 (24.9%)
Peritoneal contamination	157 out of 523 (30%)
Type of contamination	
Feculent	42 out of 157 (26.8%)
Purulent	51 out of 157 (32.5%)
Gastrointestinal content	64 out of 157 (40.7%)
Extent of contamination	
Localised	74 out of 157 (47%)
Generalised	83 out of 157 (53%)
Abdominal malignancy	121 out of 523 (23.1%)
Postoperative ICU admission	396 out of 523 (75.7%)
Mean length of ICU, days (95% CI)	4.8 (4.0–5.6)
Mean length of hospital stay, days (95% CI)	25.7 (22.9–28.5)

ASA, American Society of Anaesthesiologists; *ICU*, intensive care unit; *CI*, confidence interval

Outcomes (Table 3)

30-day postoperative mortality The risk of 30-day postoperative mortality was 21.8% (95% CI 18.3–25.6%) in the entire cohort. The risk was 24.6% (95% CI 19.3–30.7%) in male patients; 19.4% (95% CI 15.0–24.5%) in female patients; 21.4% (95% CI 15.7–28.1%) in patients who had colon resection; 24.6% (95% CI 17.5–32.9%) in patients who had small bowel resection; 20.7% (95% CI 15.4–26.7%) in patients who did not have bowel resection; 30.6% (95% CI 23.5–38.4%) in patients with peritoneal contamination; 18% (95% CI 14.2–22.4%) in patients without peritoneal contamination; 29.7% (95% CI 19.7–41.4%) in patients with localised contamination; 31.3% (95% CI 21.6–42.4%) in patients with generalised contamination; 20.7% (95% CI 13.8–29.0%) in patients with abdominal malignancy; and 22.1% (95% CI 18.2–26.5%) in patients without malignancy.

Table 2 Indications for emergency laparotomy in the included cohort

Indication	No of patients
Colon perforation	72 out of 523 (14%)
Small bowel perforation	39 out of 523 (8%)
Peptic ulcer perforation	33 out of 523 (6%)
Large bowel obstruction	92 out of 523 (18%)
Small bowel obstruction	208 out of 523 (40%)
Intestinal ischaemia	49 out of 523 (9%)
Anastomotic leak	12 out of 523 (2%)
Intraabdominal bleeding	5 out of 523 (1%)
Intraabdominal abscess	4 out of 523 (0.8%)
Intestinal fistula	4 out of 523 (0.8%)
Bleeding peptic ulcer	3 out of 523 (0.6%)
Colitis	2 out of 523 (0.4%)

In-hospital mortality The risk of in-hospital mortality was 22.6% (95% CI 19.0–26.4%) in the entire cohort. The risk was 26.4% (95% CI 20.9–32.5%) in male patients; 19.4% (95% CI 15.0–24.5%) in female patients; 22.0% (95% CI 16.2–28.7%) in patients who had colon resection; 27.7% (95% CI 20.2–36.2%) in patients who had small bowel resection; 20.2% (95% CI 15.0–26.2%) in patients who did not have bowel resection; 32.5% (95% CI 25.2–40.4%) in patients with peritoneal contamination; 18.3% (95% CI 14.5–22.7%) in patients without peritoneal contamination; 32.4% (95% CI 22.0–44.3%) in patients with localised contamination; 32.5% (95% CI 22.6–43.7%) in patients with generalised contamination; 19.0% (95% CI 12.4–27.1%) in patients with abdominal malignancy; and 23.6% (95% CI 19.6–28.1%) in patients without malignancy.

1-year mortality The risk of 1-year mortality was 40.2% (95% CI 35.9–44.5%) in the entire cohort. The risk was 43.4% (95% CI 37–50.0%) in male patients; 37.5% (95% CI 31.9–43.4%) in female patients; 43.4% (95% CI 36.1–50.9%) in patients who had colon resection; 40.0% (95% CI 31 5–49.0%) in patients who had small bowel resection; 37.6% (95% CI 31.0–44.4%) in patients who did not have bowel resection; 47.8% (95% CI 39.7–55.9%) in patients with peritoneal contamination; 36.9% (95% CI 31.9–42.1%) in patients without peritoneal contamination; 51.4% (95% CI 39.4–63.1%) in patients with localised contamination; 44.6% (95% CI 33.7–55.9%) in patients with generalised contamination; 53.7% (95% CI 44.4–62.8%) in patients with abdominal malignancy; and 36.1% (95% CI 31.4–41.0%) in patients without malignancy.

Binary logistic regression (Table 4)

30-day postoperative mortality Binary logistic regression analysis identified ASA status (OR, 2.49; 95% CI 1.82–3.38; $P < 0.0001$) and peritoneal contamination (OR, 2.00; 95% CI 1.30–3.08; $P = 0.002$) as predictors of 30-day postoperative mortality. The analyses did not identify sex (OR,

Table 3 The risk of mortality in octogenarians undergoing emergency laparotomy

Subgroups	Outcomes		
	30-day mortality	In-hospital mortality	1-year mortality
Entire cohort	114 out of 523 (21.8%)	118 out of 523 (22.6%)	210 out of 523 (40.2%)
Male	58 out of 235 (24.6%)	62 out of 235 (26.4%)	102 out of 235 (43.4%)
Female	56 out of 288 (19.4%)	56 out of 288 (19.4%)	108 out of 288 (37.5%)
Colon resection	39 out of 182 (21.4%)	40 out of 182 (22.0%)	79 out of 182 (43.4%)
Small bowel resection	32 out of 130 (24.6%)	36 out of 130 (27.7%)	52 out of 130 (40.0%)
No bowel resection	44 out of 213 (20.7%)	43 out of 213 (20.2%)	80 out of 213 (37.6%)
Peritoneal contamination	48 out of 157 (30.6%)	51 out of 157 (32.5%)	75 out of 157 (47.8%)
No contamination	66 out of 366 (18%)	67 out of 366 (18.3%)	135 out of 366 (36.9%)
Localised contamination	22 out of 74 (29.7%)	24 out of 74 (32.4%)	38 out of 74 (51.4%)
Generalised contamination	26 out of 83 (31.3%)	27 out of 83 (32.5%)	37 out of 83 (44.6%)
Abdominal malignancy	25 out of 121 (20.7%)	23 out of 121 (19.0%)	65 out of 121 (53.7%)
No malignancy	89 out of 402 (22.1%)	95 out of 402 (23.6%)	145 out of 402 (36.1%)

1.36; 95% CI 0.89, 2.06; $P = 0.150$), bowel resection (OR, 1.12; 95% CI 0.73–1.71; $P = 0.60$), or malignancy (OR, 0.92; 95% CI 0.55–1.51; $P = 0.73$) as predictors of 30-day postoperative mortality.

In-hospital mortality Binary logistic regression analysis identified ASA status (OR, 2.63; 95% CI 1.93–3.59; $P < 0.0001$) and peritoneal contamination (OR, 2.15; 95% CI 1.40–3.28; $P = 0.001$) as predictors of in-hospital mortality. The analyses did not identify sex (OR, 1.48; 95% CI 0.98, 2.24; $P = 0.06$), bowel resection (OR, 1.26; 95% CI 0.83–1.93; $P = 0.28$), or malignancy (OR, 0.76; 95% CI 0.46–1.26; $P = 0.28$) as predictors of in-hospital mortality.

1-year mortality Binary logistic regression analysis identified ASA status (OR, 1.92; 95% CI 1.50–2.46; $P < 0.0001$), peritoneal contamination (OR, 1.57; 95% CI 1.07–2.48; $P = 0.020$), and malignancy (OR, 2.06; 95% CI 1.36–3.10; $P = 0.001$) as predictors of 1-year mortality. The analyses did not identify sex (OR, 1.28; 95% CI 0.89, 1.82; $P = 0.171$) and bowel resection (OR, 1.20; 95% CI 0.84–1.72; $P = 0.32$) as predictors of 1-year mortality.

Cox proportional-hazards regression analysis

Cox proportional-hazards regression analysis taking ASA status, intraperitoneal contamination, and malignancy as covariates showed that the probability of survival 30 days postoperatively was 78.3% and identified ASA status as predictor of 30-day mortality ($P = 0.0125$).

Kaplan–Meier survival analysis (Fig. 2)

ASA-stratified survival The 30-day postoperative survival was 100% in patients with ASA 1 status, 92.8% (95% CI 85.7–97.0%) in patients with ASA 2 status, 81.9% (95% CI 76.6–86.5%) in patients with ASA 3 status, 65.6% (95% CI 57.8–72.9%) in patients with ASA 4 status, and 45.5% (95% CI

Table 4 Results of binary logistic regression analysis

Independent variables	Dependent variables					
	30-day mortality		In-hospital mortality		1-year mortality	
	OR (95% CI)	*P* value	OR (95% CI)	*P* value	OR (95% CI)	*P* value
Sex	1.36 (0.89, 2.06)	0.150	1.48 (0.98, 2.24)	0.06	1.28 (0.89, 1.82)	0.171
ASA status	2.49 (1.82–3.38)	< 0.0001	2.63 (1.93–3.59)	< 0.0001	1.92 (1.50–2.46)	< 0.0001
Peritoneal contamination	2.00 (1.30–3.08)	0.002	2.15 (1.40–3.28)	0.001	1.57 (1.07–2.48)	0.02
Bowel resection	1.12 (0.73–1.71)	0.6	1.26 (0.83–1.93)	0.28	1.20 (0.84–1.72)	0.32
Abdominal malignancy	0.92 (0.55–1.51)	0.73	0.76 (0.46–1.26)	0.28	2.06 (1.36–3.10)	0.001

ASA, American Society of Anaesthesiologists; *OR*, odds ratio; *CI*, confidence interval

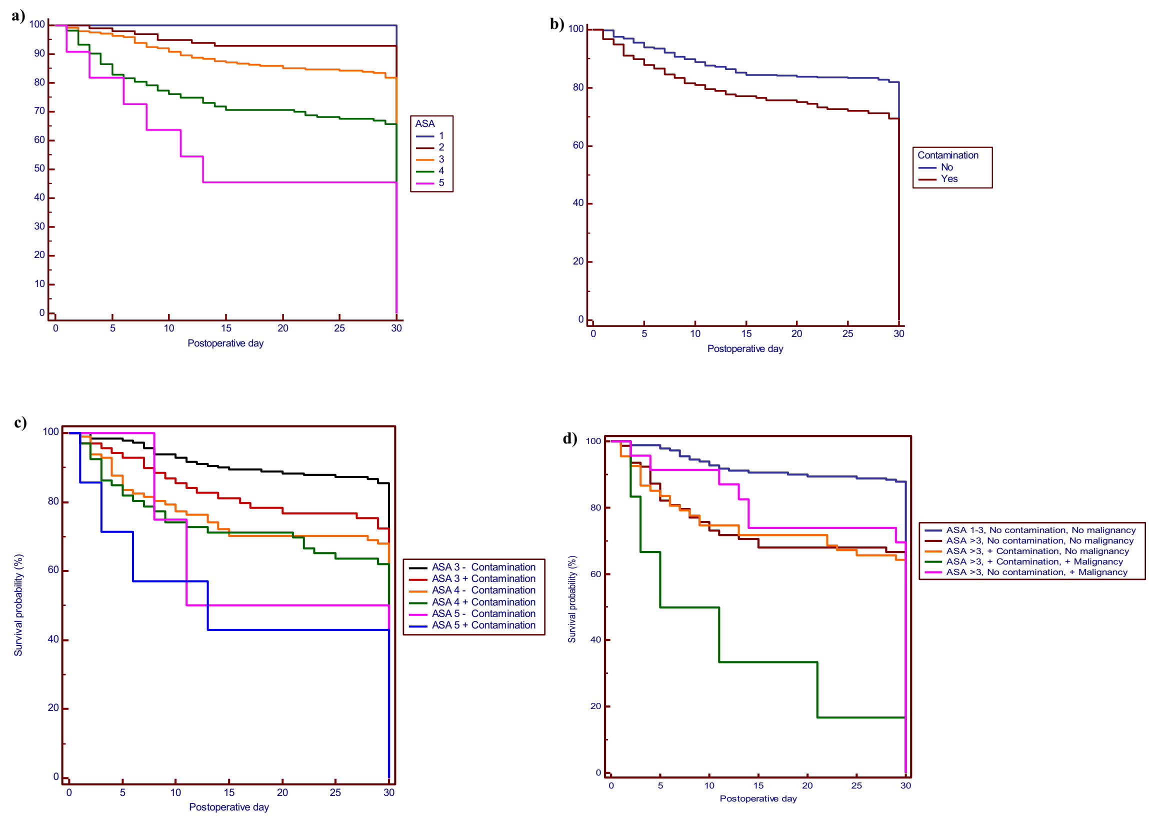

Fig. 2 Kaplan–Meier survival analysis. **a** ASA-stratified 30-day survival. **b** Peritoneal contamination-stratified 30 day survival. **c** ASA and peritoneal contamination-stratified 30-day survival. **d** ASA, peritoneal contamination, malignancy-stratified 30-day survival

16.7–76.6%) in patients with ASA 5 status. Log-rank test showed significant difference in postoperative survival among patients with different ASA status ($P < 0.0001$).

Peritoneal contamination-stratified survival The 30-day postoperative survival was 69.4% (95% CI 61.6–76.5%) in patients with peritoneal contamination and 82.0% (95% CI 77.6–85.8%) in patients without peritoneal contamination. Log-rank test showed significant difference in postoperative survival between patients with and without peritoneal contamination ($P = 0.0011$).

ASA and peritoneal contamination-stratified survival The 30-day postoperative survival was 85.6% (95% CI 79.6–90.3%) in patients with ASA 3 status without peritoneal contamination, 72.5% (95% CI 60.4–82.5%) in patients with ASA 3 status with peritoneal contamination, 68.0% (95% CI 57.8–77.1%) in patients with ASA 4 status without peritoneal contamination, 62.1% (95% CI 49.3–73.7%) in patients with ASA 4 status with peritoneal contamination, 50.0% (95% CI 6.8–93.2%) in patients with ASA 5 status without peritoneal contamination, and 42.9% (95% CI 9.9–81.6%) in patients with ASA 5 status with peritoneal contamination. Log-rank test showed significant difference in postoperative survival among patients with different ASA and peritoneal contamination status ($P < 0.0001$).

ASA, peritoneal contamination, and malignancy-stratified survival The 30-day postoperative survival was 87.8% (95% CI 82.1–92.2%) in patients with ASA 1–3 status without peritoneal contamination and without malignancy, 66.7% (95% CI 55.1–76.9%) in patients with ASA status > 3 without peritoneal contamination and without malignancy, 64.2% (95% CI 51.5–97.5%) in patients with ASA status > 3 with peritoneal contamination and without malignancy, 69.6% (95% CI 47.1–86.8%) in patients without ASA status > 3 without peritoneal contamination and with malignancy, and 16.7% (95% CI 0.4–64.1%) in patients with ASA status > 3 with peritoneal contamination and with malignancy. Log-rank test showed significant difference in postoperative survival among patients with different ASA > 3, peritoneal contamination, and malignancy ($P < 0.0001$).

Discussion

We conducted a multicentre cohort study to evaluate the risk of postoperative mortality in octogenarians undergoing emergency laparotomy. Analysis of 523 patients suggested that the risks of in-hospital mortality, 30-day postoperative mortality, and 1-year mortality in octogenarians undergoing emergency laparotomy are high. The ASA status and presence of peritoneal contamination were identified as significant predictors of in-hospital and 30-day postoperative mortality. In addition to ASA status and peritoneal contamination, the presence of abdominal malignancy was identified as significant predictor of 1-year mortality.

To the best of our knowledge, the current study is the largest cohort study in literature that evaluates the risk of mortality following emergency laparotomy specifically in octogenarians. Our findings are consistent with the findings of other studies.[8–13] Various factors may explain the relatively high risk of postoperative mortality in octogenarians undergoing emergency laparotomy. Firstly, compared with younger patients, octogenarians are likely to have higher baseline ASA status and more comorbidities, and as demonstrated in this study and in other studies, the ASA status and comorbid burden are strong predictors of postoperative mortality and morbidity.[14, 15] Moreover, octogenarians are more likely to have sarcopenia, age-related loss of skeletal muscle mass, which is a strong predictor of mortality in emergency general surgery and other settings.[3, 4] In addition to the above factors, the reduced physiological reserve and the negative effect of underlying acute abdominal pathology may explain the high risk of postoperative mortality in this group of patients.

The underlying pathology that warrants an emergency laparotomy is likely to be associated with risks of intraperitoneal contamination and need for bowel resection. Our results suggest that peritoneal contamination is a predictor of postoperative mortality in octogenarians undergoing emergency laparotomy. This is consistent with our knowledge about prognostic significance of peritoneal contamination in patients with acute abdominal pathology.[16] The extent of intraperitoneal contamination is taken into account by most of the preoperative prognostic scoring tools; however, the knowledge about the extent of contamination is only available intraoperatively, limiting the predictive value of preoperative prognostic scoring tools. Recently, intraperitoneal contamination index (Hajibandeh index) derived from combined preoperative levels of C-reactive protein, lactate, neutrophils, lymphocytes, and albumin was found to be promising in predicting the extent of intraperitoneal contamination in patients with acute abdominal pathology.[16]

It is crucial to identify the elderly patients with acute abdominal pathology who are likely or unlikely to benefit from emergency laparotomy. In order to improve outcomes in patients undergoing emergency laparotomy, many efforts have been made. These include accurate preoperative mortality and morbidity risk assessment, prediction of the need for perioperative supportive treatment in a high dependency or intensive care unit, and application of enhanced recovery protocols following emergency surgery.[17, 18] The results of our study suggests that an emergency laparotomy in a patient older than 80 with ASA status more than 3 in the presence of peritoneal contamination carries a high mortality risk. Nevertheless, such risks may not be accurately reflected by current risk predictive tools as the most commonly used preoperative mortality risk assessment tools do not take into account important predictors including advanced age, specifically being an octogenarian, frailty, and sarcopenia.[19]

The current study could potentially facilitate decision-making in the management of patients aged over 80 undergoing emergency laparotomy by providing objective information for patients, their relatives, and healthcare professionals involved in the management of such patients. Decision for operation depends on many factors including patient's wish, underlying pathology, type of procedure, and patient's baseline performance status and should be made via a multidisciplinary approach. In order to give a valid consent for a potentially life-threatening operation, patients and their relatives have a right to be informed about the estimated risk of mortality associated with the procedure. On the other hand, the healthcare professionals who are involved in the management of patients should be aware of the prognosis associated with the treatment that they offer. Therefore, all of the aforementioned factors should be taken into account when making a decision for operation in high-risk patients. Based on ethical principles, while patient's wish should be respected (autonomy), the operation should be offered to a patient who can benefit from the operation (beneficence), and when the operation is associated with a significantly high risk of mortality, it should be avoided (non-maleficence).

We are fairly confident about the robustness of the results of the current study as indicated by adequate statistical power, systematic and objective methodology, and comparable findings with other studies. However, the reported outcomes of this study should be viewed and interpreted in the context of inherent limitations. The retrospective nature of current study would subject our results to inevitable selection bias.

Directions for future research

The results of current study highlights the need for dedicated geriatric surgery pathways in the management of patients aged over 80 who need emergency laparotomy. Such pathways should follow an evidence-based multidisciplinary model of care comprising comprehensive preoperative multi-domain (medical, functional, psychological, and social) geriatric assessment and optimisation. Future studies should investigate whether the implementation of dedicated geriatric surgery pathways could improve perioperative outcomes in octogenarians undergoing emergency laparotomy. Moreover, future studies should focus on outcomes of operative versus non-operative management of patients aged over 80 who are considered to be at significantly high risk of mortality.

Conclusions

Emergency laparotomies in patients older than 80 years with ASA status more than 3 in the presence of peritoneal contamination carry a high risk of immediate postoperative and 1-year mortality. This should be taken into account in communications with patients and their relatives, consent process, and multidisciplinary decision-making process for operative or non-operative management of such patients.

Author contribution Conception and design: Shahab H; data collection: Shahab H, Shahin H, JS, JM, MA, and SM; analysis and interpretation: Shahab H and Shahin H; writing the article: Shahab H and Shahin H; critical revision of the article: all authors; final approval of the article: all authors.

Declarations

Ethics approval and consent to participate Considering the nature of this study, which was a retrospective cohort study involving non-identifiable data from hospital databases, approval by the research ethics committees was not required; however, the study was conducted in accordance with the institutions' policies and internal arrangements approved by local clinical governance units, and all authors declared compliance with the policies before being granted access to local hospital database. Considering the nature of this study, which was a retrospective cohort study involving non-identifiable data from hospital databases, there was no direct involvement of patients during the study; informed consent was not required.

Human and animal rights This study was a retrospective cohort study involving non-identifiable data from hospital databases, and there was no direct involvement of patients during the study; nevertheless, the study was conducted in compliance with the Helsinki ethical principles for medical research involving human subjects.

Conflict of interest The authors declare no competing interests.

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Full text 3

Article 3. Sarcopenia versus clinical frailty scale in predicting the risk of postoperative mortality after emergency laparotomy: a retrospective cohort study

Citation: **Hajibandeh S,** Hajibandeh S, Brown C, Harper ER, Saji AP, Hughes I, Mitra K, Rashwany H, Clayton A, Patel N, Abdelrahman T, Foliaki A, Kumar N. Sarcopenia versus clinical frailty scale in predicting the risk of postoperative mortality after emergency laparotomy: a retrospective cohort study. Langenbecks Arch Surg. 2024 Feb 14;409(1):59. doi: 10.1007/s00423-024-03252-9.

Contribution: Conception, design, data collection, data analysis, write up, and critical revision

Langenbeck's Archives of Surgery (2024) 409:59
https://doi.org/10.1007/s00423-024-03252-9

RESEARCH

Sarcopenia versus clinical frailty scale in predicting the risk of postoperative mortality after emergency laparotomy: a retrospective cohort study

Shahab Hajibandeh[1] · Shahin Hajibandeh[2] · Christopher Brown[1] · Elizabeth Ryan Harper[1] · Alwin Puthiyakunnel Saji[3] · Ioan Hughes[1] · Kalyan Mitra[1] · Hind Rashwany[1] · Amy Clayton[4] · Neil Patel[1] · Tarig Abdelrahman[1] · Antonio Foliaki[1] · Nagappan Kumar[1]

Received: 24 September 2023 / Accepted: 4 February 2024

Abstract

Objectives To compare predictive significance of sarcopenia and clinical frailty scale (CFS) in terms of postoperative mortality in patients undergoing emergency laparotomy

Methods In compliance with STROCSS statement standards, a retrospective cohort study with prospective data collection approach was conducted. The study period was between January 2017 and January 2022. All adult patients with non-traumatic acute abdominal pathology who underwent emergency laparotomy in our centre were included. The primary outcome was 30-day mortality and secondary outcomes were in-hospital mortality and 90-day mortality. The predictive value of sarcopenia and CFS were compared using the receiver operating characteristic (ROC) curve analysis and multivariable binary logistic regression analysis.

Results A total of 1043 eligible patients were included. The risk of 30-day mortality, in-hospital mortality, and 90-day mortality were 8%, 10%, and 11%, respectively. ROC curve analysis suggested that sarcopenia is a significantly stronger predictor of 30-day mortality (AUC: 0.87 vs. 0.70, P<0.0001), in-hospital mortality (AUC: 0.79 vs. 0.67, P=0.0011), and 90-day mortality (AUC: 0.79 vs. 0.67, P=0.0009) compared with CFS. Moreover, multivariable binary logistic regression analysis identified sarcopenia as an independent predictor of mortality [coefficient: 4.333, OR: 76.16 (95% CI 37.06–156.52), P<0.0001] but not the CFS [coefficient: 0.096, OR: 1.10 (95% CI 0.88–1.38), P=0.4047].

Conclusions Sarcopenia is a stronger predictor of postoperative mortality compared with CFS in patients undergoing emergency laparotomy. It cancels out the predictive value of clinical frailty scale in multivariable analyses; hence among the two variables, sarcopenia deserves to be included in preoperative predictive tools.

Keywords Laparotomy · Mortality · Sarcopenia · Frailty

Introduction

Due to aging population, the number of older adults undergoing emergency laparotomy for acute abdominal pathology has increased [1, 2]. Emergency laparotomy in older adults means encountering higher risks of postoperative complications, and more complex clinical needs due to increased number of co-morbidities, decreased physiological reserve, and increased vulnerability associated with aging-related physiological deficits [2–6]. Consequently, objective measurement of such aging-related physiological decline and vulnerability to complications in older adults has been the area of interest recently.

✉ Shahab Hajibandeh
[redacted]

1 Department of General Surgery, University Hospital of Wales, Cardiff CF14 4XW, UK

2 Department of General Surgery, Royal Stoke University Hospital, Stoke-on-Trent, UK

3 School of Medicine, Cardiff University, Cardiff, UK

4 Department of Radiology, University Hospital of Wales, Cardiff, UK

Clinical frailty scale (CFS) is an objective scale for measurement of aging-related physiological decline and vulnerability, which classifies patients between CFS 1 and CFS 9 based on extend of their frailty [7]. On the other hand, sarcopenia, aging-related loss of skeletal muscle mass, has been recognised as important measure of aging-related physiological decline and vulnerability [8]. It has been shown that CFS and sarcopenia are independent predictors of mortality in patients undergoing emergency laparotomy, and many authors recommended that they should be included in preoperative risk assessment tools [9–14]. In fact, previous cohort studies conducted by Parmer et al. [5], Youssef et al. [9], and Palaniappan et al. [14] have evaluated predictive value of CFS in patients undergoing emergency laparotomy and concluded that the CFS is an effective tool for assessing preoperative vulnerability and frailty and may be used to predict mortality and morbidity after emergency surgery [5, 9, 14]. On the other hand, several meta-analyses [10–12] have reported that sarcopenia is associated with increased risk of postoperative mortality in patients undergoing emergency laparotomy, supporting the argument that it should be incorporated into preoperative risk assessment tools [1–12].

Between sarcopenia and CFS, it is poorly understood which one is a stronger predictor of postoperative mortality. The knowledge about the stronger predictor of mortality would help to decide which one deserves to be included in preoperative predictive tools. Although the impact of sarcopenia and CFS on outcomes in patients undergoing peritoneal dialysis have been evaluated previously [15, 16], their predictive significance in patients undergoing emergency laparotomy have never been compared. Consequently, in this study, we aimed to compare predictive significance of sarcopenia and CFS in terms of postoperative mortality in patients undergoing emergency laparotomy.

Methods

Reporting standards and ethical approval

The Strengthening the Reporting of Cohort Studies in Surgery (STROCSS) guideline for observational studies [17] was followed to protocol, conduct and present this study. The Helsinki medical research ethical principles were respected, and the study proposal was approved by the Health and Care Research Wales (HCRW) and Health Research Authority (HRA) through the Integrated Research Application System (IRAS) (IRAS ID: 320962).

Study design and patient selection

A retrospective cohort study with prospective data collection approach was conducted in a tertiary general surgery centre at a teaching hospital located in South Wales. We included all patients aged over 18 who underwent emergency laparotomy due to non-traumatic abdominal pathology between January 2017 and January 2022. The prospectively maintained hospital's electronic medical record system was used to identify the eligible patients. These included local electronic theatre management system which records detail of all emergency, ambulatory, and elective operations performed in our centre, and Welsh Clinical portal, which is a national database combining clinical data from all health boards and links with the national death registry, and data obtained from general practice. The following information were available from the aforementioned medical record systems: patient demographic data, co-morbidities, procedure performed, operative findings, operative time, anaesthetic time, theatre staff detail and their seniority, admission and discharge letters, postoperative and follow-up clinic letters, and biochemical and radiological investigation results. Patients who underwent emergency laparotomy due to intestinal obstruction, intestinal ischaemia, visceral perforation, intra-abdominal sepsis of any source (collection, colitis, anastomotic leak, intestinal fistula), and intra-abdominal bleeding were included. The diagnoses were made by consultant general surgeon in charge of the patient based on clinical, biochemical, radiological, and intraoperative findings. Patients who underwent emergency laparotomy due to abdominal trauma were excluded.

Outcomes

Thirty-day postoperative mortality (death due to any cause occurring within 30 days after emergency laparotomy) was the primary outcome measure. In-hospital mortality (death due to any cause occurring during hospital stay) and 90-day postoperative mortality (death due to any cause occurring within 90 days after emergency laparotomy) were the secondary outcomes.

Definition of sarcopenia

Sarcopenia was measured by calculating cross-sectional area of both right and left psoas muscles at the level of the bottom of L3 vertebral body on the 0.625-mm-thick axial abdominal CT scan using the picture archiving and communication system (PACS) used in our centre (FUJIFILM Medical Corp. Ltd., Tokyo, Japan. Software: Synapse V5.7.240.16413). This value was adjusted based on each patient's height to calculate psoas muscle index (PMI) (mm^2/m^2). The age and sex specific cut-off values reported by Kim et al. [18] were used to define sarcopenia (Supplementary Table 1)

Definition of clinical frailty scale

CFS was defined and classed as CFS 1 (very fit), CFS 2 (well, no active disease symptoms), CFS 3 (managing well, medical problems are well controlled, not regularly active), CFS 4 (vulnerable, not dependent, symptoms limit activities), CFS 5 (mildly frail, more evident slowing, need help in high order instrumental activities of daily living), CFS 6 (moderately frail, need help with all outside activities and with keeping house), CFS 7 (severely frail, completely dependent for personal care), CFS 8 (very severely frail, completely dependent, approaching the end of life), and CFS 9 (terminally ill, approaching the end of life, life expectancy <6 months) [7]. (Supplementary Table 2)

Data collection

The prospectively maintained electronic hospital records were used as the source for data collection. An electronic data collection sheet was created which collected data on the following parameters: age, gender, American Society of Anesthesiologists (ASA) status, indication for laparotomy, procedure performed, need for bowel resection, presence of peritoneal contamination, CFS, sarcopenia, and mortality outcomes. All steps of the data collection were performed by two independent authors, and an independent third author was consulted in the event of disagreement. All authors were members of direct clinical team who worked as staff in department of general surgery. Data collection was performed by members of the direct care team who had legitimate access to the participants' personal identifiable information and had automatic access to the medical records. The data were anonymised at the source by data-masking technique through which the patient's hospital number was masked.

Data synthesis and statistical analyses

The MedCalc 13.0 software was used for statistical analyses. The demographics, clinical characteristics, and outcome data were summarised with mean ± standard deviation (SD) or median and interquartile range (IQR) for continuous variables, and percentages for categorical variables. The continuous variables were compared using *t* test or Mann–Whitney test as appropriate and dichotomous variables were compared using chi-squared test. The predictive values of sarcopenia and CFS were compared using the receiver operating characteristic (ROC) curve analysis through which the standard error of the area under the curve (AUC) and an exact binomial confidence interval for the AUC were calculated. Moreover, multivariable binary logistic regression model was constructed in which 30-day mortality was defined as the dependent variable, and the following variables were defined as independent variables: age, age ≥ 80, ASA status, need for bowel resection, presence of peritoneal contamination, CFS, and sarcopenia. All statistical tests were two-tailed and statistical significance was assumed at $P < 0.05$.

Results

Baseline characteristics of the included population

Between January 2017 and January 2021, 1069 patients underwent emergency laparotomy due to non-traumatic abdominal pathology; 26 patients were excluded due to unavailable perioperative data. Consequently, 1043 patients were included for analysis. The study flow chart is shown in Fig. 1. Ninety-day follow up data were available for all patients. The mean age of the included patients was 62 (95% CI 60–64), and 19% were ≥ 80 years old. In terms of sex, 49% were male, and 51% were female. Eight percent of patients were classed as ASA I, 36% as ASA II, 41% as ASA III, 14% as ASA IV, and 1% as ASA V. Bowel resection was required in 54% of patients, and 28% had peritoneal contamination. The median CFS was 2 (IQR 1–3); 33% of patients were classed as CFS 1, 26% as CFS 2, 18% as CFS 3, 10% as CFS 4, 6% as CFS 5, 6% as CFS 6, 1% as CFS 7, 0.1% as CFS 8, and 0.1% as CFS 9. Sarcopenia was present in 11% of patients. The baseline characteristics of the included patients are summarised in Table 1.

Postoperative mortality

The risks of 30-day mortality, in-hospital mortality, and 90-day mortality were 8%, 10%, and 11%, respectively. Table 2 highlights the differences in characteristics of the patients who survived longer than 30 days and those who died within 30 days. The patients who died were older (71 vs. 61, $P< 0.001$); they were more likely to be over 80 years old (30 % vs. 19%, P=0.016); they were more likely to have ASA status IV (41% vs. 12%, $P< 0.001$) and ASA status V (6% vs. 0.4%, $P< 0.001$); they were more likely to have peritoneal contamination (42% vs. 26%, P=0.003) and bowel resection (65% vs. 53%, P=0.003); they had higher CFS score (3 vs. 2; $P< 0.001$) and were more likely to have sarcopenia (78% vs. 5%, $P< 0.001$).

Sarcopenia versus clinical frailty scale

ROC curve analysis

ROC curve analysis suggested that sarcopenia was a significantly stronger predictor of 30-day mortality (AUC: 0.87 vs. 0.70, P<0.0001), in-hospital mortality (AUC: 0.79 vs.

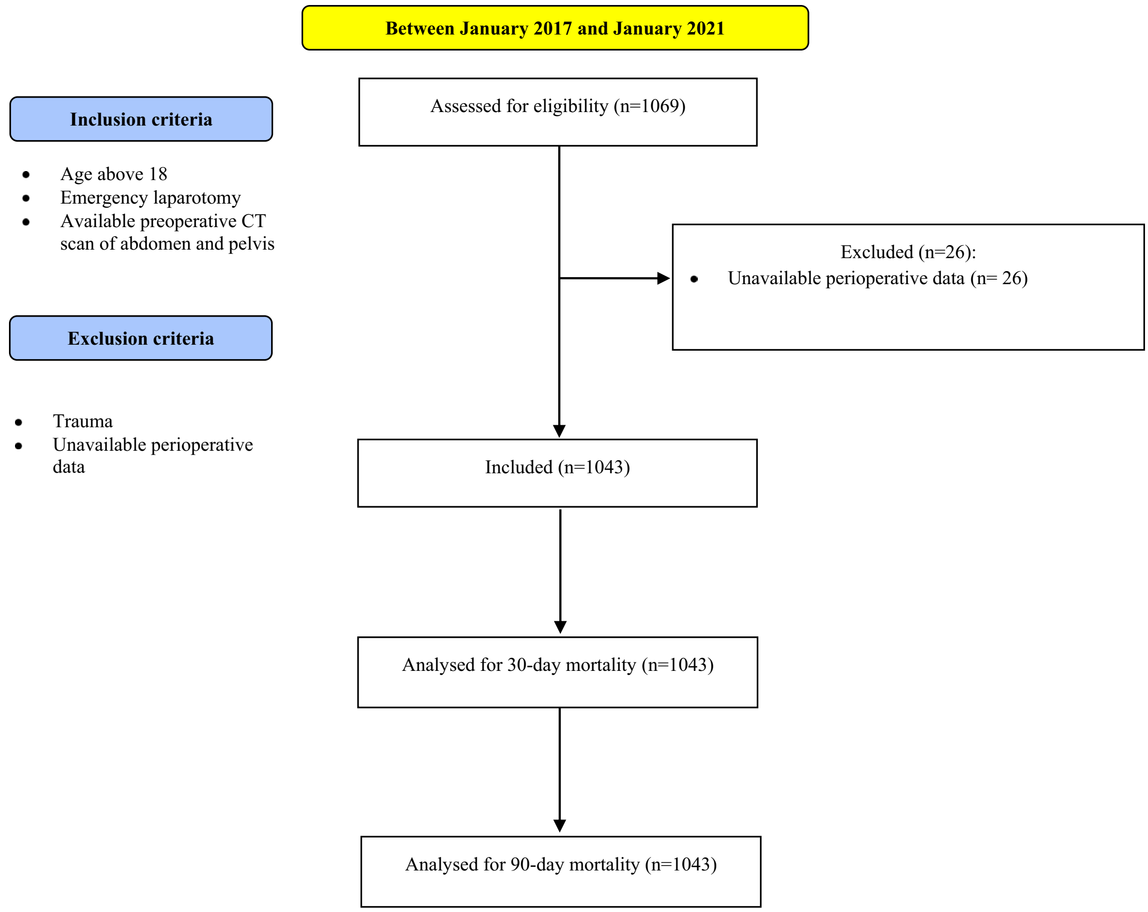

Fig. 1 The study flow diagram

0.67, P=0.0011), and 90-day mortality (AUC: 0.79 vs. 0.67, P=0.0009) compared with CFS (Fig. 2).

Multivariable binary logistic regression analysis

Multivariable binary logistic regression identified sarcopenia [coefficient: 4.333, OR: 76.16 (95% CI 37.06–156.52), P<0.0001], ASA status [coefficient: 1.039, OR: 2.83 (95% CI 1.79–4.47), P<0.0001], and peritoneal contamination [coefficient: 0.856, OR: 2.37 (95% CI 1.15–4.91), P=0.0197] as independent predictors of 30-day mortality while the following variables did not predict the 30-day mortality: age [coefficient: 0.004, OR: 1.00 (95% CI 0.97–1.03), P=0.8035], age ≥ 80 [coefficient: −0.877, OR: 0.42 (95% CI 0.15–1.12), P=0.0829], bowel resection [coefficient: −0.463, OR: 0.63 (95% CI 0.33–1.22), P=0.1688], and CFS [coefficient: 0.096, OR: 1.10 (95% CI 0.88–1.38), P=0.4047] (Table 3).

Discussion

Objective measurement of aging-related physiological decline and vulnerability to complications in older adults undergoing emergency laparotomy has been the area of interest recently. Considering that sarcopenia and CFS are two commonly used measures of aging-related physiological decline and vulnerability, we aimed to compare predictive significance of sarcopenia and CFS in terms of postoperative mortality in patients undergoing emergency laparotomy. Analysis of 1043 patients suggested that

Table 1 Baseline characteristics of the included patients

Number of patients	1043
Age, mean (95% CI)	62 (60–64)
Age ≥ 80	203 (19%)
Male, *n* (%)	514 (49%)
Female, *n* (%)	529 (51%)
ASA, *n* (%)	
I	79 (8%)
II	377 (36%)
III	430 (41%)
IV	148 (14%)
V	9 (1%)
Indication for laparotomy, *n* (%)	
Small bowel obstruction	411 (39%)
Large bowel obstruction	150 (14%)
Perforated peptic ulcer	58 (6%)
Small bowel perforation	39 (4%)
Colonic perforation	176 (17%)
Intestinal ischaemia	55 (4%)
Intra-abdominal collection	32 (3%)
Colitis	55 (5%)
Anastomotic leak	29 (3%)
Other	38 (4%)
Need for bowel resection, *n* (%)	559 (54%)
Peritoneal contamination, *n* (%)	289 (28%)
Neutrophils ($\times 10^9$/L), median (IQR)	8.7 (5.8–12.1)
CRP (mg/L), median (IQR)	1.3 (1–2)
Lactate (mmol/L), median (IQR)	45 (9–149)
Albumin (mmol/L), median (IQR)	35 (28–39)
Clinical frailty scale, median (IQR)	2 (1–3)
Clinical frailty scale, *n* (%)	
1	342 (33%)
2	267 (26%)
3	189 (18%)
4	108 (10%)
5	64 (6%)
6	61 (6%)
7	10 (1%)
8	1 (0.1%)
9	1 (0.1%)
Sarcopenia, *n* (%)	109 (11%)
30-day mortality, *n* (%)	83 (8%)
In-hospital mortality, *n* (%)	105 (10%)
90-day mortality, *n* (%)	109 (11%)

CI Confidence interval, *ASA* American Society of Anesthesiologists, *IQR* interquartile range

sarcopenia is a stronger predictor of postoperative mortality compared with CFS in patients undergoing emergency laparotomy. Moreover, it cancels out the predictive value of clinical frailty scale in multivariable analyses.

Although this study is the first in the literature comparing the predictive significance of sarcopenia and CFS in patients undergoing emergency laparotomy, other researchers have evaluated predictive significance of sarcopenia and CFS separately; hence, we can compare our findings with findings of other studies. Consistent with the findings of current study, Park et al. [11] conducted a meta-analysis including 6737 patients from 20 studies which showed that sarcopenia is associated with increased risk of mortality following emergency laparotomy. Yang et al. [12] and Brzeszczyńska et al. [13] reported similar findings in two different meta-analyses. Youssef et al. [9] analysed 191 patients and concluded that CFS can predict postoperative morbidity and mortality in patients undergoing emergency laparotomy [9]. This was consistent with findings of the study by Parmer et al. [5] which analysed 937 older adults undergoing emergency laparotomy. Palaniappan et al. [14] analysed 2246 patients undergoing emergency laparotomy and reported that AUC of CFS for predicting postoperative mortality was 0.71, which is consistent with the findings of current study. All of the above would support external validity of our findings.

Based on the available evidence, there is no doubt that both sarcopenia and CFS are predictors of mortality in patients undergoing emergency laparotomy and many authors recommended that they should be included in preoperative risk assessment tools. However, the important question is "which one should be included in the preoperative risk assessment tools?". The results of current study suggests that sarcopenia may be a better reflector of patient's aging-related physiological decline and vulnerability in comparison to age, being an octogenarian, and CFS; the effects of all were cancelled out by sarcopenia in multivariable analyses. Consequently, we believe that among the two variables, sarcopenia deserves to be included in preoperative predictive tools.

There is increasing effort to take into account frailty into risk predictive tools; however, appropriate measure of frailty is subject of debate. Considering that CFS and sarcopenia are currently popular measures of frailty, it is important to understand which one is the stronger predictor. It is particularly important when developing a model as inclusion of multiple variables that measure the same thing within the

Table 2 Comparison of baseline characteristics between patients who survived longer than 30 days and those died within 30 days

	Patients survived longer than 30 days (n = 960)	Patients died within 30 days (n = 83)	P value*
Age, mean (95% CI)	61 (60-62)	71 (69-73)	< 0.001
Age ≥ 80	178 (19%)	25 (30%)	0.016
Male, *n* (%)	476 (49%)	38 (46%)	0.582
Female, *n* (%)	484 (51%)	45 (54%)	0.582
ASA, *n* (%)			
I	78 (8%)	1 (1%)	0.039
II	372 (39%)	5 (6%)	< 0.001
III	392 (41%)	38 (46%)	0.446
IV	114 (12%)	34 (41%)	< 0.001
V	4 (0.4%)	5 (6%)	< 0.001
Need for bowel resection, *n* (%)	505 (53%)	54 (65%)	0.003
Peritoneal contamination, *n* (%)	254 (26%)	35 (42%)	0.003
Clinical frailty scale, median (IQR)	2 (1-3)	3 (2-5)	< 0.001
Sarcopenia, *n* (%)	44 (5%)	65 (78%)	< 0.001

*Continuous variables were compared using *t* test or Mann–Whitney test as appropriate and dichotomous variables were compared using chi-squared test

CI Confidence interval, *ASA* American Society of Anesthesiologists, *IQR* interquartile range

same model decreases the accuracy of the model. This study is a novel study that compares predictive significance of two measures of frailty. In emergency general surgery setting, comparison of sarcopenia and CFS is very important and is subject of interest. It has never been compared in emergency laparotomy. The knowledge provided by the results of current study has implications for researchers with interest in perioperative care of patients requiring emergency laparotomy. Consistent with previous literature, we have demonstrated that measures of frailty are predictors of mortality following emergency laparotomy. The unique finding of the current study is that among the sarcopenia and CFS, the former needs to be tested and incorporated into preoperative risk assessment tools. Consequently, the results of current study encourages other researchers to either incorporate sarcopenia into previously available risk assessment tools or develop and validate new preoperative risk assessment tools including sarcopenia as one of the variables.

The current study has the following limitations. Retrospective nature of the study would subject the results to inevitable risk of selection bias. The study was a single-centre study; although the results are consistent with the available literature, the generalizability of findings should be done with caution due to single-centre nature of the study. We excluded 26 patients due to unavailable perioperative data; however, considering that the sample size of the study was relatively large, we do not believe the aforementioned exclusion affected our findings.

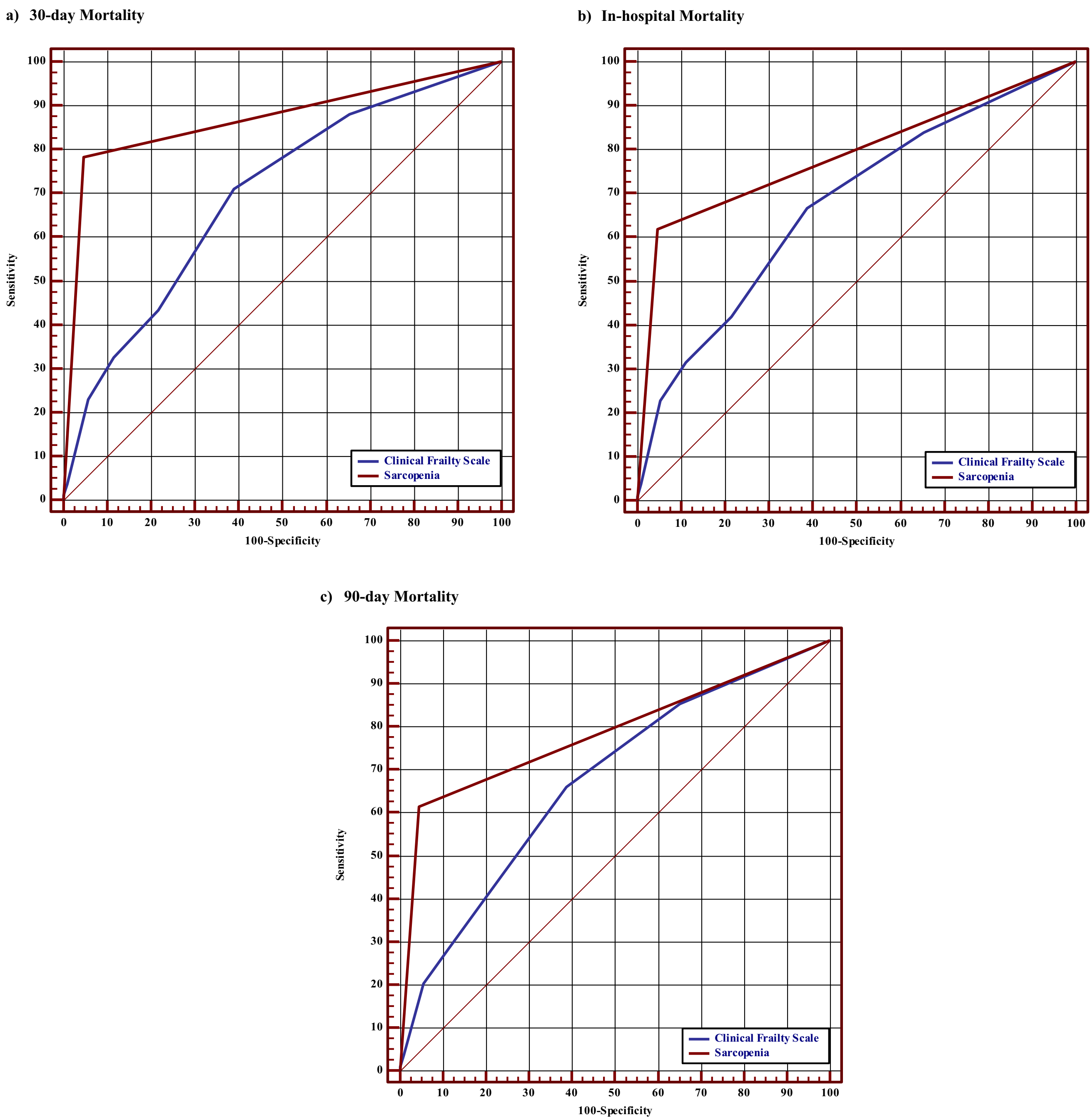

Fig. 2 ROC curves for comparison of sarcopenia and clinical frailty scale in predicting: **a** 30-day mortality; **b** in-hospital mortality; **c** 90-day mortality

Table 3 Results of multivariable binary logistic regression

	30-day mortality as dependent variable		
Independent variables	Coefficient	OR (95% CI)	*P* value
Age	0.004	1.00 (0.97–1.03)	0.8035
Age ≥ 80	−0.877	0.42 (0.15–1.12)	0.0829
ASA status	1.039	2.83 (1.79–4.47)	<0.0001
Bowel resection	−0.463	0.63 (0.33–1.22)	0.1688
Peritoneal contamination	0.865	2.37 (1.15–4.91)	0.0197
Sarcopenia	4.333	76.16 (37.06–156.52)	<0.0001
Clinical frailty scale	0.096	1.10 (0.88–1.38)	0.4047

OR Odds ratio, *CI* confidence interval, *ASA* American Society of Anesthesiologists

Conclusions

Sarcopenia is a stronger predictor of postoperative mortality compared with CFS in patients undergoing emergency laparotomy. It cancels out the predictive value of clinical frailty scale in multivariable analyses; hence among the two variables, sarcopenia deserves to be included in preoperative predictive tools.

Supplementary Information The online version contains supplementary material available at https://doi.org/10.1007/s00423-024-03252-9.

Acknowledgements We would like to thank Maureen Edgar (Research Governance Manager), Alun Meggy (Clinical Trials Manager), and Rachel Norman (Registration and Permissions Improvement Manager) in the Cardiff & Vale University Health Board for their support in registration, protocoling, and approval of the study.

Authors' contributions Conception and design: Shahab H. Data collection: IH, KM, APS, HR, Shahab H. Analysis and interpretation: All authors. Writing the article: Shahab H, Shahin H. Critical revision of the article: All authors. Final approval of the article: All authors.

Declarations

Ethical approval This study was approved by the Health Research Authority (HRA) and Health and Care Research Wales (HCRW) through the Integrated Research Application System (IRAS) (IRAS ID: 320962). Moreover, the study was approved by local research and development (RD) department (R&D reference: 8446/AUG/2022). The included population in this study is the same as the included population in our recently published article; however, the research question, study design, analyses, and results are entirely different and independent.

Consent to participate Due to retrospective design of the study and use of non-identifiable data, patient's consent was not required

Conflict of interest The authors declare no competing interests.

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Full text 4

Article 4. Synergistic effect of sarcopenia and ASA status in predicting mortality after emergency laparotomy: a systematic review and meta-analysis with meta-regression

Citation: Al-Sarireh A, Al-Sarireh H, Ambler O, Hajibandeh S, **Hajibandeh S**. Synergistic effect of sarcopenia and ASA status in predicting mortality after emergency laparotomy: a systematic review and meta-analysis with meta-regression. Updates Surg. 2025 Apr;77(2):591-603. doi: 10.1007/s13304-025-02105-4.

Contribution: Conception, design, data collection, data analysis, write up, and critical revision

Updates in Surgery (2025) 77:591–603
https://doi.org/10.1007/s13304-025-02105-4

ORIGINAL ARTICLE

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Synergistic effect of sarcopenia and ASA status in predicting mortality after emergency laparotomy: a systematic review and meta-analysis with meta-regression

Ahmad Al-Sarireh[1] · Hashim Al-Sarireh[2] · Olivia Ambler[3] · Shahin Hajibandeh[4] · Shahab Hajibandeh[3]

Received: 28 November 2024 / Accepted: 7 January 2025 / Published online: 16 January 2025

Abstract
The aim of this study was to investigate the relationship between sarcopenia and American Society of Anesthesiologists (ASA) status in predicting post-operative mortality after emergency laparotomy. A PRISMA-compliant systematic review and meta-analysis (using random effects modelling) was performed searching for studies reporting 30-day mortality risk in patients with sarcopenia undergoing emergency laparotomy. The ASA status of sarcopenic and non-sarcopenic patients was determined, and the effect of difference in ASA status on 30-day mortality in sarcopenic and non-sarcopenic patients was determined via a meta-regression model. The risk of bias and certainty was assessed using the QUIPS tool and the GRADE system, respectively. Seven studies comprising 2663 patients were included. Thirty-day mortality risk was 22.9% (95% CI 11.6–40.0%) in sarcopenic patients and 6.2% (95% CI 2.9–13.0%) in non-sarcopenic patients; the risk was significantly higher in sarcopenic patients (OR: 4.452, $p=0.016$). In sarcopenic patients, ASA status IV–V increased the risk of mortality (Coefficient: 0.07612, $p<0.0001$), while ASA status I–II (Coefficient: −0.09039, $p<0.0001$) or ASA status III (Coefficient: 0.01300, $p=0.344$) did not. In non-sarcopenic patients, ASA status III (Coefficient: 0.06830, $p<0.0001$) and ASA status IV–V (Coefficient: 0.17809, $p<0.0001$) increased the risk of mortality, while ASA status I-II (Coefficient: −0.05841, $p<0.0001$) did not. The GRADE certainty was moderate. Sarcopenia and ASA status are two independent predictors of mortality after emergency laparotomy with no significant collinearity. Sarcopenia and ASA status synergistically increase the risk of mortality after emergency laparotomy. ASA status IV and ASA status III are critical thresholds for increased risk of mortality in sarcopenic and non-sarcopenic patients, respectively.

Keywords American Society of Anesthesiologists · Sarcopenia · Laparotomy · Mortality

Introduction

Emergency laparotomy accounts for over 30,000 operations performed annually in the United Kingdom [1], but it still carries a high risk of mortality despite recent improvements [2]. Therefore, decisions around emergency laparotomy require multidisciplinary perioperative consideration and planning which are heavily dependent on detailed knowledge about predictors of mortality in patients undergoing such high-risk procedures. Our understanding of predictors of mortality after emergency laparotomy has evolved extensively over recent years. Modern predictors include objective measures of age-related physiological decline such as sarcopenia, the clinical frailty scale, objective measures of patient's health and functional capacity such as American Society of Anesthesiologists (ASA) status, and objective measures of the severity of underlying pathology such as a peritoneal contamination index (Hajibandeh index), and the need for bowel resection [3].

The available pre-operative risk assessment tools which are commonly used for predicting mortality after emergency laparotomy have two major disadvantages. First, they lack

Ahmad Al-Sarireh and Hashim Al-Sarireh are joint first authors.

✉ Shahab Hajibandeh
[redacted]

1 University of Cambridge, Cambridge, UK

2 University of Leeds, Leeds, UK

3 Department of General Surgery, Morriston Hospital, Swansea, UK

4 Department of General Surgery, Royal Stoke University Hospital, Stoke-on-Trent, UK

objective measurement of age-related physiological decline and vulnerability [4]. Second, they contain too many variables measuring the same feature resulting in collinearity in the model, which reduces the accuracy of the predictive tool [4]. Hajibandeh et al. [3] conducted a strict multivariable analysis of all modern predictors of mortality after emergency laparotomy and identified only three independent predictors without collinearity: Hajibandeh index, sarcopenia, and ASA status [3]. Ming et al. [5] also demonstrated that combining ASA status with sarcopenia provides simple alternative to the more complex established risk assessment tools [5].

While sarcopenia and ASA status are strong predictors of mortality after emergency laparotomy, the association between the two variables has not been adequately evaluated. Whether the prognostic significance of ASA status varies between sarcopenic and non-sarcopenic patients undergoing emergency laparotomy is poorly understood. Therefore, we aimed to conduct a systematic review and meta-analysis with meta-regression to investigate the relationship between sarcopenia and ASA status in predicting post-operative mortality after emergency laparotomy.

Methods

Methodological and reporting compliance

The study was conducted and reported in compliance with the Cochrane Handbook for Systematic Reviews (version 6.4) [6] and the Preferred Reporting Items for Systematic reviews and Meta-Analyses (PRISMA) 2020 statement standards [7], respectively.

Registration and protocol

The study followed a pre-defined protocol which was prospectively registered in PROSPERO which is a publicly available international database of prospectively registered systematic reviews (PROSPERO registration number: CRD42024607701).

Eligibility criteria

Study design

All retrospective and prospective studies (randomised controlled trials, cohort studies, and case–control studies) were considered eligible for inclusion in this study. Systematic reviews, meta-analyses, scoping reviews, review articles, single-arm studies, case series, case reports, and correspondence articles were excluded.

Population

All adult patients aged 18 or over with acute non-traumatic abdominal pathology who underwent emergency laparotomy were eligible. The non-traumatic abdominal pathologies of interest included visceral perforation, intestinal obstruction, intestinal ischemia, intra-abdominal bleeding, and intra-abdominal sepsis of any source (intra-abdominal collection, colitis, anastomotic leak, and intestinal fistula).

Prognostic factor

Combined sarcopenia and ASA status were considered as prognostic factor of interest. The prognostic significance of each ASA status in sarcopenic and non-sarcopenic patients were evaluated.

Outcomes

30-Day mortality defined as death due to any cause within 30 days of emergency laparotomy was the outcome of interest.

Based on the above criteria, a study was only defined as eligible if it reported ASA status, sarcopenia, and 30-day mortality in adult patients undergoing emergency laparotomy.

Information sources and search strategy

A comprehensive search strategy consisting of proper search keywords, limits, thesaurus headings, and operators was created, adopted, and applied on the following electronic sources: Scopus®, MEDLINE®, the Cochrane Central Register of Controlled Trials, the Cumulative Index to Nursing and Allied Health Literature, the International Standard Randomised Controlled Trial Number Registry, the International Clinical Trials Registry Platform, ClinicalTrials.gov, and the Grey Literature Network Service (Appendix I). Two authors with expertise in evidence synthesis designed and applied the search strategy on 01 October 2024 with no language restrictions.

Study selection, data collection, and data items

Two authors independently screened the identified articles through titles and abstracts against the eligibility criteria and retrieved the full text of potentially eligible articles. Articles that met the eligibility criteria were selected for inclusion. If there was discrepancy in the findings of the first two authors, a third author provided an opinion on eligibility. The data

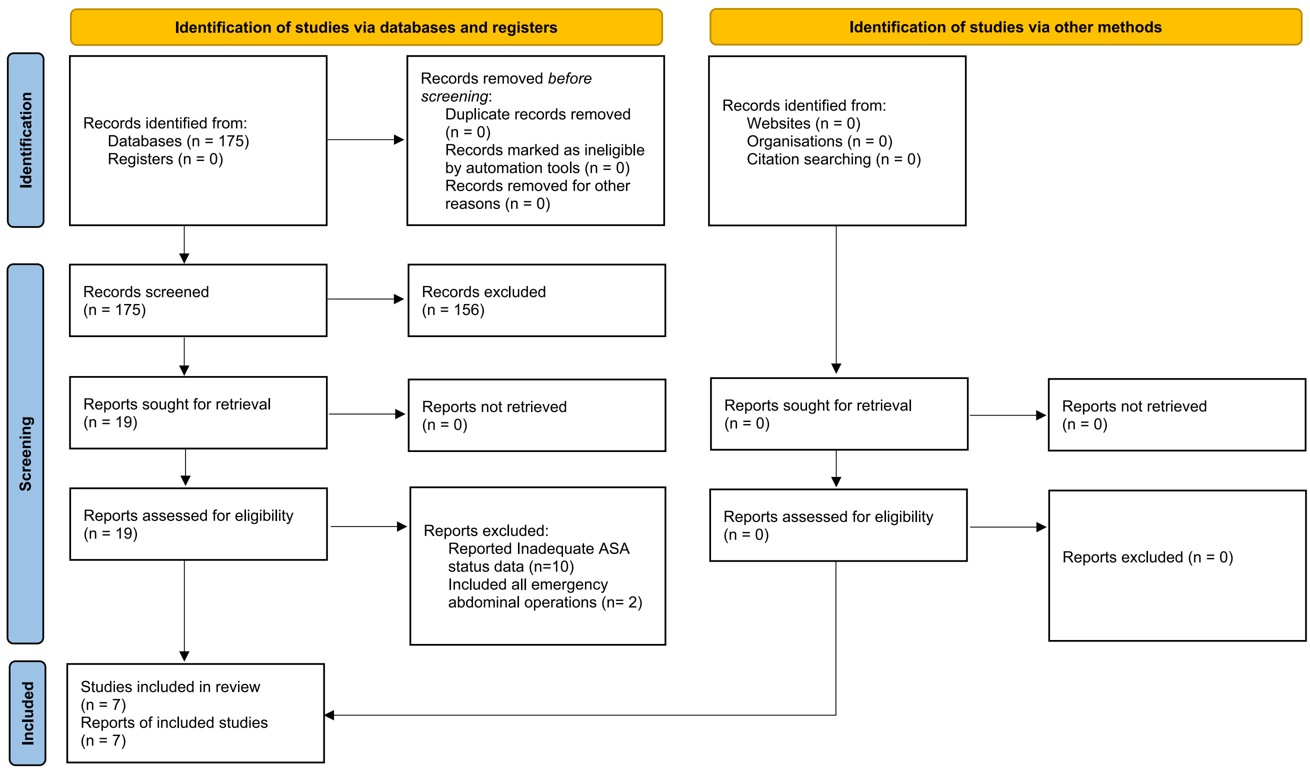


Fig. 1 Study PRISMA flow diagram

items were determined at the protocol development stage by the authors with expertise in the field and after selection of eligible studies by the authors with expertise in evidence synthesis using a pilot-testing technique of randomly selected studies. Data items were collected in an electronic data collection sheet by two independent authors. These included information about the bibliometric parameters, study design, included population and their demographic parameters, ASA status, sarcopenia, and operative mortality.

Study risk-of-bias assessment

The risk of bias in study participation, study attrition, prognostic factor measurement, outcome measurement, study confounding, and statistical analysis were judged using the Quality In Prognosis Studies (QUIPS) tool [8]. The risk of bias in the included studies was assessed by two independent authors. If there was any discrepancy in assessment by the first two authors, a third author provided opinion.

Effect measures and synthesis methods

Comprehensive Meta-Analysis Version 2.0 software was employed for meta-analysis. A proportion meta-analysis model was constructed to calculate pooled risk of 30-day mortality in patients with and without sarcopenia. A comparison meta-analysis model was constructed to compare the risk of 30-day mortality between the patients with and without sarcopenia; odds ratio (OR) was calculated as summary effect measure. Meta-regression was performed to evaluate the effect of each ASA status level on 30-day mortality in patients with and without sarcopenia. Individual patients were considered a unit of analysis. Random-effects modelling was used for analyses and forest plots with 95% confidence intervals (CIs) were constructed to present the results. Statistical heterogeneity was measured as I^2 using Cochran's Q test (χ^2), and heterogeneity was classified as low when I^2 was 0–25%, moderate when I^2 was 25–75%, and high when I^2 was 75–100%. Sensitivity analyses (leave-one-out analysis and separate analysis for studies with low overall risk of bias) were performed if the outcome was reported by a minimum of four studies.

Reporting bias assessment

The protocol planned to evaluate the risk of reporting bias by constructing a funnel plot if the outcome was reported by at least ten studies; however, because the outcome was reported by less than ten studies, reporting bias could not be evaluated.

Table 1 Baseline characteristics of the included studies

Authors, year, country	Journal	Design	Sample size			Age* mean (SD)	Male* (n/total)	ASA status* (n/total)				
			Total	Sarcopenia	No Sarcopenia			I	II	III	IV	V
Hajibandeh et al., 2024, UK	Ann Surg	Retrospective cohort	1043	109	934	75 (16) vs 61 (18)	51/109 vs 463/934	1/109 vs 78/934	18/109 vs 359/934	51/109 vs 379/934	34/109 vs 114/934	5/109 vs 4/934
Uyeda et al., 2023, UK	Abdom Radiol	Retrospective cohort	297	75	222	78 (3) vs 78 (2)	32/75 vs 95/222	9/75 vs 14/222	7/75 vs 44/222	46/75 vs 128/222	13/75 vs 36/222	0/75 vs 0/222
Barazanchi et al., 2022, New Zealand	Eur J Trauma Emerg Surg	Retrospective cohort	167	84	83	76 (7) vs 75 (7)	35/84 vs 50/83	1/84 vs 5/83	28/84 vs 18/83	48/84 vs 46/83	6/84 vs 13/83	1/84 vs 1/83
Body et al., 2022, UK	Ann Surg	Retrospective cohort	536	179	357	75 (3) Vs 68 (6)	82/179 vs 164/357	12/179 vs 45/357	64/179 vs 162/357	70/179 vs 109/357	30/179 vs 37/357	3/179 vs 4/357
Wu et al., 2022, China	World J Emerg Surg	Retrospective cohort	228	56	172	61 (15) vs 57 (16)	34/56 vs 104/172	0/56 vs 7/172	19/56 vs 79/172	25/56 vs 71/172	12/56 vs 14/172	0/56 vs 1/172
Tan et al., 2022, Singapore	Ann Acad Med Singap	Retrospective cohort	289	49	240	78 (6) vs 75 (7)	37/49 vs 130/240	3/49 vs 6/240	12/49 vs 81/240	26/49 vs 119/240	8/49 vs 32/240	0/49 vs 2/240
Kubo et al., 2019, Japan	Ann Gastroenterol Surg	Retrospective cohort	103	50	53	68 (17) vs 69 (16)	17/50 vs 31/53	5/50 vs 5/53	14/50 vs 8/53	28/50 vs 36/53	3/50 vs 4/53	0/50 vs 0/53

ASA American Society of Anesthesiologists, *SD* standard deviation

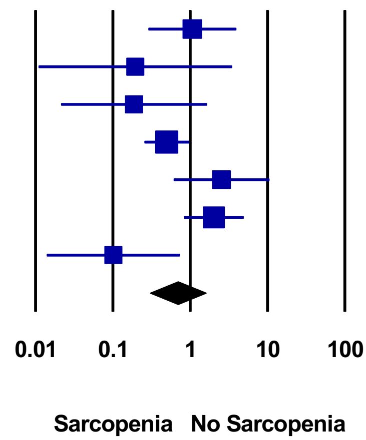
*Sarcopenia group versus no sarcopenia group

A) ASA I

Comparison of ASA I status between patients with and without sarcopenia

Study name	Odds ratio	Lower limit	Upper limit	Z-Value	p-Value
Kubo 2019	1.067	0.289	3.932	0.097	0.923
Wu 2022	0.195	0.011	3.474	-1.112	0.266
Barazanchi 2022	0.188	0.021	1.645	-1.510	0.131
Body 2022	0.498	0.256	0.968	-2.057	0.040
Tan 2022	2.543	0.614	10.538	1.287	0.198
Uyeda 2022	2.026	0.839	4.894	1.569	0.117
Hajibandeh 2024	0.102	0.014	0.738	-2.260	0.024
	0.695	0.304	1.587	-0.864	0.387

Odds ratio and 95% CI



B) ASA II

Comparison of ASA II status between patients with and without sarcopenia

Study name	Odds ratio	Lower limit	Upper limit	Z-Value	p-Value
Kubo 2019	2.188	0.827	5.788	1.577	0.115
Body 2022	0.670	0.463	0.970	-2.123	0.034
Tan 2022	0.637	0.315	1.287	-1.257	0.209
Uyeda 2022	0.416	0.179	0.970	-2.032	0.042
Wu 2022	0.605	0.322	1.134	-1.568	0.117
Barazanchi 2022	1.806	0.904	3.606	1.675	0.094
Hajibandeh 2024	0.317	0.188	0.534	-4.312	0.000
	0.715	0.449	1.138	-1.415	0.157

Odds ratio and 95% CI

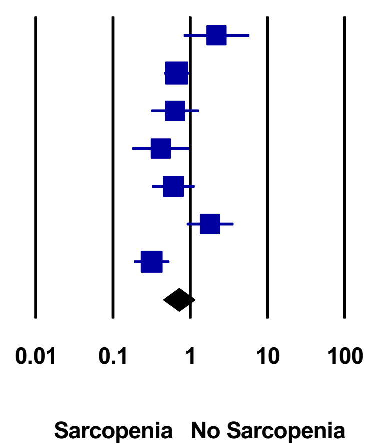
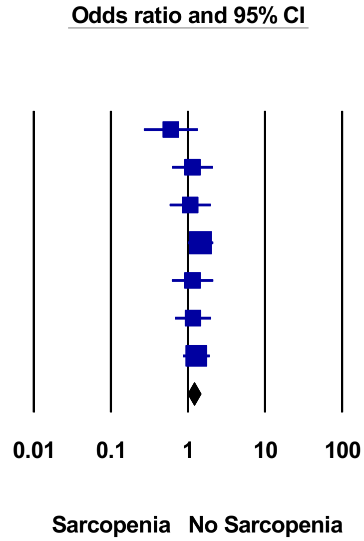


Fig. 2 Forest plots for comparison of ASA status between patients with and without sarcopenia: **A** ASA I; **B** ASA II; **C** ASA III; **D** ASA IV-V

C) ASA III

Comparison of ASA III status between patients with and without sarcopenia

Study name	Odds ratio	Lower limit	Upper limit	Z-Value	p-Value
Kubo 2019	0.601	0.269	1.341	-1.243	0.214
Wu 2022	1.147	0.625	2.107	0.443	0.658
Barazanchi 2022	1.072	0.582	1.977	0.224	0.823
Body 2022	1.461	1.004	2.127	1.980	0.048
Tan 2022	1.149	0.621	2.127	0.444	0.657
Uyeda 2022	1.165	0.682	1.990	0.558	0.577
Hajibandeh 2024	1.288	0.865	1.918	1.244	0.213
	1.206	0.993	1.465	1.888	0.059



D) ASA IV-V

Comparison of ASA IV-V status between patients with and without sarcopenia

Study name	Odds ratio	Lower limit	Upper limit	Z-Value	p-Value
Kubo 2019	0.782	0.166	3.682	-0.311	0.756
Tan 2022	1.182	0.510	2.738	0.391	0.696
Uyeda 2022	1.083	0.540	2.173	0.225	0.822
Wu 2022	2.855	1.245	6.543	2.479	0.013
Barazanchi 2022	0.448	0.171	1.175	-1.633	0.103
Body 2022	1.742	1.058	2.868	2.182	0.029
Hajibandeh 2024	3.853	2.490	5.962	6.055	0.000
	1.499	0.858	2.620	1.422	0.155

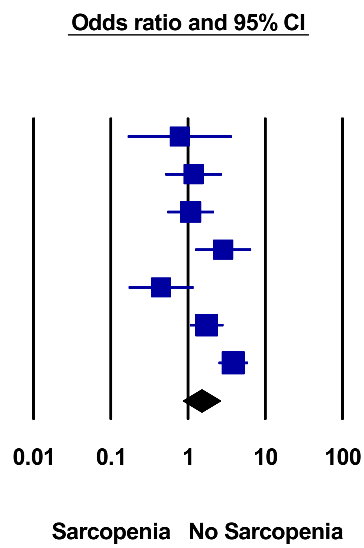


Fig. 2 (continued)

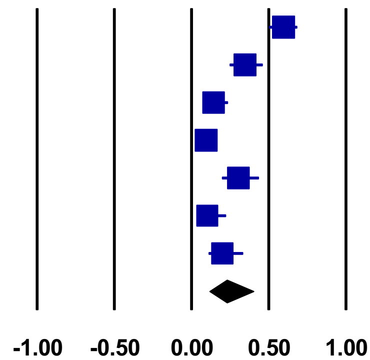
Certainty assessment

The Grading of Recommendations Assessment, Development and Evaluation (GRADE) system was used for assessment of the certainty of evidence for operative mortality [9].

A) Patients with sarcopenia

30-day mortality in patients with sarcopenia

Study name	Event rate	Lower limit	Upper limit	Z-Value	p-Value
Hajibandeh 2024	0.596	0.502	0.684	1.999	0.046
Uyeda 2023	0.347	0.248	0.461	-2.612	0.009
Barazanchi 2022	0.143	0.083	0.235	-5.746	0.000
Body 2022	0.095	0.060	0.147	-8.843	0.000
Wu 2022	0.304	0.198	0.435	-2.857	0.004
Tan 2022	0.102	0.043	0.223	-4.608	0.000
Kubo 2019	0.200	0.111	0.333	-3.921	0.000
	0.229	0.116	0.400	-2.937	0.003



B) Patients without sarcopenia

30-day mortality in patients without sarcopenia

Study name	Event rate	Lower limit	Upper limit	Z-Value	p-Value
Hajibandeh 2024	0.019	0.012	0.030	-16.511	0.000
Uyeda 2023	0.194	0.147	0.251	-8.398	0.000
Barazanchi 2022	0.120	0.066	0.210	-5.895	0.000
Body 2022	0.036	0.021	0.062	-11.594	0.000
Wu 2022	0.087	0.053	0.140	-8.689	0.000
Tan 2022	0.038	0.020	0.070	-9.551	0.000
Kubo 2019	0.057	0.018	0.161	-4.733	0.000
	0.062	0.029	0.130	-6.554	0.000

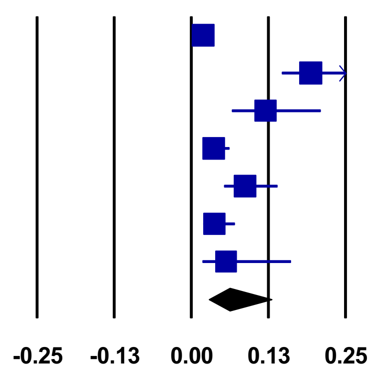


Fig. 3 Forest plots for proportion meta-analysis of 30-day mortality in: **A** patients with sarcopenia; **B** patients without sarcopenia

Comparison of 30-day mortality between patients with and without sarcopenia

Study name	Odds ratio	Lower limit	Upper limit	Z-Value	p-Value
Hajibandeh 2024	75.177	41.121	137.439	14.033	0.000
Uyeda 2023	2.209	1.236	3.947	2.676	0.007
Barazanchi 2022	1.217	0.495	2.993	0.427	0.669
Body 2022	2.777	1.317	5.854	2.684	0.007
Wu 2022	4.562	2.096	9.931	3.825	0.000
Tan 2022	2.917	0.933	9.118	1.841	0.066
Kubo 2019	4.167	1.074	16.162	2.063	0.039
	4.452	1.323	14.976	2.413	0.016

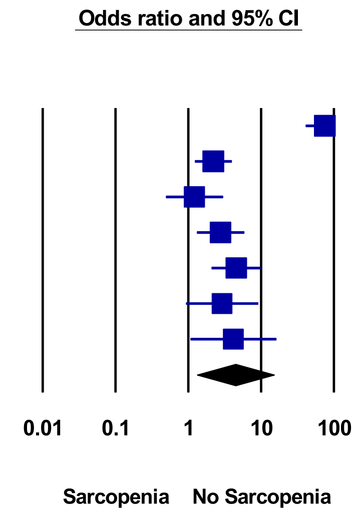


Fig. 4 Forest plot for comparison of 30-day mortality between patients with and without sarcopenia

Deviation from the registered protocol

The study remained compliant with the registered protocol with no deviations.

Results

Study selection and study characteristics

Search of the information sources resulted in 175 articles; 156 articles were excluded directly by screening their titles and abstracts. The full-text review of the remaining 19 articles resulted in exclusion of 12 articles (10 studies did not report adequate ASA status data; 2 studies included all emergency abdominal operations). Consequently, seven comparative retrospective cohort studies [3, 10–15] comprising 2663 patients were included; 602 patients were sarcopenic and 2061 patients were not sarcopenic. The study PRISMA flow diagram is shown in Fig. 1 and baseline characteristics of the included studies are shown in Table 1.

Risk of bias in studies

Supplementary Fig. 1 shows overall risk-of-bias graph and the risk-of-bias judgement for each domain of QUIPS tool for each study. All the included studies were judged to be of low risk of bias in study participation, study attrition, prognostic factor measurement, outcome measurement, and statistical analysis. The risk of bias due to study confounding was judged to be low in five studies, and high in two studies.

ASA status

The patients with and without sarcopenia were comparable in terms of ASA I status (5% vs 8%; OR: 0.695, 95% CI 0.304–1.587, $p=0.387$); ASA II status (27% vs 36%; OR: 0.715, 95% CI 0.449–1.138, $p=0.157$), ASA III status (49% vs 43%; OR: 1.206, 95% CI 0.993–1.465, $p=0.059$), and ASA IV–V status (19% vs 13%; OR: 1.499, 95% CI 0.858–2.620, $p=0.155$) (Fig. 2).

30-Day mortality

The pooled risk of 30-day mortality was 22.9% (95% CI 11.6–40.0%) in patients with sarcopenia and 6.2% (95% CI 2.9–13.0%) in patients without sarcopenia (Fig. 3). The risk of 30-day mortality was higher in patients with sarcopenia (OR: 4.452, 95% CI 1.323–14.976, $p=0.016$) (Fig. 4). The level of between-study heterogeneity was high ($I^2=94\%$) and the GRADE certainty of evidence was moderate.

ASA status and sarcopenia, and 30-day mortality

In patients with sarcopenia, ASA status IV–V increased the risk of 30-day mortality (coefficient: 0.07612, $p<0.0001$), while ASA status I–II (coefficient: -0.09039, $p<0.0001$) or ASA status III (coefficient: 0.01300, $p=0.344$) did not increase the risk of 30-day mortality (Fig. 5 and Table 2). In patients without sarcopenia, ASA status III (coefficient: 0.06830, $p<0.0001$) and ASA status IV–V (coefficient: 0.17809, $p<0.0001$) increased the risk of 30-day mortality, while ASA status I–II (coefficient: -0.05841,

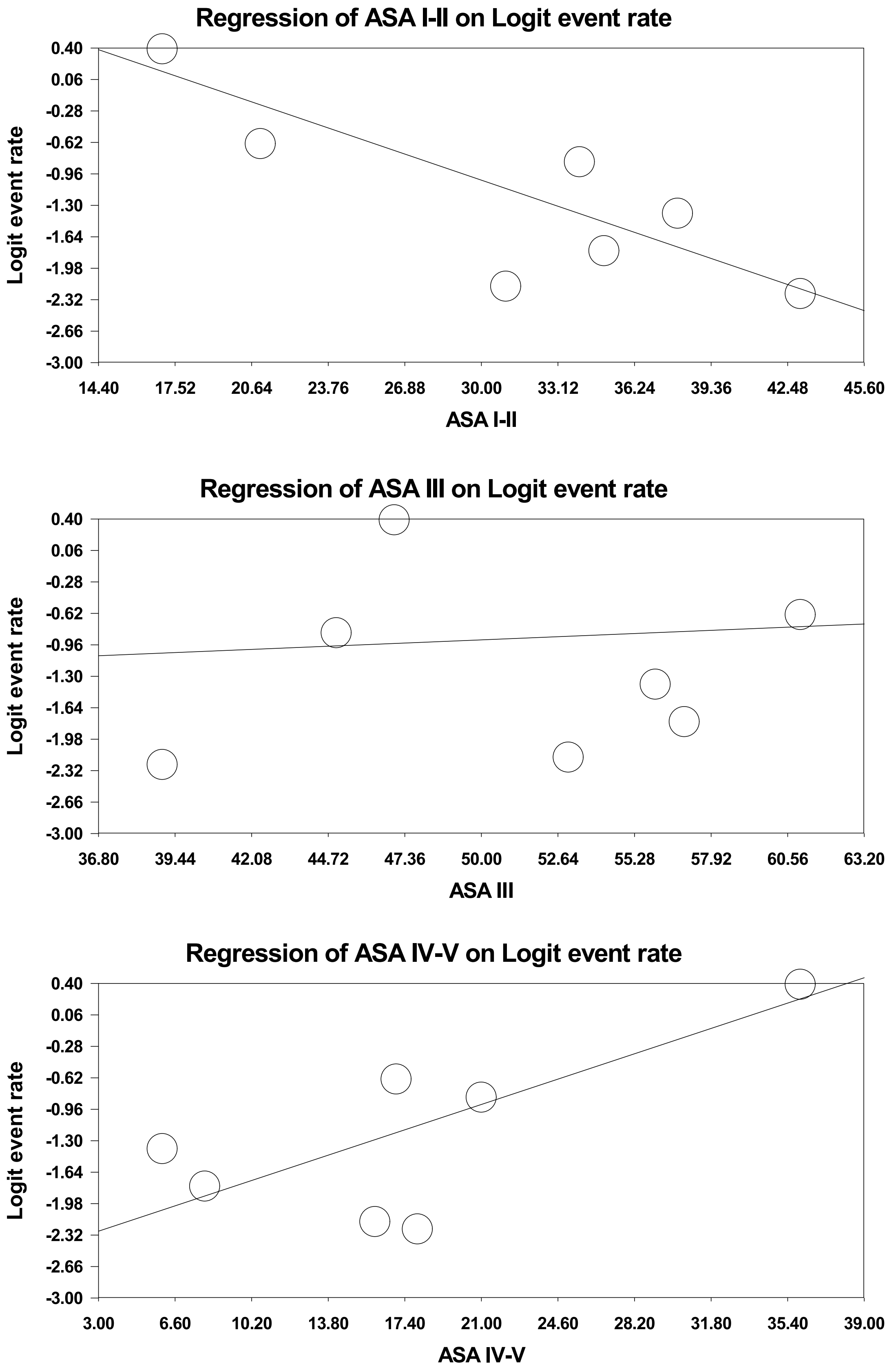


Fig. 5 Meta-regression analysis for effect of ASA status on 30-day mortality in patients with sarcopenia

Table 2 Results of meta-regression analysis for effect of ASA status on 30-day mortality in patients with and without sarcopenia

	Patients with sarcopenia				Patients without sarcopenia			
	Coefficient	Lower limit	Upper limit	*p* value	Coefficient	Lower limit	Upper limit	*p* value
ASA I-II	−0.09039	−0.11082	−0.06995	< 0.0001	−0.05841	−0.07452	−0.04229	< 0.0001
ASA III	0.01300	−0.01398	0.03997	0.34491	0.06830	0.04922	0.08804	< 0.0001
ASA IV-V	0.07612	0.05648	0.09575	< 0.0001	0.17809	0.105	0.25117	< 0.0001

ASA American Society of Anesthesiologists

$p < 0.0001$) did not increase the risk of 30-day mortality (Fig. 6 and Table 2).

Sensitivity analyses

Leave-one-out analysis and separate analysis for studies with low overall risk of bias did not affect direction of effect size (Supplementary Fig. 2).

Discussion

We conducted a systematic review and meta-analysis with meta-regression to investigate the relationship between sarcopenia and ASA status in predicting post-operative mortality after emergency laparotomy. Analysis of 2663 patients from seven studies confirmed that ASA status remains an independent predictor of post-operative mortality in patients with and without sarcopenia. It confirmed a synergistic effect of ASA status and sarcopenia on mortality after emergency laparotomy, and highlighted that ASA status and sarcopenia are not likely to cause collinearity in predictive models. ASA status IV is critical threshold for increased risk of mortality in sarcopenic patients and ASA status III is critical threshold for increased risk of mortality in non-sarcopenic patients. The GRADE certainty of evidence was moderate.

This study is the first meta-analysis evaluating the combined effect of sarcopenia and ASA status on mortality after emergency laparotomy. Consequently, the results cannot be compared with another similar systematic review; nevertheless, the external validity of the findings of current study can be confirmed by findings of other studies. Ming et al. [5] conducted a retrospective study of 500 patients undergoing emergency laparotomy which concluded that combined sarcopenia and ASA status is strong predictor of mortality after emergency laparotomy with area under the curve (AUC) of 0.84 [5]. In another study, Hajibandeh et al. [4] conducted a retrospective cohort study of 1,043 patients undergoing emergency laparotomy which concluded that combined ASA status, sarcopenia, and Hajibandeh index is excellent predictor of mortality after emergency laparotomy with AUC of 0.96 [4]; this was found to be superior to National Emergency Laparotomy Audit (NELA) score in predicting mortality after emergency laparotomy [16]. Moreover, Akhtar et al. [17] conducted a systematic review of 10,861 patients which concluded that high ASA status is associated with high risk of mortality after emergency laparotomy [17].

The risk of post-operative mortality was higher in patients with sarcopenia than patients without sarcopenia. This is not a novel finding on its own as negative impact of sarcopenia on mortality after emergency laparotomy has already been shown in the previous systematic reviews [18]. The most important finding of the current study is that sarcopenia does not cancel out the predictive significance of ASA status which suggests that both variables should be included in pre-operative mortality risk assessment tools. Collinearity of variables in a predictive tool reduces the accuracy of the model and it is very important to recognise the variables with and without collinearity before including them in a model. While it may be argued that there is apparent collinearity between sarcopenia and ASA status as sarcopenic patients are likely to have higher ASA status, the results of this study do not support this argument, because ASA IV or V status increased the risk of mortality in sarcopenic patients. However, such possible collinearity may explain why ASA III status did not increase mortality in sarcopenic patients, but it increased the mortality in non-sarcopenic patients.

The current study has some limitations. The included studies had a retrospective design, and their results may be subject to selection bias. The statistical between-study heterogeneity was high, and it may be explained by the fact that the included studies defined and measured sarcopenia differently; however, we did downgrade the certainty of the evidence to compensate for this limitation. The relationship between ASA status, sarcopenia, and post-operative mortality was assessed using a meta-regression model which is well-recognised approach in meta-analysis; however, the most robust technique in evaluation of such association is direct comparison of mortality in different ASA status groups; due to lack of access to patient level data, such analyses were not possible. The publication bias could not be

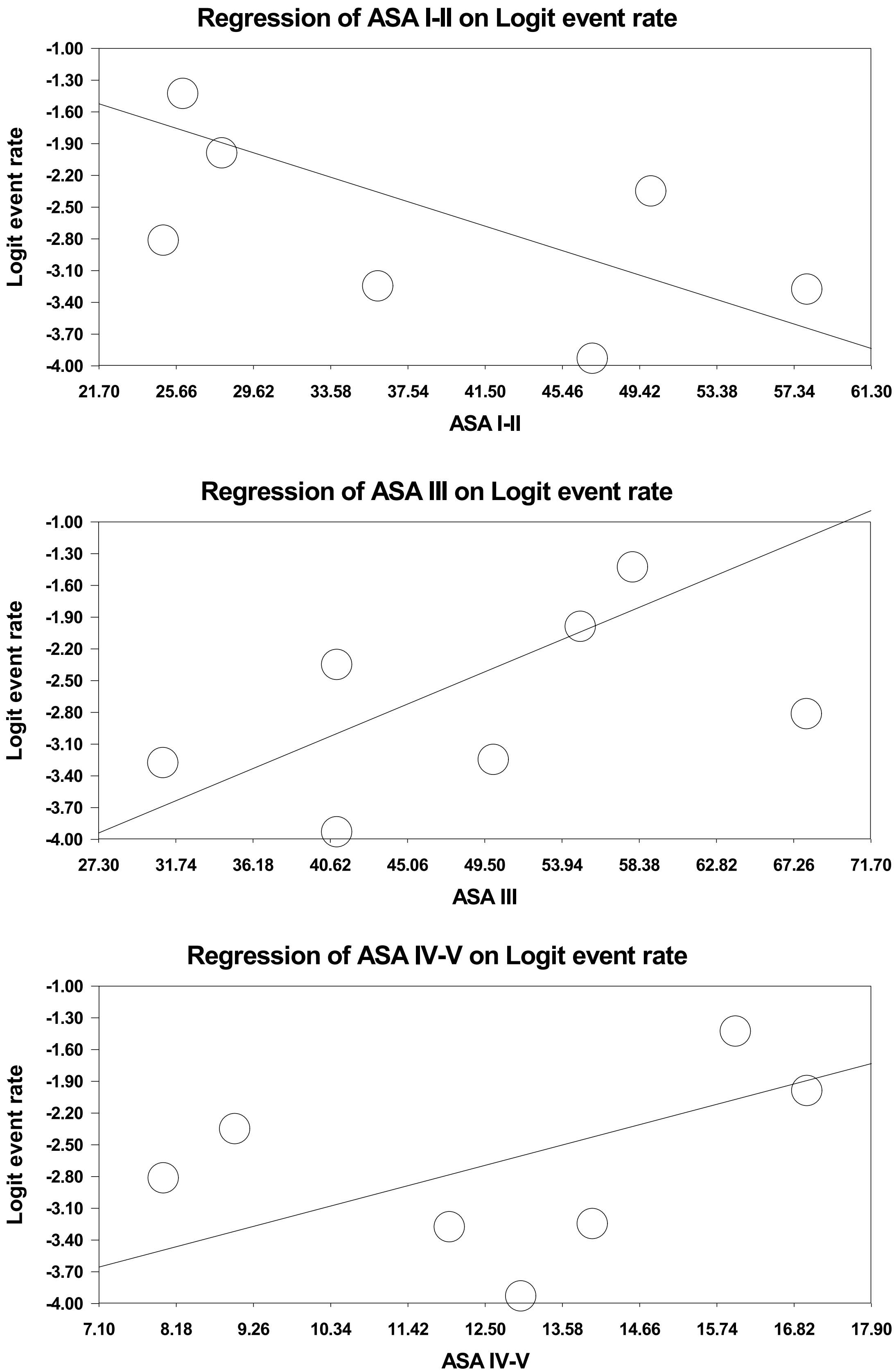


Fig. 6 Meta-regression analysis for effect of ASA status on 30-day mortality in patients without sarcopenia

assessed formally due to not having more than ten eligible studies.

Conclusions

Sarcopenia and ASA status are two independent predictors of mortality after emergency laparotomy with no significant collinearity. Sarcopenia and ASA status synergistically increase the risk of mortality after emergency laparotomy. ASA status IV and ASA status III are critical thresholds for increased risk of mortality in sarcopenic and non-sarcopenic patients, respectively.

Appendix I

Literature search strategy

Search number	Search description	Action
Number 1	Sarcopenia	Titles, abstracts, keywords
Number 2	MeSH term: [sarcopenia]	Explode all trees
Number 3	Number 1 OR Number 2	Combined with OR
Number 4	Emergency near 2 laparotomy	Titles, abstracts, keywords
Number 5	Laparotomy	Titles, abstracts, keywords
Number 6	Number 4 OR Number 5	Combined with OR
Number 7	Number 3 AND Number 6	Combined with AND

Author contributions Conception and design: Shahab H. Data collection: AA, HA, Shahab H. Analysis and interpretation: AA, HA, OA, Shahin H, Shahab H. Writing the article: AA, HA, OA, Shahin H, Shahab H. Critical revision for important intellectual content: AA, HA, OA, Shahin H, Shahab H. Final approval of the article: AA, HA, OA, Shahin H, Shahab H.

Funding The authors received no financial support for the research, authorship, and/or publication of this article.

Availability of data and materials The data and materials related to this study will be available upon reasonable request from the corresponding author.

Declarations

Conflict of interest The authors declared no potential conflicts of interest with respect to the research, authorship, and/or publication of this article.

Human and animal rights This study is a systematic review with meta-analysis of outcomes which does not include research directly involving human or animal participation. PROSPERO registration number: CRD42024607701.

Informed consent This study is a systematic review which does not include direct involvment of individual patients, hence informed consent was not applicable.

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Full text 5

Article 5. Intraperitoneal contamination index (Hajibandeh index) predicts nature of peritoneal contamination and risk of postoperative mortality in patients with acute abdominal pathology: a prospective multicentre cohort study

Citation: **Hajibandeh S,** Shah J, Hajibandeh S, Murali S, Stephanos M, Ibrahim S, Asqalan A, Mithany R, Wickramasekara N, Mansour M. Intraperitoneal contamination index (Hajibandeh index) predicts nature of peritoneal contamination and risk of postoperative mortality in patients with acute abdominal pathology: a prospective multicentre cohort study. Int J Colorectal Dis. 2021 May;36(5):1023-1031. doi: 10.1007/s00384-020-03822-5.

Contribution: Conception, design, data collection, data analysis, write up, and critical revision

International Journal of Colorectal Disease (2021) 36:1023–1031
https://doi.org/10.1007/s00384-020-03822-5

ORIGINAL ARTICLE

Intraperitoneal contamination index (Hajibandeh index) predicts nature of peritoneal contamination and risk of postoperative mortality in patients with acute abdominal pathology: a prospective multicentre cohort study

Shahab Hajibandeh[1] · Jigar Shah[2] · Shahin Hajibandeh[3] · Sreedutt Murali[1] · Mina Stephanos[1] · Sherif Ibrahim[1] · Ahmad Asqalan[1] · Reda Mithany[1] · Nuwan Wickramasekara[1] · Moustafa Mansour[2]

Accepted: 15 December 2020 / Published online: 6 January 2021

Abstract

Objectives To assess whether intraperitoneal contamination index (ICI) (Hajibandeh index) derived from combined levels of CRP, lactate, neutrophils, lymphocytes, and albumin can predict the nature of intraperitoneal contamination in patients with acute abdominal pathology and to assess whether ICI can predict postoperative mortality in patients undergoing emergency laparotomy.

Methods In order to prospectively validate the ICI, developed and validated retrospectively in our previous study, a multicentre prospective cohort study was conducted between January 2019 and June 2020 including all adult patients who presented with acute abdominal pathology requiring emergency laparotomy. ROC curve analysis was performed to determine discrimination and cut-off values of preoperative ICI that could predict the nature of intraperitoneal contamination and postoperative mortality.

Results Overall, 269 patients were included in the prospective validation cohort which were compared with 234 patients in the primary cohort and 234 patients in the retrospective validation cohort. The analyses identified ICI of 24.76 as cut-off value for purulent contamination (AUC: 0.78, $P < 0.0001$; sensitivity: 82.4%, specificity: 60.9%); ICI of 33.84 as cut-off value for feculent contamination (AUC: 0.78, $P < 0.0001$; sensitivity: 82%, specificity: 67.8%), and ICI of 33.47 as cut-off value for postoperative mortality (AUC: 0.70, $P < 0.0001$; sensitivity: 72.7%, specificity: 58.47%). The results of the prospective validation cohort were comparable with the results of the primary and retrospective validation cohorts.

Conclusions Hajibandeh index predicts the presence of purulent and feculent intraperitoneal contamination in patients with acute abdominal pathology and postoperative mortality in patients undergoing emergency laparotomy. Future studies should investigate the effect of ICI use on the accuracy of preoperative prognostic scoring tools and on patient selection for operative or non-operative management of underlying abdominal pathology.

Keywords Laparotomy · Mortality · Morbidity · Peritonitis · Contamination

Shahab Hajibandeh, Jigar Shah, and Shahin Hajibandeh equally contributed to this paper and joined first authorship is proposed

✉ Shahab Hajibandeh
[redacted]

1 Department of General Surgery, Glan Clwyd Hospital, Rhyl, Denbighshire, UK

2 Department of General Surgery, North Manchester General Hospital, North Manchester Care Organisation, Manchester, UK

3 Department of General Surgery, Sandwell and West Birmingham Hospitals NHS Trust, Birmingham, UK

Introduction

Intraabdominal sepsis due to the presence of intraperitoneal contamination increases the risk of morbidity and mortality associated with emergency laparotomy [1]. Knowledge about the nature of intraperitoneal contamination in patients presenting with acute abdominal pathology before the decision to operate would allow more accurate preoperative mortality and morbidity risk assessment and would potentially guide more appropriate management decisions. Many preoperative prognostic scoring tools that are used to predict the risk of mortality and morbidity following emergency laparotomy take the nature of intraperitoneal contamination into account [2]. However, the knowledge about the nature of contamination is only available intraoperatively which limits the predictive value of preoperative prognostic scoring tools. Therefore, identifying a reliable biomarker that could help to predict the nature of peritoneal contamination before the decision to operate, along with clinical and radiological findings, is crucial.

We recently developed an intraperitoneal contamination index (ICI) (Hajibandeh Index) derived from combined levels of C-reactive protein (CRP), lactate, neutrophils, lymphocytes, and albumin [3]. The ICI included the levels of CRP, neutrophil, and lactate as nominator considering the fact that their levels increase during sepsis [4–7], and included the levels of albumin and lymphocytes as denominator considering the fact that their levels decrease during sepsis [4, 8]. The retrospective development and validation of the ICI suggested that ICI, as a predictive measure which is purely derived from biomarkers, was promising in predicting purulent and feculent contamination in patients with acute abdominal pathology with the area under the curve (AUC) of greater than 70 and sensitivity of greater than 80% [3].

Considering that in our previous study the developed ICI was validated retrospectively in a single centre, we aimed to conduct a multicentre prospective study to prospectively validate the already developed ICI. This would potentially provide more robust evidence on the predictive value of ICI in patients presenting with acute abdominal pathology.

Objectives

The objectives of the current study were:

- To assess whether ICI could predict the presence of purulent and feculent contamination in patients with acute abdominal pathology in a prospective setting
- To assess whether ICI could predict the risk of postoperative mortality in patients with acute abdominal pathology undergoing emergency laparotomy

Methods

In compliance with the Strengthening the Reporting of Cohort Studies in Surgery (STROCSS) guideline for observational studies, we conducted and presented this multicentre prospective cohort study [9]. This study was performed according to an agreed predefined protocol which was registered locally and will be available on request. Considering the nature of this study, patient consent and approval by the Research Ethics Committees was not required; however, the study was conducted in accordance with institutions' policies and internal arrangements approved by local Clinical Governance Units.

Study design and patient selection

We performed a multicentre prospective cohort study involving three general surgery centres located in the North Wales and North West of England. The study period was between January 2019 and June 2020. All consecutive patients of any gender aged over 18 who presented to either of the above three centres with acute abdominal pathology requiring emergency laparotomy were considered eligible for inclusion. The indications of interest for emergency laparotomy included visceral perforation, small bowel obstruction, large bowel obstruction, intestinal ischaemia, incarcerated abdominal wall hernia, intraabdominal sepsis of any source, intraabdominal bleeding, and intraabdominal abscess. We excluded the patients with underlying haematological malignancy resulting in chronic elevated levels of neutrophils or lymphocytes, patients who did not have available preoperative levels of CRP, neutrophils, lactate, lymphocytes, or albumin, and those who underwent laparotomy secondary to trauma.

Intraperitoneal contamination index

The formula for ICI is presented in Fig. 1. As described above and in our previous study, the proposed ICI included the levels of CRP, neutrophil, and lactate as nominator and the levels of albumin and lymphocytes as denominator. The proposed ICI as a potential predictor of the nature of intraperitoneal contamination was tested in a prospective cohort; however, for comparison purposes, we also presented the results of previous study in which the index was tested in the primary cohort and retrospective validation cohort.

Outcome measures

Primary outcome The nature of intraperitoneal contamination, classified as serous, purulent, or feculent based on the intraoperative finding of the operating surgeon, was considered as the primary outcome measure. The operating surgeon classified the contamination as purulent or feculent. In presence of turbid fluid, the operating surgeon assessed the nature of contamination very carefully and in absence of obvious pus or faecal material, turbid fluid was classed as serous or no contamination.

Secondary outcome Postoperative mortality defined as death due to any cause within 30 days of emergency laparotomy was considered as a secondary outcome measure.

$$\text{Intraperitoneal Contamination Index (Hajibandeh Index)} = \frac{\text{CRP (mg/L)} \times \text{Lactate (mmol/L)} \times \text{Neutrophils } (\times 10^9/\text{L})}{\text{Albumin (g/L)} \times \text{Lymphocytes } (\times 10^9/\text{L})}$$

Fig. 1 Formula for intraperitoneal contamination index (Hajibandeh Index)

Data collection

All steps of data collection were performed by two independent authors and an independent third author was consulted in the event of disagreement. An electronic data collection proforma was developed which contained data on the following parameters: patients' demographic data (age and sex), American Society of Anaesthesiologists (ASA) score, indication for emergency laparotomy, performed procedure, preoperative biomarker levels, the nature of intraperitoneal contamination, and postoperative mortality. The authors who were involved in collecting the data on intraperitoneal contamination were not involved in collecting data on preoperative biomarker levels and were blinded in terms of results of ICI calculation. Moreover, the operating surgeons were not aware of the results of the ICI calculation.

Data synthesis and statistical analyses

The MedCalc 13.0 software was used for statistical analyses. The demographics, clinical characteristics, and outcome data were presented using simple descriptive statistics. Data were summarised with mean ± standard deviation (SD) or median and interquartile range (IQR) for continuous variables, and frequencies/percentages for categorical variables. All statistical tests were two-tailed and statistical significance was assumed at $P < 0.05$. To assess whether ICI could predict the presence of purulent and feculent contamination in patients with acute abdominal pathology, receiver operating characteristic (ROC) curve analysis was performed to evaluate discrimination of ICI. The method described by DeLong et al. was used for the calculation of the standard error of the area under the curve (AUC) and an exact binomial confidence interval was calculated for the AUC [10]. We calculated associated sensitivity and specificity for all possible threshold values of ICI and we determined the optimal criterion value as the cut-off value of ICI for the nature of intraperitoneal contamination. Binary logistic regression models were constructed to investigate whether ICI greater than the calculated cut-off values can predict the presence of intraperitoneal contamination. The intraperitoneal contamination was considered as dependent variables and the ICI greater than the calculated cut-off values as independent variables. To assess whether ICI could predict the risk of postoperative mortality, we first performed ROC curve analysis (methods described above) to determine the cut-off value and associated sensitivity and specificity of ICI for postoperative mortality. We then performed binary logistic regression models considering postoperative mortality as the dependent variable and the ICI greater than the calculated cut-off value as the independent variable. A two-sided CI with 95% confidence level was used to indicate statistical significance. It was hypothesised that the risk of intraperitoneal contamination in patients undergoing emergency laparotomy ranges between 20 and 30%; therefore, it was estimated that a minimum number of 172 patients would be required to achieve 80% power with 95% confidence level.

Results

Baseline patient characteristics

Overall, a total of 269 patients were included in the prospective validation cohort. The mean age of the included patients was 64.2 (95% CI 62.3 to 66.1) and 123 out of 269 (46%) were male. In terms of ASA status, 9 out of 269 (3%) patients were classified as ASA 1; 54 out of 269 (20%) as ASA 2; 158 out of 269 (59%) as ASA 3; 43 out of 269 (16%) as ASA 4; 5 out of 269 (2%) as ASA 5. The indication for emergency laparotomy was small bowel obstruction in 94 out of 269 (35%) patients, perforated diverticulitis in 41 out of 269 (15%) patients, perforated colonic tumour in 6 out of 269 (2%) patients, small bowel perforation in 10 out of 269 (4%) patients, perforated peptic ulcer in 27 out of 269 (10%), perforated appendicitis in 2 out of 269 (1%) patients, perforated gallbladder in 1 out of 269 (0.4%) patients, large bowel obstruction in 34 out of 269 (12.5%), intraabdominal abscess in 4 out of 269 (1.5%), intestinal ischaemia in 25 out of 269 (9%), anastomotic leak in 3 out of 269 (1%), Meckel's diverticulitis in 2 out of 269 (1%), intraabdominal bleeding in 5 out of 269 (2%), colitis in 5 out of 269 (2%), and other indications in 10 out of 269 (4%). The study flow chart, the baseline characteristics of the included population, and the preoperative biomarker levels in all cohorts (primary cohort, retrospective validation cohort, and prospective validation cohort) are demonstrated in Fig. 2, Table 1, and Table 2 respectively.

Intraperitoneal contamination

Prospective validation cohort

The median ICI was 25.2 (4.5 to 121.1) in the prospective validation cohort. The nature of intraperitoneal contamination

Table 1 Baseline characteristics of the included population

	Primary development cohort	Retrospective validation cohort	Prospective validation cohort
Number of patients	234	234	269
Age, mean (95% CI)	62.4 (60.2 to 64.6)	60.2 (58.0 to 62.3)	64.2 (62.3 to 66.1)
Male, *n* (%)	106 out of 234 (45%)	100 out of 234 (43%)	123 out of 269 (46%)
Female, *n* (%)	128 out of 234 (55%)	134 out of 234 (57%)	146 out of 269 (54%)
ASA, *n* (%)			
1	33 out of 234 (14%)	23 out of 234 (10%)	9 out of 269 (3%)
2	76 out of 234 (33%)	85 out of 234 (36%)	54 out of 269 (20%)
3	78 out of 234 (33%)	94 out of 234 (40%)	158 out of 269 (59%)
4	40 out of 234 (17%)	30 out of 234 (13%)	43 out of 269 (16%)
5	7 out of 234 (3%)	2 out of 234 (1%)	5 out of 269 (2%)
Indication for laparotomy, *n* (%)			
Small bowel obstruction	84 out of 234 (36%)	88 out of 234 (38%)	94 out of 269 (35%)
Perforated diverticulitis	37 out of 234 (16%)	30 out of 234 (13%)	41 out of 269 (15%)
Perforated colonic tumour	5 out of 234 (2%)	6 out of 234 (2%)	6 out of 269 (2%)
Small bowel perforation	11 out of 234 (5%)	14 out of 234 (6%)	10 out of 269 (4%)
Perforated peptic ulcer	28 out of 234 (12%)	23 out of 234 (10%)	27 out of 269 (10%)
Perforated appendicitis	0 out of 234 (0%)	0 out of 234 (0%)	2 out of 269 (1%)
Perforated gallbladder	0 out of 234 (0%)	0 out of 234 (0%)	1 out of 269 (0.4%)
Large bowel obstruction	28 out of 234 (12%)	39 out of 234 (17%)	34 out of 269 (13%)
Intraabdominal abscess	18 out of 234 (8%)	12 out of 234 (5%)	4 out of 269 (2%)
Intestinal ischaemia	8 out of 234 (3%)	5 out of 234 (2%)	25 out of 269 (9%)
Anastomotic leak	4 out of 234 (2%)	4 out of 234 (2%)	3 out of 269 (1%)
Meckel's diverticulitis	3 out of 234 (1%)	1 out of 234 (0.4%)	2 out of 269 (1%)
Intraabdominal bleeding	1 out of 234 (0.4%)	1 out of 234 (0.4%)	5 out of 269 (2%)
Colitis	2 out of 234 (1%)	0 out of 234 (0%)	5 out of 269 (2%)
Other	5 out of 234 (2%)	11 out of 234 (5%)	10 out of 269 (4%)

CI, confidence interval; *ASA*, American Society of Anaesthesiologists

was classified as serous in 75% (202 out of 269) of patients, purulent in 6% (17 out of 269), and feculent in 19% (50 out of 269) (Table 3).

Purulent contamination ROC curve analysis identified ICI of 24.76 as the cut-off value for purulent contamination (Fig. 3). The ICI had an AUC of 0.78 (95% CI 0.72–0.83, $P < 0.0001$) with a sensitivity of 82.4% (95% CI 56.6–96.2%) and specificity of 60.89% (95% CI 53.8–67.7%). Binary logistic regression analysis confirmed that ICI greater than 24.76 was an independent predictor of purulent contamination (OR: 7.27, 95% CI 2.02–26.10, $P = 0.0004$) (Table 3).

Table 2 Preoperative biomarkers in the primary and validation cohorts

	Primary development cohort	Retrospective validation cohort	Prospective validation cohort
Neutrophils$^{\$}$ (× 10^9/L)	10.1 (6.4–13.2)	10.1(6.4–13.5)	9.6 (5.9–13.9)
Lymphocytes$^{\$}$ (× 10^9/L)	1.1(0.7–1.7)	1(0.7–1.6)	1.1(0.7–1.6)
CRP$^{\$}$ (mg/L)	77 (23–199)	69 (16.2–210)	52 (41–71)
Lactate$^{\$}$ (mmol/L)	1.2 (1–2)	1.3 (1–2)	1.6 (1.1–2.3)
Albumin$^{\$}$ (mmol/L)	29 (23–36)	32 (23–38)	31 (25–38)
ICI$^{\$}$	32.2 (4.9 to 144.3)	23.3 (3.6–130.4)	25.2 (4.5–121.1)

CI, confidence interval; *WBC*, white blood cells; *CRP*, C-reactive protein; *ICI*, intraperitoneal contamination index

$^{\$}$ Median (interquartile range) was calculated

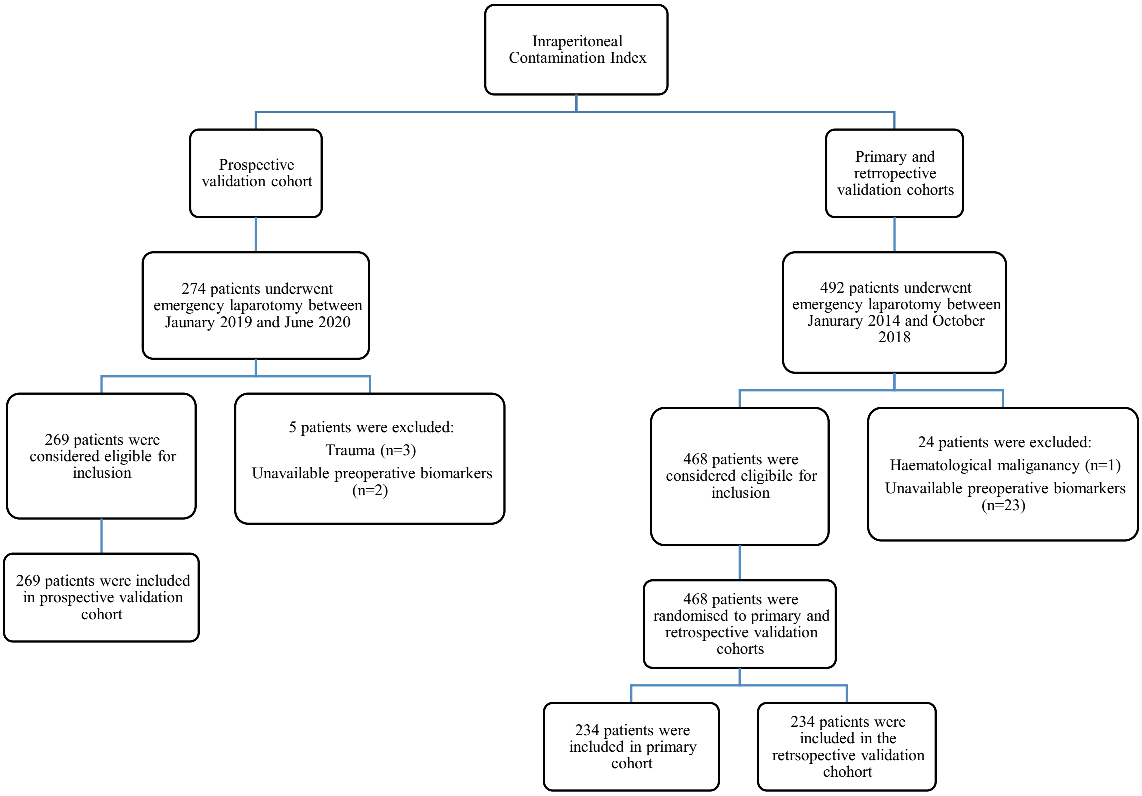

Fig. 2 The study flow chart

Feculent contamination ROC curve analysis identified an ICI of 33.84 as the cut-off value for feculent contamination (Fig. 3). The ICI had AUC of 0.78 (95% CI 0.72–0.83, $P < 0.0001$) with sensitivity of 82.0% (95% CI 68.6–91.4%) and specificity of 67.8% (95% CI, 60.9–74.2%). Binary logistic regression analysis confirmed that ICI greater than 33.84 was an

Table 3 Intraperitoneal contamination index and the nature of intraperitoneal contamination

	Primary development cohort	Retrospective validation cohort	Prospective validation cohort
ICI, median (interquartile range)	32.2 (4.9–144.3)	23.3 (3.6–130.4)	25.2 (4.5–121.1)
Intraperitoneal contamination, *n* (%)			
Serous	172 out of 234 (73.5%)	162 out of 234 (69.2%)	202 out of 269 (75%)
Purulent	32 out of 234 (13.7%)	44 out of 234 (18.8%)	17 out of 269 (6%)
Feculent	30 out of 234 (12.8%)	28 out of 234 (12%)	50 out of 269 (19%)
ROC curve analysis of ICI for purulent contamination			
Cut-off value	24.77	24.32	24.76
AUC (95% CI)	0.73 (0.67–0.79)	0.83 (0.77–0.88)	0.78 (0.72–0.83)
Sensitivity, % (95% CI)	84.4% (67.2–94.7%)	90.9% (78.3–97.5%)	82.4% (56.6–96.2%)
Specificity, % (95% CI)	59.9% (52.1–67.3%)	69.1% (61.4–76.1%)	60.89% (53.8–67.7%)
OR (95% CI)	5.96 (2.21–16.10)	11.96 (4.05–31.72)	7.27 (2.02–26.10)
ROC curve analysis of ICI for feculent contamination			
Cut-off value	33.7	33.41	33.84
AUC (95% CI)	0.78 (0.71–0.83)	0.79 (0.73–0.85)	0.78 (0.72–0.83)
Sensitivity, % (95% CI)	86.7% (69.3–96.2%)	85.7% (67.3–96.0%)	82.0% (68.6–91.4%)
Specificity, % (95% CI)	64.0% (56.3–71.1%)	73.5% (66.0–80.0%)	67.8% (60.9–74.2%)
OR (95% CI)	8.57 (2.89–25.45)	9.26 (3.10–27.67)	8.43 (3.97–17.91)

ICI, intraperitoneal contamination index; *ROC*, receiver operating characteristic; *AUC*, area under the curve; *OR*, odds ratio; *CI*, confidence intervals independent predictor of feculent contamination (OR: 8.43, 95% CI 3.97–17.91, $P < 0.0001$) (Table 3).

Comparison with the primary and retrospective validation cohorts

Purulent contamination The cut-off value for purulent contamination was comparable among the primary cohort (24.77), retrospective validation cohort (24.32), and prospective validation cohort (24.76). The ICI had comparable AUC for purulent contamination among the primary cohort (0.73, 95% CI 0.67–0.79), retrospective validation cohort (0.83, 95% CI 0.77–0.88), and prospective validation cohort (0.78, 95% CI 0.72–0.83). The sensitivity of ICI for purulent contamination was comparable among the primary cohort (84.4%, 95% CI 67.2–94.7%), retrospective validation cohort (90.9%, 95% CI 78.3–97.5%), and prospective validation cohort (82.4%, 95% CI 56.6–96.2%). The specificity of ICI for purulent contamination was comparable among the primary cohort (59.9%, 95% CI 52.1–67.3%), retrospective validation cohort (69.1%, 95% CI 61.4–76.1%), and prospective validation cohort (60.89%, 95% CI 53.8–67.7%) (Table 3).

Feculent contamination The cut-off value for feculent contamination was comparable among the primary cohort (33.7), retrospective validation cohort (33.41), and prospective validation cohort (33.84). The ICI had comparable AUC for feculent contamination among the primary cohort (0.78, 95% CI 0.71–0.83), retrospective validation cohort (0.79, 95% CI 0.73–0.85), and prospective validation cohort (0.78, 95% CI 0.72–0.83). The sensitivity of ICI for feculent contamination was comparable among the primary cohort (86.7%, 95% CI 69.3–96.2%), retrospective validation cohort (85.7%, 95% CI 67.3–96.0%), and prospective validation cohort (82.0%, 95% CI 68.6–91.4%). The specificity of ICI for feculent contamination was comparable among the primary cohort (64.0%, 95%

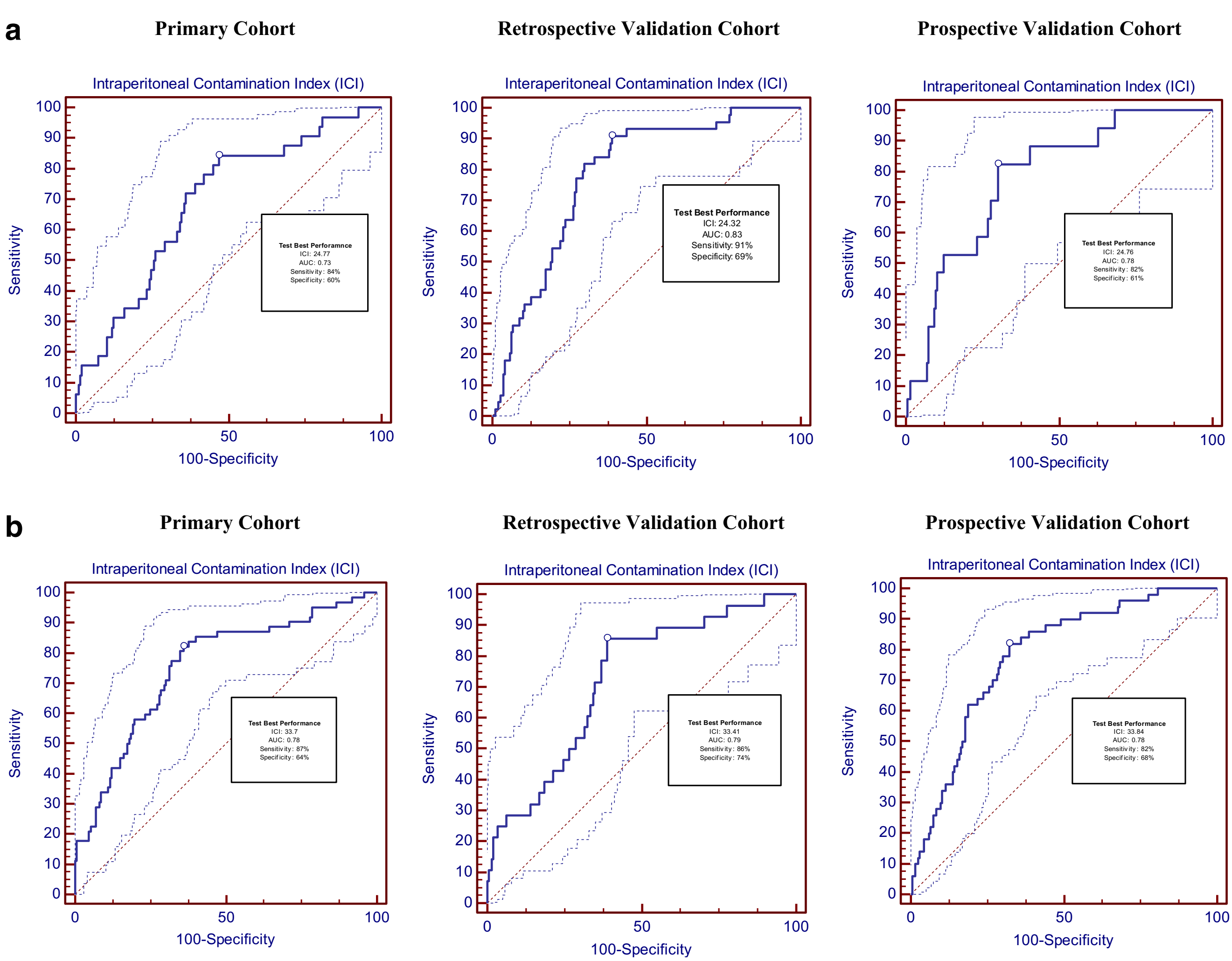

Fig. 3 Results of ROC curve analyses of intraperitoneal contamination index (ICI) for **a** purulent contamination and **b** feculent contamination

CI 56.3–71.1%), retrospective validation cohort (73.5%, 95% CI 66.0–80.0%), and prospective validation cohort (67.8%, 95% CI 60.9–74.2%) (Table 3).

Postoperative mortality

In the prospective cohort, 33 out of 269 patients died within 30 days of the operation. The risk of postoperative mortality was 12.3% (95% CI 8.6–16.8%). ROC curve analysis identified an ICI of 33.47 as the cut-off value for postoperative mortality (Fig. 4). The ICI had an AUC of 0.70 (95% CI 0.64–0.75, $P <$ 0.0001) with a sensitivity of 72.7% (95% CI 54.5–86.7%) and specificity of 58.47% (95% CI 51.9–64.8%). Binary logistic regression analysis showed that ICI > 33.47 (OR: 3.24, 95% CI 1.48–7.11, $P = 0.002$) was an independent predictor of postoperative mortality.

Discussion

In our previous study, we developed an intraperitoneal contamination index to predict the extent of intraabdominal contamination in patients presenting with acute abdominal pathology and testing the index in the primary and validation cohorts suggested that ICI could predict purulent and feculent contamination in patients with acute abdominal pathology with AUC of greater than 70 and sensitivity of greater than 80% [3]. We aimed to validate the ICI in a prospective cohort and analysis of 269 patients confirmed that ICI can independently predict the presence of purulent and feculent contamination in patients with acute abdominal pathology. Moreover, ICI was an independent predictor of postoperative mortality in patients undergoing emergency laparotomy. The cut-off value, AUC, sensitivity, and specificity of ICI found in the prospective validation cohort were comparable with the calculated values in the primary and retrospective validation cohorts.

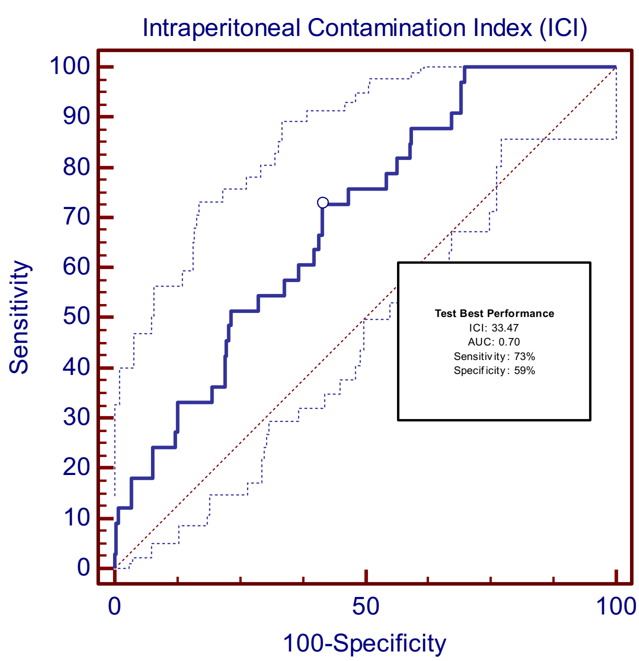

Fig. 4 Results of ROC curve analysis of intraperitoneal contamination index (ICI) for postoperative mortality

Considering that the current study was prospective in nature and was conducted in more than one centre, the findings are considered to be more robust with a lower risk of bias. To the best of our knowledge, the ICI is currently the best available preoperative predictor of intraperitoneal contamination in patients with underlying abdominal pathology. It is cost efficient, economical, and non-time consuming to calculate the ICI as it is derived from the most basic biomarkers that are routinely checked in every patient presenting to any surgical setting. Moreover, the ICI, together with clinical and radiological findings, could potentially improve the accuracy of preoperative prognostic scoring tools that consider intraperitoneal contamination to predict the risk of postoperative mortality and morbidity. This could potentially facilitate better decision-making in terms of operative versus non-operative management of the underlying pathology. Calculating ICI could, for example, play a role in selecting patients with perforated diverticulitis for conservative management versus those who are likely to require operative intervention from the outset. A similar argument could be made for the management of patients with perforated peptic ulcers or anastomotic leaks. It is however recognised that decisions are ultimately guided by clinical findings and by putting into consideration patients' comorbidities. The effectiveness of ICI use in the above settings needs further evaluation in future studies.

We noted that although ICI has a very good accuracy and sensitivity in predicting purulent and feculent contamination, its specificity was relatively lower. One possible explanation for this could be cases of intestinal ischaemia. In fact, in cases of intestinal ischaemia, the levels of neutrophil, lactate, and CRP would increase significantly resulting in a high ICI without evidence of intraperitoneal contamination. Nevertheless, we decided against the exclusion of the cases with intestinal ischaemia in order to test the ICI in a sample which is a true representation of patients presenting with acute abdominal pathology and to avoid the risk of selection bias.

Hajibandeh index is the only available index in the literature that aims to predict the nature of peritoneal contamination before performing an operation. However, the presence of peritoneal contamination is taken into account by many prognostic tools. Mannheim peritonitis index (MPI) is an index that takes eight variables into account to predict the prognosis of patients with peritonitis [11, 12]. One of the variables of MPI is the nature of intraperitoneal peritoneal contamination. Similar to MPI, other tools such as the National Emergency Laparotomy Audit (NELA) risk calculator and the

Portsmouth-Physiological and Operative Severity Score for the enumeration of Mortality and morbidity (P-POSSUM) risk calculator consider peritoneal contamination as one of the main variables to predict the risks of postoperative morbidity and mortality [13–16]. All of the available tools including MPI, NELA, and P-POSSUM are limited to intraoperative findings of peritoneal contamination as the knowledge about the nature of peritoneal contamination is not available preoperatively. We believe that the Hajibandeh index could potentially improve the preoperative predictive value of the aforementioned tools by making the preoperative estimation of peritoneal contamination more accurate.

The reported outcomes of this study should be viewed and interpreted in the context of inherent limitations. Firstly, we excluded patients with underlying haematological malignancy and trauma patients; therefore, the predictive value of ICI in these cohorts of patients remains unknown. Secondly, the ICI may be associated with false-positive prediction in cases of intestinal ischaemia. Finally, considering that ICI is a novel index, there has not been adequate number of studies in the literature to investigate its predictive value and to assess whether its predictive value could be translated into real practice. Nevertheless, we are confident about the robustness of the results of the current study as indicated by adequate statistical power, systematic and objective methodology, and comparable findings among the primary, retrospective validation, and prospective validation cohorts.

Future directions

Future studies should investigate the effect of ICI use on the accuracy of preoperative prognostic scoring tools in terms of the prediction of postoperative mortality. Moreover, future studies should focus on the effect of ICI use on patient selection for operative versus non-operative management of underlying abdominal pathology such as perforated diverticulitis, perforated peptic ulcers, and anastomotic leaks.

Conclusion

Hajibandeh index predicts the presence of purulent and feculent intraperitoneal contamination in patients with acute abdominal pathology and postoperative mortality in patients undergoing emergency laparotomy. Future studies should investigate the effect of ICI use on the accuracy of preoperative prognostic scoring tools and on patient selection for operative or non-operative management of underlying abdominal pathology.

Author contributions Conception and design: SH

Data collection: SH, JS, SH, SM, MS, SI, AA, RM, NW

Analysis and interpretation: SH, SH, JS

Writing the article: SH, SH, JS

Critical revision of the article: All authors

Final approval of the article: All authors

SH, JS, and SH equally contributed to this paper and joined first authorship is proposed

Compliance with ethical standards

Conflict of interest The authors declare that they have no conflict of interest.

Ethical approval The study was conducted with respect to the institution's policy and internal arrangements approved by the local Clinical Governance Unit.

Informed consent and patient details Considering the design of this study, patient consent was not required.

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Full text 6

Article 6. Hajibandeh Index versus NELA score in predicting mortality following emergency laparotomy: A retrospective Cohort Study

Citation: **Hajibandeh S,** Hajibandeh S, Waterman J, Miller B, Johnson B, Higgi A, Hale J, Pearce D, Evans L, Satyadas T, Mansour M, Havard T, Maw A. Hajibandeh Index versus NELA score in predicting mortality following emergency laparotomy: A retrospective Cohort Study. Int J Surg. 2022 Jun;102:106645. doi: 10.1016/j.ijsu.2022.106645.

Contribution: Conception, design, data collection, data analysis, write up, and critical revision

International Journal of Surgery 102 (2022) 106645

Contents lists available at ScienceDirect

International Journal of Surgery

journal homepage: www.elsevier.com/locate/ijsu

Retrospective Cohort Study

Hajibandeh Index versus NELA score in predicting mortality following emergency laparotomy: A retrospective Cohort Study

Shahab Hajibandeh [a,b,*,1], Shahin Hajibandeh [c,1], Jennifer Waterman [b], Bethany Miller [b], Bethan Johnson [b], Adnan Higgi [b], Jay Hale [b], Dafydd Pearce [b], Louis Evans [b], Thomas Satyadas [d], Moustafa Mansour [e], Tim Havard [b], Andrew Maw [f]

[a] Department of General Surgery, University Hospital of Wales, Cardiff & Vale NHS Trust, Cardiff, United Kingdom
[b] Department of General Surgery, Royal Glamorgan Hospital, Cwm Taf University Health Board, Pontyclun, United Kingdom
[c] Hepatobiliary and Pancreatic Surgery and Liver Transplant Unit, Queen Elizabeth Hospital, Birmingham, United Kingdom
[d] Department of Hepatobiliary and Pancreatic Surgery, Manchester Royal Infirmary Hospital, Manchester, United Kingdom
[e] Department of General Surgery, North Manchester General Hospital, North Manchester Care Organisation, Manchester, United Kingdom
[f] Department of General Surgery, Glan Clwyd Hospital, Betsi Cadwaladr University Health Board, Rhyl, United Kingdom

ARTICLE INFO

Keywords:
Laparotomy
Mortality
Hajibandeh index
NELA

ABSTRACT

Objectives: To compare performance of the Hajibandeh Index (HI) and National Emergency Laparotomy Audit (NELA) score in predicting postoperative mortality in patients undergoing emergency laparotomy.

Methods: In compliance with STROCSS guidelines for observational studies a cohort study was conducted. All patients aged over 18 who underwent emergency laparotomy between January 2014 and January 2021 in our centre were considered eligible for inclusion. The HI and NELA indices in predicting 30-day and 90-day post-operative mortality were compared. The discrimination of each test was evaluated using Receiver Operating Characteristic (ROC) curve analysis, classification using the classification table and calibration using a plotted diagram of the expected versus observed mortality rates.

Results: Analysis of 700 patients showed that the predictive performance of the HI and NELA models were comparable (30-day mortality: AUC: 0.86 vs 0.87, P = 0.557; 90-day mortality: AUC: 0.81 vs 0.84, P = 0.0607). In terms of 30-day mortality, HI was significantly better than the NELA model in predicting postoperative mortality in patients aged over 80 (AUC: 0.85 vs 0.72, P = 0.0174); however, the performances of both tools were comparable in patients with ASA status above 3 (AUC: 0.82 vs 0.82, P = 0.9775), patients with intra-peritoneal contamination (AUC: 0.77 vs 0.85, P = 0.0728) and patients who needed a bowel resection (AUC: 0.85 vs 0.88, P = 0.2749). In terms of 90-day mortality, HI was significantly better than the NELA model in predicting mortality in patients aged over 80 (AUC: 0.82 vs 0.71, P = 0.0214); however, NELA had better predictive value in patients with intraperitoneal contamination (AUC: 0.76 vs 0.85, P = 0.0268); the performances of both tools were comparable in patients with ASA status above 3 (AUC: 0.77 vs 0.80, P = 0.2582), and patients who needed a bowel resection (AUC: 0.81 vs 0.86, P = 0.05). Both tools were comparable in terms of classification and calibration.

Conclusions: Hajibandeh index was better than the NELA score in predicting postoperative 30-day and 90-day mortality in patients aged over 80 undergoing emergency laparotomy. Its performance in predicting 30-day and 90-day mortality was comparable with NELA score in other subgroups except 90-day mortality in patients with intraperitoneal contamination where the performance of NELA was better. We encourage other researchers to validate HI in predicting mortality following emergency laparotomy.

* Corresponding author. Department of General Surgery, University Hospital of Wales, Cardiff & Vale NHS Trust, Cardiff, United Kingdom.
E-mail address: [redacted] (S. Hajibandeh).

[1] Shahab Hajibandeh and Shahin Hajibandeh equally contributed to this paper and joined first authorship is proposed.

https://doi.org/10.1016/j.ijsu.2022.106645
Received 8 February 2022; Received in revised form 30 March 2022; Accepted 8 April 2022
Available online 6 May 2022
1743-9191/

1. Introduction

Emergency laparotomy carries a high risk of morbidity and mortality [1]. Modern predictors of mortality following emergency laparotomy include age over 80, American Society of Anesthesiologists (ASA) status above 3, sarcopenia (age-related loss of skeletal muscle mass), presence of intraperitoneal contamination, and the need for a bowel resection [2–4]. In order to identify patients at high risk of morbidity and mortality following emergency laparotomy, there has been increasing effort to develop and validate accurate risk-prediction models over recent years. An accurate risk-prediction model would facilitate the preoperative risk assessment, the prediction of the need for perioperative support in critical care units, objective discussion between patients and relatives and multidisciplinary decision making when deciding on operative or non-operative treatment high risk patients.

Commonly used risk-prediction models for predicting mortality following emergency laparotomy include the Portsmouth-physiological and operative severity score for the enumeration of mortality and morbidity (P-POSSUM) [5] and the National Emergency Laparotomy Audit (NELA) score [6]. Although P-POSSUM was initially the most commonly used model for predicting mortality following emergency laparotomy [7], it lost its popularity due to concerns about inaccuracy in some subgroups of patients and potential overestimation of mortality [8, 9]. The predictive value of the NELA score and P-POSSUM model have been compared recently and the routine use of NELA model instead of P-POSSUM has been recommended [10,11].

The Hajibandeh Index (HI), which is derived from combined levels of C-reactive protein (CRP), lactate, neutrophils, lymphocytes and albumin, was developed and validated in our previous studies [12,13]. It was shown that HI predicts the presence of intraperitoneal contamination in patients with acute abdominal pathology and postoperative mortality in patients undergoing emergency laparotomy [12]. The HI includes levels of CRP, neutrophils and lactate as nominators considering the fact that their levels increase in presence of abdominal sepsis. It includes levels of albumin and lymphocytes as denominators because their levels decrease in presence of abdominal sepsis [12,13].

In this study we aimed to compare the performance of the HI and NELA model in predicting postoperative mortality in patients undergoing emergency laparotomy.

2. Methods

The Strengthening the Reporting of Cohort Studies in Surgery (STROCSS) guideline for observational studies was followed to protocol, conduct and present this retrospective cohort study [14]. The study was registered in Chinese Clinical Trial Registry (Registration number: ChiCTR2200056183) [15]. The study was compliant with the Helsinki medical research ethical principles and the institutions' policies recommended by local Clinical Governance Unit. Due to retrospective nature of the study, use of non-identifiable hospital data, and indirect involvement of patients in the study, the Research Ethics Committees approval and patient consent were not required.

2.1. Study design and patient selection

A retrospective cohort study was conducted in a General Surgery Department located in the South Wales. The study period was January 2014 to January 2021. All patients aged over 18 who underwent emergency laparotomy in our centre during the aforementioned study period were considered eligible for inclusion. The indications of interest for emergency laparotomy included small bowel obstruction, large bowel obstruction, visceral perforation, intestinal ischaemia, intra-abdominal collection, intraabdominal bleeding, and intraabdominal sepsis of any source (anastomotic leak, colitis, intestinal fistula). The list of procedures of interest during emergency laparotomy was not exhaustive and included colectomies, small bowel resection, repair of perforated viscus, adhesiolysis, creation of defunctioning stoma, achievement of haemostasis, drainage of intraabdominal collection and peritoneal irrigation. The patients who underwent laparotomy secondary to trauma were excluded. Moreover, patients who did not have available preoperative levels of CRP, neutrophils, lactate, lymphocytes or albumin and the patients with underlying haematological malignancy resulting in chronic elevated levels of neutrophils or lymphocytes were excluded.

2.2. The risk-prediction tools

Hajibandeh Index. Hajibandeh Index (HI) includes preoperative levels of CRP, neutrophils and lactate as nominators and preoperative levels of albumin and lymphocytes as denominators [12]. The formula for calculating HI is shown in Appendix I.

NELA risk score. The NELA model includes patient characteristics (age and gender), ASA status, preoperative laboratory tests (haemoglobin, white blood cell count, sodium, potassium, creatinine, and urea), heart rate, systolic blood pressure, the Glasgow coma score, cardiac and respiratory signs, operative severity, peritoneal soiling, intraoperative blood loss, severity of malignancy, and urgency of surgery [16].

2.3. Outcome measures

The primary outcome of this study was 30-day postoperative mortality which was defined as death due to any cause occurring within 30 days following emergency laparotomy. Secondary outcome measure was 90-day postoperative mortality defined as death due to any cause occurring within 90 days after emergency laparotomy.

2.4. Data collection

An electronic proforma was created that collected data on the following parameters: patients' demographic data (age and sex), ASA status, indication for emergency laparotomy, performed procedure, components of the HI, components of the NELA score, presence and nature of intraperitoneal contamination, 30-day mortality and 90-day mortality. All steps of the data collection were performed by two independent authors and an independent third author was consulted in the event of disagreement. The authors who were involved in data collection were not involved in data analyses.

2.5. Data synthesis and statistical analyses

The demographics, clinical characteristics and outcome data were presented using simple descriptive statistics. Data were summarized with mean ± standard deviation (SD) or median and interquartile range (IQR) for continuous variables, and frequencies/percentages for categorical variables. The performance of HI and NELA were compared in terms of discrimination, classification, and calibration. In order to evaluate the discrimination of each risk-prediction tool, Receiver Operating Characteristic (ROC) curve analysis was performed using the method described by DeLong et al. [17]; we determined the standard error of the Area Under the Curve (AUC) and calculated an exact Binomial Confidence Interval for the AUC [16]. Moreover, we calculated associated sensitivity and specificity for all possible threshold values and we determined the optimal criterion value as a cut-off value. In order to evaluate classification of each risk predictive tool, binary logistic regression models were constructed and the classification table was created by cross-classifying the observed values and the predicted values for postoperative mortality. The classification table would help to determine proportion of cases who were correctly classified as dead or alive. In order to evaluate the calibration of each tool, we divided the study cohort into 10 sequential groups of equal size and determined the expected and observed mortality rates for each group. The plotted diagram of the expected and observed mortality rates were created and was visually assessed to determine the calibration. Finally, in order to assess whether the risk-prediction tools overestimate or underestimate the risk of postoperative mortality, the observed deaths to expected deaths ratio (O/E ratio) was calculated. All statistical tests were two-tailed and statistical significance was assumed at $P < 0.05$. Although sample size calculation is not applicable for retrospective studies, the statistical power of study was determined to be 85% based on sample size of 700 patients, accuracy of 86% and 87% for HI and NELA, respectively. The MedCalc 13.0 software was used for statistical analyses.

2.6. Subgroup analyses

We performed subgroup analyses for patients aged over 80, patients with ASA status above 3, patients with intraperitoneal contamination, and patients who needed bowel resection.

3. Results

3.1. Baseline patient characteristics

A total of 700 patients met the eligibility criteria of the study and were included. Fig. 1 demonstrates the study flow chart. The mean age of the included patients was 63 (95% CI 62–65); 261 out of 700 (37%) were male and 439 out of 700 (63%) were female. In terms of ASA status, 35 out of 700 (5%) patients were classified as ASA 1; 245 out of 700 (35%) as ASA 2; 273 out of 700 (39%) as ASA 3; 131 out of 700 (19%) as ASA 4; 16 out of 700 (2%) as ASA 5. The indication for emergency laparotomy was small bowel obstruction in 270 out of 700 (39%) patients, large bowel obstruction in 81 out of 700 (11%), perforated peptic ulcer in 34 out of 700 (5%), small bowel perforation in 43 out of 700 (6%), colonic perforation in 110 out of 700 (16%), intestinal ischaemia in 54 out of 700 (8%), intraabdominal collection in 31 out of 700 (4%), intraabdominal bleeding in 14 out of 700 (2%), colitis in 26 out of 700 (4%), anastomotic leak in 28 out of 700 (4%), and intestinal fistula in 9 out of 700 (1%). Intraperitoneal contamination was present in 222 out of 700 (32%) patients and 120 out of 700 (17%) patients had underlying abdominal malignancy. The median preoperative HI and NELA risk scores were 19.01 (3.89–87.28) and 6.70% (2.1–20.65), respectively. The baseline characteristics of the included population are shown in Table 1.

3.2. Postoperative mortality

One hundred and one out of 700 (14.4%) patients died within 30 days after the operation and 127 out of 700 (18.1%) patients died within 90 days after the operation.

3.3. Hajibandeh Index versus NELA

3.3.1. 30-day mortality

Discrimination. ROC curve analysis showed that the AUC for HI was 0.86 (95% CI 0.83–0.88, $P < 0.0001$) and the AUC for the NELA score was 0.87 (95% CI 0.84–0.89, $P < 0.0001$). The cut of value for HI was calculated as 26 (sensitivity: 94% and specificity: 66%) and for NELA score was calculated as 20 (sensitivity: 72% and specificity: 83%). There was no difference in discrimination between HI and NELA score (P =

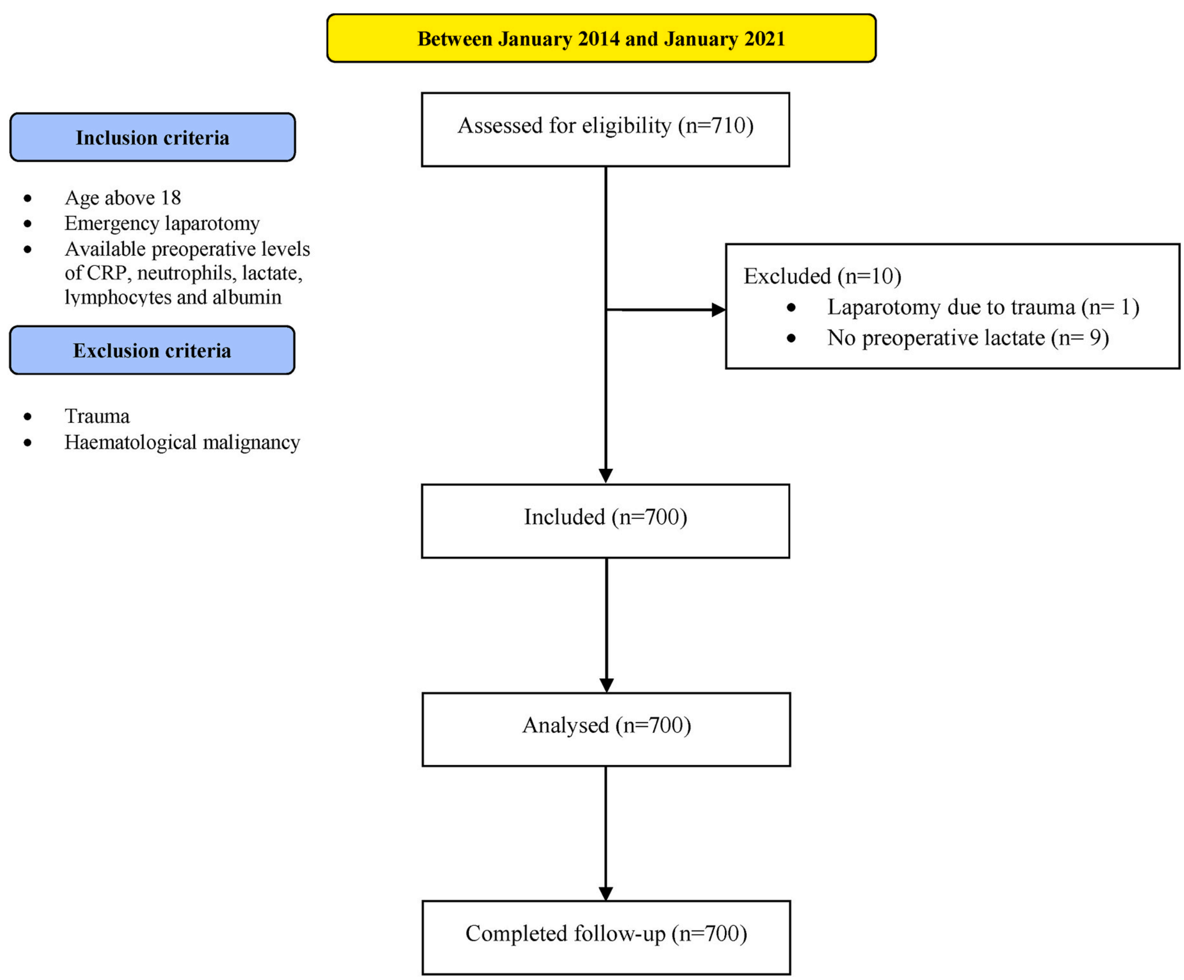

Fig. 1. The study flow diagram.

Table 1
Baseline characteristics of the included population.

Number of patients	700
Age, mean (95% CI)	63 (62–65)
Male, n (%)	261 out of 700 (37%)
Female, n (%)	439 out of 700 (63%)
ASA, n (%)	
1	35 out of 700 (5%)
2	245 out of 700 (35%)
3	273 out of 700 (39%)
4	131 out of 700 (19%)
5	16 out of 700 (2%)
Indication for laparotomy, n (%)	
Small bowel obstruction	270 out of 700 (39%)
Large bowel obstruction	81 out of 700 (11%)
Perforated peptic ulcer	34 out of 700 (5%)
Small bowel perforation	43 out of 700 (6%)
Colonic perforation	110 out of 700 (16%)
Intestinal ischaemia	54 out of 700 (8%)
Intraabdominal collection	31 out of 700 (4%)
Intraabdominal bleeding	14 out of 700 (2%)
Colitis	26 out of 700 (4%)
Anastomotic leak	28 out of 700 (4%)
Intestinal fistula	9 out of 700 (1%)
Procedure performed, n (%)	
Colectomy (right, left, sub-total, total)	278 out of 700 (40%)
Small bowel resection	131 out of 700 (19%)
Adhesiolysis	113 out of 700 (16%)
Defunctioning stoma	41 out of 700 (6%)
Repair of perforated viscus	35 out of 700 (5%)
Wash-out	24 out of 700 (3%)
Intestinal bypass	23 out of 700 (3%)
Enterotomy	14 out of 700 (2%)
Drainage of intraabdominal collection	13 out of 700 (2%)
Other procedures	28 out of 700 (4%)
Intraperitoneal contamination, n (%)	222 out of 700 (32%)
Malignancy, n (%)	120 out of 700 (17%)
Preoperative HI, median (IQR)	19.01 (3.89–87.28)
Preoperative NELA risk, median (IQR)	6.70 (2.1–20.65)
30-day mortality	101 out of 700 (14.4%)
90-day mortality	127 out of 700 (18.1%)

CI: confidence interval; ASA: American Society of Anesthesiologists; HI: Hajibandeh Index; NELA: National Emergency Laparotomy Audit.

0.557) (Fig. 2a).

Classification. Analysis of classification table showed that HI classified 86% of cases correctly and NELA score classified 87% of cases correctly. There was no difference in classification between HI and NELA score (P = 0.836).

Calibration. The statistical analysis of the relationship between the observed and expected mortality rates and visual assessment of the calibration diagram suggested that HI (P = 0.0081) and NELA (P = 0.0012) were well-calibrated (Fig. 3).

O/E ratio. The observed number of deaths were 101 patients and the expected number of deaths based on HI and NELA score were 103 and 111, respectively. The calculated O/E ratio for HI and NELA score were 0.98 and 0.91, respectively.

3.3.2. 90-day mortality

Discrimination. ROC curve analysis showed that the AUC for HI was 0.81 (95% CI 0.77–0.83, P < 0.0001) and the AUC for NELA score was 0.84 (95% CI 0.81–0.87, P < 0.0001). The cut of value for HI was calculated as 18 (sensitivity: 92% and specificity: 58%) and for NELA score was calculated as 11 (sensitivity: 82% and specificity: 71%). There was no difference in discrimination between HI and NELA score (P = 0.0607) (Fig. 4a).

Classification. Analysis of classification table showed that HI classified 83% of cases correctly and NELA score classified 84% of cases correctly. There was no difference in classification between HI and NELA score (P = 0.849).

Calibration. The statistical analysis of the relationship between the observed and expected mortality rates and visual assessment of the calibration diagram suggested that HI (P = 0.0082) and NELA (P = 0.0003) were well-calibrated (Fig. 5).

O/E ratio. The observed number of deaths were 127 patients and the expected number of deaths based on HI and NELA score were 126 and 113, respectively. The calculated O/E ratio for HI and NELA score were 1.01 and 1.12, respectively.

3.4. Subgroup analysis (Table 2)

3.4.1. 30-day mortality

Patients aged over 80. The AUC for HI was 0.85 (95% CI 0.78–0.90, P < 0.0001) and the AUC for NELA score was 0.72 (95% CI 0.64–0.79, P = 0.0003). HI had significantly better discrimination than NELA score (P = 0.0174) (Fig. 2b). There was no difference in classification (81% vs 80%, P = 0.858) and calibration between HI and NELA score.

Patients with ASA status ≥3. The AUC for HI was 0.82 (95% CI 0.78–0.86, P < 0.0001) and the AUC for NELA score was 0.82 (95% CI 0.78–0.86, P < 0.0001). There was no difference in discrimination (P = 0.9775) (Fig. 2c), classification (81% vs 80%, P = 0.858) and calibration between HI and NELA score.

Patients with intraperitoneal contamination. The AUC for HI was 0.77 (95% CI 0.71–0.83, P < 0.0001) and the AUC for NELA score was 0.85 (95% CI 0.79–0.89, P < 0.0001). There was no difference in discrimination (P = 0.0728) (Fig. 2d), classification (80% vs 79%, P = 0.861) and calibration between HI and NELA score.

Patients who needed bowel resection. The AUC for HI was 0.85 (95% CI 0.82–0.89, P < 0.0001) and the AUC for NELA score was 0.88 (95% CI 0.85–0.91, P < 0.0001). There was no difference in discrimination (P = 0.2749) (Fig. 2e), classification (86% vs 87%, P = 0.836) and calibration between HI and NELA score.

3.4.2. 90-day mortality

Patients aged over 80. The AUC for HI was 0.82 (95% CI 0.75–0.88, P < 0.0001) and the AUC for NELA score was 0.71 (95% CI 0.63–0.78, P

Table 2
Performance of Hajibandeh Index versus NELA in predicting mortality following emergency laparotomy.

		30-day Mortality			90-day Mortality		
		HI	NELA	P-value	HI	NELA	P-value
All patients	AUC (95% CI)	0.86 (0.83–0.88)	0.87 (0.84–0.89)	0.557	0.81 (0.77–0.83)	0.84 (0.81–0.87)	0.0607
	Classification	86%	87%	0.836	83%	84%	0.849
Patients aged above 80	AUC (95% CI)	0.85 (0.78–0.90)	0.72 (0.64–0.79)	0.0174	0.82 (0.75–0.88)	0.71 (0.63–0.78)	0.0214
	Classification	81%	80%	0.858	74%	78%	0.508
Patients with ASA status ≥3	AUC (95% CI)	0.82 (0.78–0.86)	0.82 (0.78–0.86)	0.9775	0.77 (0.73–0.81)	0.80 (0.76–0.84)	0.2582
	Classification	81%	80%	0.858	76%	78%	0.737
Patients with intraperitoneal contamination	AUC (95% CI)	0.77 (0.71–0.83)	0.85 (0.79–0.89)	0.0728	0.76 (0.70–0.81)	0.85 (0.79–0.89)	0.0268
	Classification	80%	79%	0.861	78%	79%	0.863
Patients who needed bowel resection	AUC (95% CI)	0.85 (0.82–0.89)	0.88 (0.85–0.91)	0.2749	0.81 (0.76–0.84)	0.86 (0.82–0.89)	0.05
	Classification	86%	87%	0.836	83%	85%	0.699

AUC: Area Under the Curve; CI: confidence interval; ASA: American Society of Anesthesiologists; HI: Hajibandeh Index; NELA: National Emergency Laparotomy Audit.

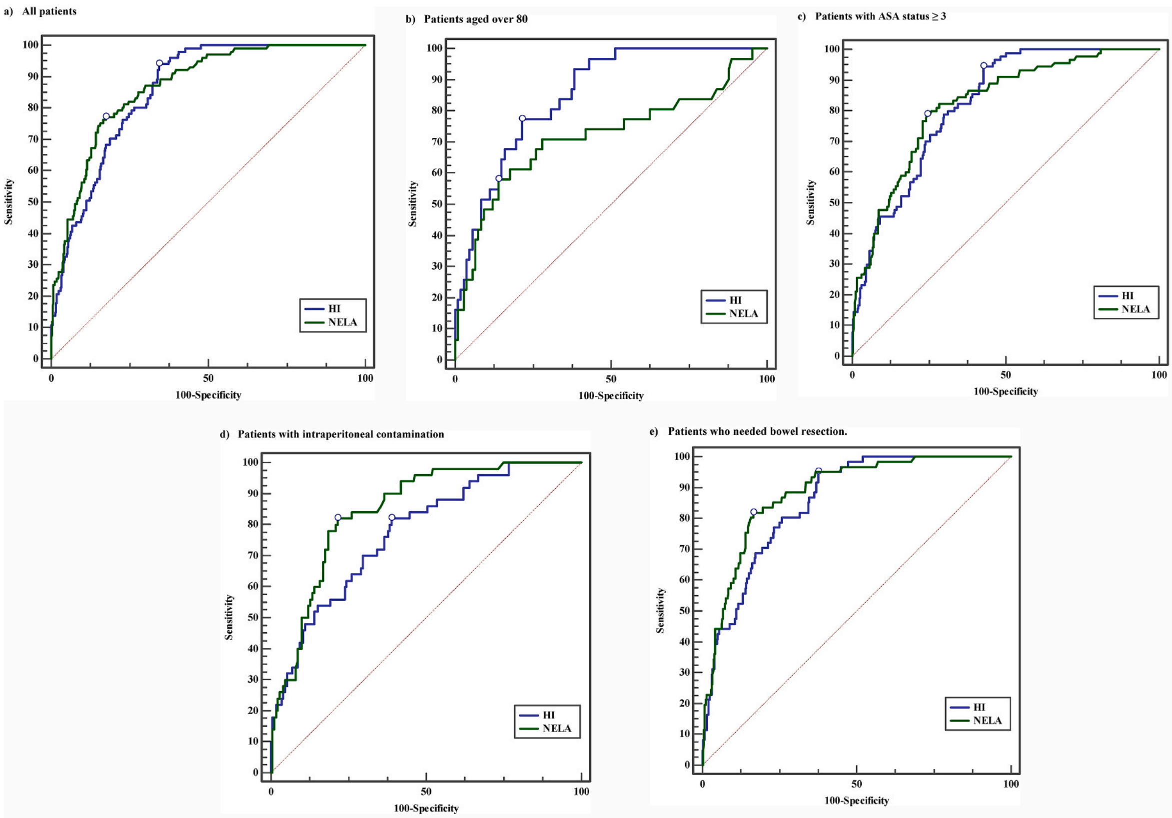

Fig. 2. Comparison of Hajibandeh Index (HI) and NELA score in predicting 30-day postoperative mortality: a) All patients; b) Patients aged over 80; c) Patients with ASA status ≥3; d) Patients with intraperitoneal contamination; e) Patients who needed bowel resection.

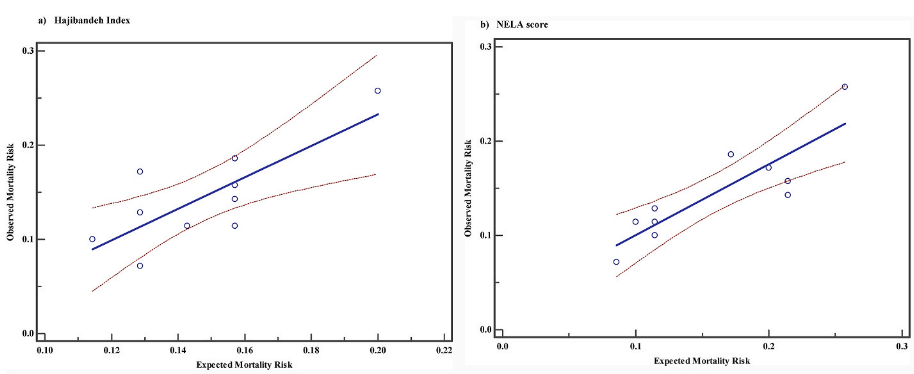

Fig. 3. The calibration diagram based on the relationship between the observed and expected 30-day mortality risks: a) Hajibandeh Index; b) NELA score.

= 0.0001). HI had significantly better discrimination than NELA score (P = 0.0214) (Fig. 4b). There was no difference in classification (74% vs 78%, P = 0.508) and calibration between HI and NELA score.

Patients with ASA status ≥3. The AUC for HI was 0.77 (95% CI 0.73–0.81, P < 0.0001) and the AUC for NELA score was 0.80 (95% CI 0.76–0.84, P < 0.0001). There was no difference in discrimination (P = 0.2582) (Fig. 4c), classification (76% vs 78%, P = 0.737) and calibration between HI and NELA score.

Patients with intraperitoneal contamination. The AUC for HI was 0.76 (95% CI 0.70–0.81, P < 0.0001) and the AUC for NELA score was 0.85 (95% CI 0.79–0.89, P < 0.0001). NELA score had significantly better discrimination than HI (P = 0.0268) (Fig. 4d). There was no difference in classification (78% vs 79%, P = 0.863) and calibration between HI and NELA score.

Patients who needed bowel resection. The AUC for HI was 0.81 (95% CI 0.76–0.84, P < 0.0001) and the AUC for NELA score was 0.86 (95% CI 0.82–0.89, P < 0.0001). There was no difference in discrimination (P = 0.05) (Fig. 4e), classification (83% vs 85%, P = 0.699) and calibration between HI and NELA score.

4. Discussion

In this study we aimed to compare the performance of the HI and NELA models in predicting postoperative mortality in patients undergoing emergency laparotomy. Analysis of 700 patients showed that the predictive performance of HI and NELA model were comparable in terms of discrimination, classification, and calibration; however, the predictive performance of HI was significantly better than the NELA model in patients aged over 80 undergoing emergency laparotomy. The performance of both predictive tools were comparable in patients with ASA status above 3, patients with intraperitoneal contamination and patients who needed a bowel resection.

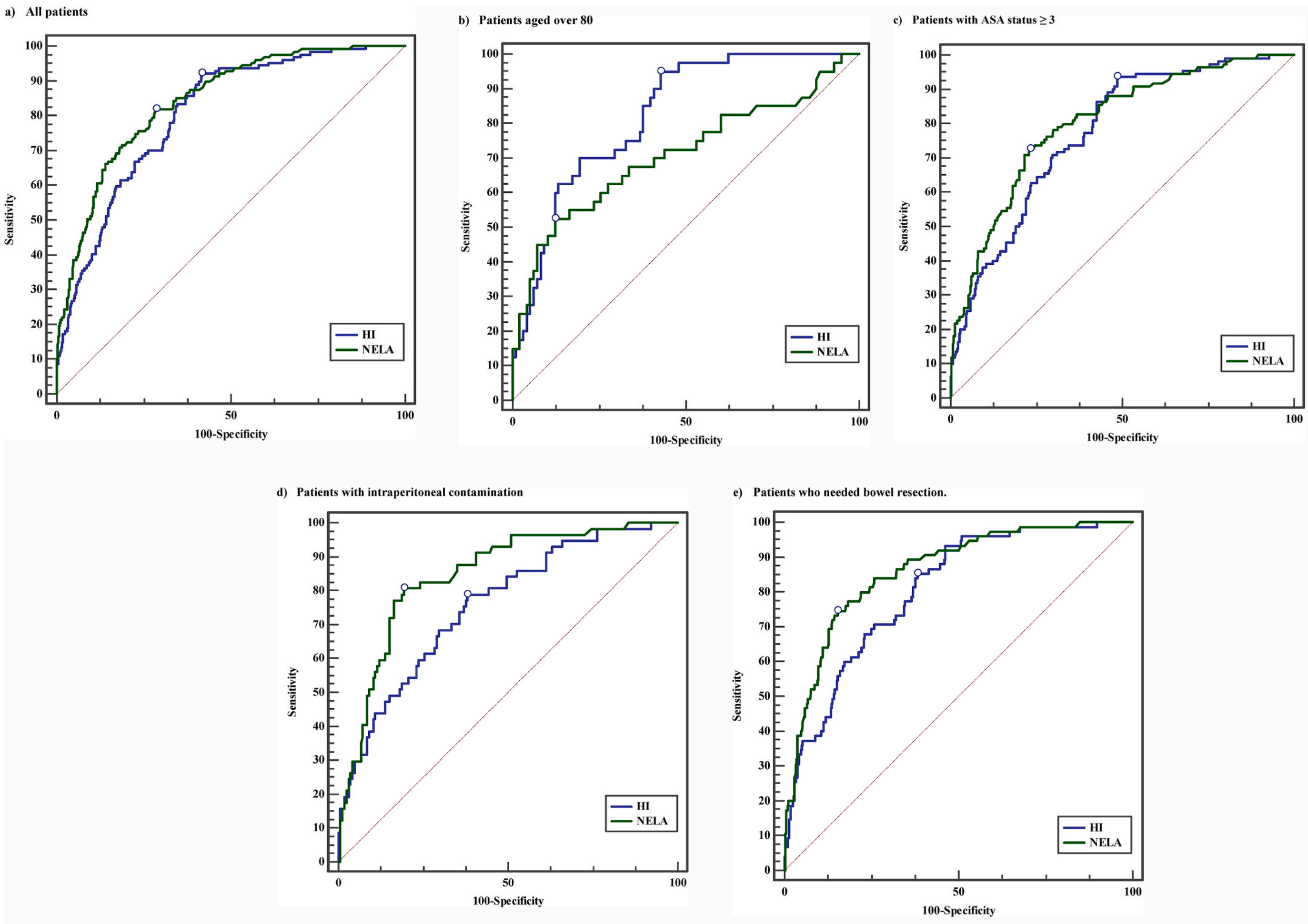

Fig. 4. Comparison of Hajibandeh Index (HI) and NELA score in predicting 90-day postoperative mortality: a) All patients; b) Patients aged over 80; c) Patients with ASA status ≥3; d) Patients with intraperitoneal contamination; e) Patients who needed bowel resection.

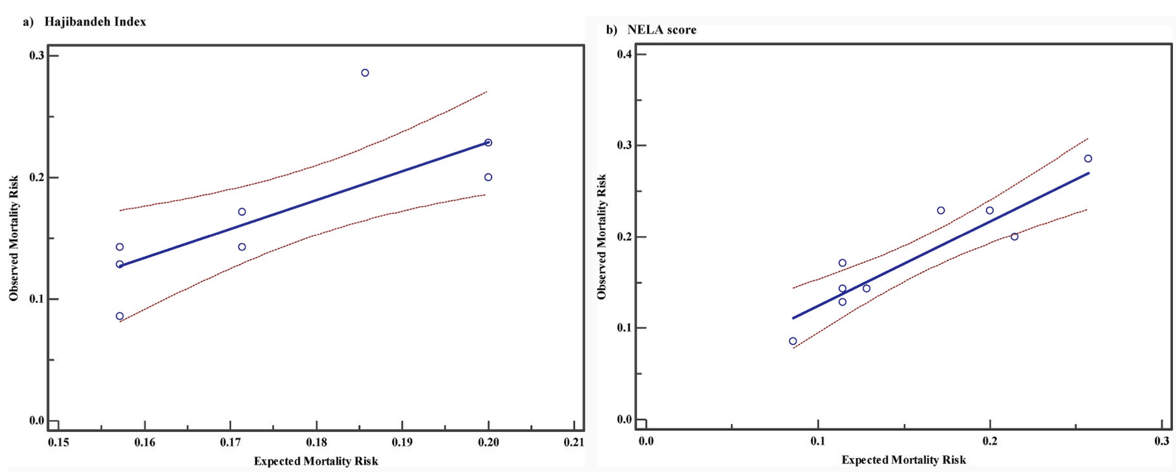

Fig. 5. The calibration diagram based on the relationship between the observed and expected 90-day mortality risks: a) Hajibandeh Index; b) NELA score.

The HI was initially developed to predict the nature of intraperitoneal contamination and it was shown that it can predict the presence of purulent and feculent intraperitoneal contamination in patients with acute abdominal pathology [12,13]. Moreover, it was shown that HI can predict postoperative mortality in patients undergoing emergency laparotomy [12]. Consistent with our previous findings, this study has demonstrated that HI has very good performance in predicting postoperative mortality in patients undergoing emergency laparotomy. The predictive performance of the NELA model found in the current study was consistent with the findings of previous studies [10,11]. The risks of postoperative mortality found in this study are consistent with the risks reported in other studies [18–20]. All of the above support the external validity of the findings of the current study.

Although the components of HI and NELA models are very different, it was interesting to see that HI and NELA have comparable performance in predicting mortality following emergency laparotomy. HI is derived from the most basic but very objectively selected biomarkers while the NELA model includes several variables including patient characteristics (age and gender), the ASA status, preoperative laboratory tests, haemodynamic status, the Glasgow coma score, cardiac and respiratory signs, operative severity, peritoneal soiling, intraoperative blood loss, severity of malignancy and urgency of surgery. While of comparable performance of HI and NELA model is considered promising for HI, it suggests that NELA model may not efficiently take into account the parameters that it asks for.

The most important finding of the current study was that the predictive performance of HI was significantly better than the NELA model in patients aged over 80 undergoing emergency laparotomy. We have previously demonstrated that emergency laparotomy in patients aged over 80 is associated with significantly higher risk of postoperative mortality compared with younger patients [2,3]. Underestimating the risk of postoperative mortality in such patients may result in inaccurate preoperative risk assessment, inaccurate prediction of postoperative needs and failure in identifying the patients who are likely or unlikely to benefit from a high-risk major operation.

The good performance of HI in predicting postoperative mortality can be easily explained. We know from the available evidence that severe sepsis and septic shock are major predictors of mortality [21]. The intraabdominal sepsis due to presence of intestinal ischaemia, tissue necrosis, or peritoneal contamination result in an increase in the levels of CRP, neutrophil, and lactate and result in a decrease in the levels of albumin and lymphocyte [12,13]. Therefore, it is reasonable to assume that the more severe the underlying sepsis due to abdominal pathology, the higher the HI. Considering that severe sepsis can negatively affect haemodynamic status, mental state, and severity of the operation, it can be argued that HI would inevitably take into account the following parameters of the NELA model: preoperative laboratory tests, haemodynamic status, the Glasgow coma score, cardiac and respiratory signs, operative severity, and peritoneal soiling.

The systematic and objective methodology and adequate statistical power of the current study highlights the robustness of the results. However, the reported outcomes of this study should be viewed and interpreted in the context of inherent limitations. The retrospective nature of current study would subject our results to inevitable selection bias. We tried to minimise such effects by recruiting two independent authors for data collection, separating the authors who are involved in data collection and data analyses and performing appropriate subgroup analyses. Moreover, the study was performed in a single centre; this may affect the generalisability of the findings. HI is a novel predictive tool which has been evaluated only in few studies; more studies are required to confirm its predictive values.

5. Conclusion

Hajibandeh index was better than the NELA score in predicting postoperative 30-day and 90-day mortality in patients aged over 80 undergoing emergency laparotomy. Its performance in predicting 30-day and 90-day mortality was comparable with NELA score in other subgroups except 90-day mortality in patients with intraperitoneal contamination where the performance of NELA was better. We encourage other researchers to validate HI in predicting mortality following emergency laparotomy.

Sources of funding

None.

Ethical approval

The study was compliant with the Helsinki medical research ethical principles and the institutions' policies recommended by local Clinical Governance Unit. Due to retrospective nature of the study, use of non-identifiable hospital data, and indirect involvement of patients in the study, the Research Ethics Committees approval and patient consent were not required.

Research registration unique identifying number (UIN)

Registry: Chinese Clinical Trial Registry.
Registration number: ChiCTR2200056183.
Link: Chinese Clinical Trial Register (ChiCTR) - The world health organization international clinical trials registered organization registered platform.

Guarantor

Shahab Hajibandeh.

Data statement

The information about the data presented in this article will be accessible on request.

Provenance and peer review

Not commissioned, externally peer-reviewed.

CRediT authorship contribution statement

Shahab Hajibandeh: Conceptualization, Methodology, Formal analysis, Investigation, Data curation, Writing – original draft, Writing – review & editing, Supervision. **Shahin Hajibandeh:** Conceptualization, Methodology, Formal analysis, Investigation, Data curation, Writing – original draft, Writing – review & editing. **Jennifer Waterman:** Data curation, Validation, Writing – review & editing. **Bethany Miller:** Data curation, Validation, Writing – review & editing. **Bethan Johnson:** Data curation, Validation, Writing – review & editing. **Adnan Higgi:** Data curation, Validation, Writing – review & editing. **Jay Hale:** Data curation, Validation, Writing – review & editing. **Dafydd Pearce:** Data curation, Validation, Writing – review & editing. **Louis Evans:** Data curation, Validation, Writing – review & editing. **Thomas Satyadas:** Data curation, Validation, Writing – review & editing, Supervision. **Moustafa Mansour:** Data curation, Validation, Writing – review & editing, Supervision. **Tim Havard:** Data curation, Validation, Writing – review & editing, Supervision. **Andrew Maw:** Data curation, Validation, Writing – review & editing, Supervision.

Declaration of competing interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.ijsu.2022.106645.

Appendix I

$$\text{Hajibandeh Index} = \frac{\text{CRP (mg/L)} \times \text{Lactate (mmol/L)} \times \text{Neutrophils } (\times 10^9/\text{L})}{\text{Albumin (g/L)} \times \text{Lymphocytes } (\times 10^9/\text{L})}$$

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Full text 7

Article 7. Prognostic significance of socioeconomic deprivation in patients undergoing emergency laparotomy: A retrospective cohort study

Citation: Hajibandeh S, Efstathiou A, Hajibandeh S, Al-Sarireh A, Al-Sarireh H, Duffaydar H, Stechman M, Egan RJ, Lewis WG. Prognostic significance of socioeconomic deprivation in patients undergoing emergency laparotomy: A retrospective cohort study. World J Surg. 2024 Oct;48(10):2433-2442. doi: 10.1002/wjs.12332.

Contribution: Conception, design, data collection, data analysis, write up, and critical revision

Received: 26 June 2024 | Accepted: 21 August 2024

DOI: 10.1002/wjs.12332

ORIGINAL SCIENTIFIC REPORT

World Journal of Surgery

Prognostic significance of socioeconomic deprivation in patients undergoing emergency laparotomy: A retrospective cohort study

Shahab Hajibandeh[1,2] | **Anastasia Efstathiou**[2] | **Shahin Hajibandeh**[3] | **Ahmad Al-Sarireh**[4] | **Hashim Al-Sarireh**[5] | **Hamza Duffaydar**[1] | **Michael Stechman**[2] | **Richard John Egan**[1,6] | **Wyn G. Lewis**[1,2]

[1]Department of General Surgery, Morriston Hospital, Swansea, UK

[2]Department of General Surgery, University Hospital of Wales, Cardiff, UK

[3]Department of General Surgery, Royal Stoke University Hospital, Stoke-on-Trent, UK

[4]University of Cambridge, Cambridge, UK

[5]University of Leeds, Leeds, UK

[6]School of Medicine, Swansea University, Swansea, UK

Correspondence

Shahab Hajibandeh, Department of Hepatobiliary and Pancreatic Surgery, Morriston Hospital, Swansea, UK.

Email: [redacted]

Abstract

Objectives: Deprivation is a complex, multifaceted concept and not synonymous with poverty. The aim of this study was to assess the prognostic influence of the multiple deprivation index on emergency laparotomy (EL) outcome.

Methods: STROCSS statement standards were followed to conduct a retrospective cohort study. Consecutive 1723 adult patients [median age (range): 66 (18–98), 762 M, and 961 F] undergoing EL over eight years (2014–22) at two hospitals [a tertiary teaching center and district general hospital (DGH)] were studied. Deprivation scores and ranks were derived from patients' postcodes using the Welsh Index of Multiple Deprivation and ranks categorized into quartiles. Primary outcome measure was a 30-day operative mortality (OM).

Results: OM risk was higher in the most deprived quartile (Q1) compared with the least deprived quartile (Q4) (13.2% vs. 7.9% and $p = 0.008$). Deprivation was an independent predictor of OM on both univariate (unadjusted OR: 1.75, 95% CI 1.17–2.61, and $p = 0.006$) and multivariable logistic regression analyses (OR: 1.03, 95% CI 1.01–1.06, and $p = 0.023$; adjusted for age ≥80 years, American Society of Anesthesiologists grade, need for bowel resection, and peritoneal contamination). Deprivation had poor discriminatory value in predicting OM (AUC: 0.56 and 95% CI 0.54–0.59). Subgroup analysis showed that although the risk of OM was lower in the tertiary center compared with the DGH (7.9% vs. 14.5% and $p < 0.001$), the predictive significance of deprivation was similar in both hospitals (AUC: 0.54 vs. 0.56 and $p = 0.674$).

Conclusion: Deprivation is an independent but modest predictor of OM after EL. The potential prognostic value of incorporating deprivation into preoperative risk assessment algorithms deserves further evaluation.

Shahab Hajibandeh, Anastasia Efstathiou and Shahin Hajibandeh are joint first authors.

Richard John Egan and Wyn G. Lewis are joint senior authors.

KEYWORDS
laparotomy, mortality, socioeconomic deprivation

1 | INTRODUCTION

Emergency laparotomy (EL) is a high stakes critical procedure, performed on some of the sickest patients treated by the National Health Service. It requires swift decision-making, a high degree of technical skill, and comprehensive strategic and multidisciplinary perioperative management. EL accounts for over 30,000 operations annually in the United Kingdom, half of the general surgery workload, and up to 90% of all surgical deaths. For over a decade now, the National Emergency Laparotomy Audit (NELA) has focused on the need to address these poor outcomes and reconfigure services to improve access to specialist emergency surgical services, which resulted in improvement in operative mortality (OM) from 12.7% to 9.2%.[1]

The main predictors of 30-day OM after EL include American Society of Anesthesiologists (ASA) status,[2] sarcopenia,[3,4] clinical frailty,[4] age over 80 years,[5] peritoneal contamination,[6] and the need for bowel resection.[6] The main focus of the existing relevant literature relates to the prognostic value of first, the patient's underlying abdominal pathology and second, the patient's physiological physical fitness. The prognostic significance of patients' socioeconomic status and deprivation related to their geographical area of residence has not been characterized. Deprivation is multidimensional and determined based on various domains including income, employment, health, education, access to services, housing, community safety, and physical environment.[7] Socioeconomic deprivation refers to unmet needs caused by lack of financial and nonfinancial resources[6] and may affect individuals' health-seeking behavior, exposure to lifestyle-related risk factors,[8,9] prevalence and severity of comorbidities,[10–12] and access to healthcare.[13] The negative impact of deprivation on postoperative outcomes has been reported and related to several surgical pathologies,[13–18] but whether or not deprivation affects OM in patients undergoing EL is poorly understood. This cohort study aimed to evaluate the effect of deprivation on OM after EL. The primary hypothesis was that patients living in more deprived geographical areas would experience significantly poorer OM than patients living in less deprived areas. The setting was two hospital sites in Wales—a tertiary center and a district general hospital (DGH).

2 | METHODS

2.1 | Study design, reporting standards, and ethical compliance

The study design was a retrospective cohort study with prospective data collection approach. The design, protocol, and conduct of the study were compliant with the standards recommended by the Strengthening the Reporting of Cohort Studies in Surgery (STROCSS) guideline for observational studies.[19] Due to the retrospective nature of the study, use of non-identifiable hospital data and indirect patient involvement, ethical approval, and patient consent were not required. However, the study was compliant with the Helsinki medical research ethical principles and the policies recommended by local Clinical Governance Units.

2.2 | Setting and period

The study was conducted in two centers found in South Wales; a tertiary general surgery center and a DGH providing emergency and elective services to a population of approximately 472,400 and 450,000 people, respectively. The study period was January 1, 2014, to January 1, 2022.

2.3 | Participant selection

The prospectively kept hospital electronic medical record systems were used to find eligible patients. All adult patients (age ≥18 years) undergoing EL due to non-traumatic acute abdominal pathologies, including small bowel obstruction, large bowel obstruction, visceral perforation, intestinal ischemia, intra-abdominal collection, intra-abdominal bleeding, and intra-abdominal sepsis of any source (anastomotic leak, colitis, and intestinal fistula) in the hospitals, were considered eligible for inclusion. Patients in whom deprivation status could not be assessed and those who undergoing EL for abdominal trauma were excluded.

2.4 | Socioeconomic deprivation

The socioeconomic status of each patient was determined using the Welsh Index of Multiple

Deprivation (WIMD), which is the Welsh Government's official measure of multiple deprivation that is both an area-based measure and a measure of relative deprivation.[7] The WIMD is derived from a weighted sum of the deprivation score for eight different domains including income, employment, health, education, access to services, housing, community safety, and physical environment. WIMD ranks all small areas in Wales from 1 (most deprived) to 1909 (least deprived).[7] The WIMD rank for each patient was found based on their home address. Subsequently, each patient was distributed to a quartile based on the WIMD rank: quartile 1 (Q1) if WIMD rank was between 1 and 478; quartile 2 (Q2) if WIMD rank was between 479 and 955; quartile 3 (Q3) if WIMD rank was between 956 and 1432; and quartile 4 (Q4) if WIMD rank was between 1433 and 1909. Q1 was defined as the most deprived quartile and Q4 the least deprived quartile.

2.5 | Primary outcome

The primary outcome measure was OM, defined as death due to any cause occurring within 30 days of EL.

2.6 | Data collection

The following data items for each patient were collected: age, sex, ASA status, clinical frailty score, indication for EL, the procedure performed, peritoneal contamination, need for bowel resection, WIMD rank, rank for each domain of deprivation, and mortality outcomes. Data collection steps were performed by two independent authors, and an independent third author was consulted in case of disagreement. Hospital medical records were used as sources for data collection. Follow-up data were collected using the Welsh Clinical portal, a national electronic database combining clinical data from all health boards which links with the national death registry, and data obtained from general practice.

2.7 | Data synthesis and statistical analyses

Simple descriptive statistics, including median and interquartile range for continuous variables and frequencies/percentages for dichotomous variables, were used to summarize data. The Mann–Whitney test and the chi-squared test was used to compare continuous and dichotomous variables, respectively. Receiver operating characteristic (ROC) curve analysis was performed to determine discriminative performance of the multiple deprivation index and other domains of deprivation in predicating a 30-day OM by calculating the area under the curve using the method described by DeLong et al.[20] Binary logistic regression model was constructed to calculate odds ratio (OR) of OM for each deprivation quartile using the most deprived quartile as the reference. A stepwise multivariable binary logistic regression model was constructed in which OM was defined as the dependent variable and the following variables were defined as independent variables: multiple deprivation index, age ≥80 years, ASA status, need for bowel resection, and presence of peritoneal contamination. All statistical tests were two-tailed, and statistical significance was set at $p < 0.05$. MedCalc® Statistical Software version 22.002 (MedCalc Software Ltd, Ostend, Belgium) was used for statistical analyses.

2.8 | Subgroup analysis

Subgroup analysis was performed for patients who underwent EL in each hospital.

3 | RESULTS

A total of 1769 patients who underwent EL in the relevant time period were included; 46 patients were excluded because their deprivation status could not be determined. Consequently, 1723 patients were eligible for inclusion. In terms of deprivation quartile, 576 patients were distributed to Q1 (the most deprived quartile), 424 patients to Q2, 210 patients to Q3, and 513 patients to Q4 (the least deprived Quartile). Follow-up data were available for all patients. Figure 1 shows the study flow diagram.

3.1 | Baseline characteristics of the included population

Baseline characteristics of the included population for each socioeconomic deprivation quartile can be found in Table 1. Comparison of the most deprived and the least deprived quartiles showed that the most deprived cohort was younger (median age: 63 vs. 70 years, $p < 0.001$) but there was no difference between the two quartiles in terms of sex (male: 45.8% vs. 44.7% and $p = 0.991$), ASA grade (ASA 1: 7.1% vs. 6.9% and $p = 0.957$; ASA 2: 33.9% vs. 37.9% and $p = 0.118$; ASA 3: 41.7% vs. 40.9% and $p = 0.964$; ASA 4: 16.5% vs. 12.0% and $p = 0.060$; and ASA 5: 0.9% vs. 0.4% and $p = 0.545$), clinical frailty score (median: 2 vs. 2, $p = 0.521$), indication for laparotomy (small bowel obstruction: 37.3% vs. 41.5% and $p = 0.134$; large bowel obstruction: 11.3%

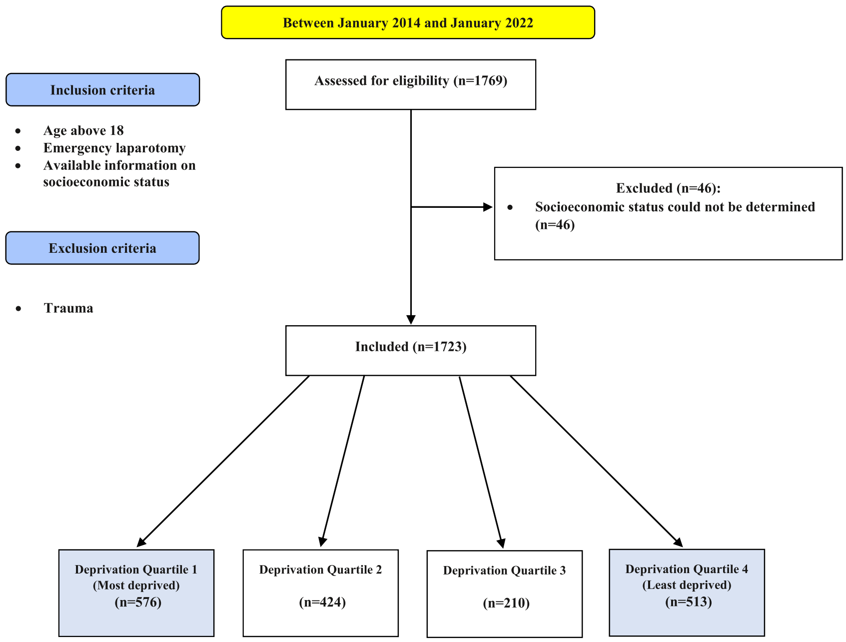

FIGURE 1 The study flow diagram. [Colour figure can be viewed at wileyonlinelibrary.com]

vs. 14.7% and p = 0.083; perforated peptic ulcer: 6.8% vs. 5.7% and p = 0.617; small bowel perforation: 5.6% vs. 3.6% and p = 0.194; colonic perforation: 17.9% vs. 15.3% and p = 0.354; intestinal ischemia: 6.6% vs. 4.2% and p = 0.125; and other indications: 14.6% vs. 13.0% and p = 0.587), need for bowel resection (55.7% vs. 56.2% and p = 0.643), and peritoneal contamination (31.1% vs. 25.6% and p = 0.082).

3.2 | Thirty-day operative mortality

The risk of OM was 10.6% (182 out of 1723) in the entire cohort, 13.2% (76 out of 576) in Q1, 10.1% (43 out of 424) in Q2, 10.5% (22 out of 210) in Q3, and 7.9% (41 out of 513) in Q4. The risk was higher in the most deprived quartile compared with the least deprived quartile (p = 0.0076) (Table 2).

3.3 | Binary logistic regression analysis

Univariate logistic regression analysis showed that the risk of OM was higher in the most of deprived quartile compared with the least deprived quartile (unadjusted OR: 1.75, 95% CI 1.17–2.61, and p = 0.006). The risk was comparable between Q2 and Q4 (unadjusted OR: 1.30, 95% CI 0.83–2.03, and p = 0.253) and between Q3 and Q4 (unadjusted OR: 1.35, 95% CI 0.78–2.32, and p = 0.284) (Table 3). Stepwise multivariate logistic regression analysis showed multiple deprivation to be an independent predictor of OM (adjusted OR: 1.03, 95% CI 1.01–1.06, and p = 0.023) (Table 4).

3.4 | ROC curve analysis

ROC curve analysis suggested that multiple socioeconomic deprivation had poor discrimination in predicting the risk of OM (AUC: 0.56, 95% CI 0.54–0.590, and Figure 2).

3.5 | Domains of deprivation

Among the domains of deprivation, income (OR: 1.0017, 95% CI 1.0004–1.0030, and p = 0.012) and employment (OR: 0.9986, 95% CI 0.9975–0.9998, and p = 0.021) were predictors of OM; however, health (OR: 0.9993, 95% CI 0.9983–1.0003, and p = 0.199), education (OR: 0.9998, 95% CI 0.9991–1.0005, and p = 0.542), access to services (OR: 0.9998, 95% CI 0.9994–1.0003, and p = 0.418), housing (OR: 0.9999, 95% CI 0.9995–1.0002, and p = 0.472), community safety (OR: 1.0004, 95% CI 1.0000–1.0009, and p = 0.078), and physical environment (OR: 1.0004, 95% CI 1.0000–1.0009, and p = 0.714) did not predict OM (Table 5). All domains had poor discrimination in predicting OM (Figure 3 and Table 5): income (AUC: 0.56 and 95% CI 0.54–0.58); employment (AUC: 0.57 and 95% CI 0.55–0.59), health (AUC: 0.57 and 95% CI 0.55–0.59), education (AUC: 0.56 and 95% CI 0.54–0.59), access to services (AUC: 0.55 and 95% CI 0.53–

TABLE 1 Baseline characteristics of the included population for each socioeconomic deprivation quartile.

		Socioeconomic deprivation quartile				
	All patients	1 (most deprived)	2	3	4 (least deprived)	*p*-value[a,b]
No of patients	1723	576	424	210	513	
Age, median (IQR)	66 (51–77)	63 (49–74)	64 (50–76)	69 (54–77)	70 (54–80)	<0.0001
Age ≥80	338 (19.6%)	93 (16.1%)	73 (17.2%)	41 (19.5%)	131 (25.0%)	0.0002
Male, *n* (%)	762 (44.2%)	264 (45.8%)	181 (42.7%)	83 (39.5%)	234 (44.7%)	0.9907
Female, *n* (%)	961 (55.8%)	312 (54.2%)	243 (57.3%)	127 (60.5%)	279 (53.3%)	0.9907
ASA, *n* (%)						
1	112 (6.5%)	41 (7.1%)	24 (5.7%)	11 (5.2%)	36 (6.9%)	0.9571
2	635 (36.9%)	195 (33.9%)	162 (38.2%)	80 (38.1%)	198 (37.9%)	0.1179
3	699 (40.6%)	240 (41.7%)	166 (39.2%)	79 (37.6%)	214 (40.9%)	0.9638
4	260 (15.1%)	95 (16.5%)	64 (15.1%)	38 (18.1%)	63 (12.0%)	0.0595
5	17 (1.0%)	5 (0.9%)	8 (1.9%)	2 (1.0%)	2 (0.4%)	0.5446
Clinical frailty scale, median (IQR)	2 (1–4)	2 (1–4)	2 (1–3)	2 (1–3)	2 (1–3)	0.5208
Indication for laparotomy, *n* (%)						
Small bowel obstruction	676 (39.2%)	215 (37.3%)	164 (38.7%)	80 (38.1%)	217 (41.5%)	0.1344
Large bowel obstruction	218 (12.7%)	65 (11.3%)	46 (10.8%)	30 (14.3%)	77 (14.7%)	0.0832
Perforated peptic ulcer	99 (5.7%)	39 (6.8%)	20 (4.7%)	10 (4.8%)	30 (5.7%)	0.6175
Small bowel perforation	85 (4.9%)	32 (5.6%)	24 (5.7%)	10 (4.8%)	19 (3.6%)	0.1935
Colonic perforation	290 (16.8%)	103 (17.9%)	71 (16.7%)	36 (17.1%)	80 (15.3%)	0.3541
Intestinal ischemia	105 (6.1%)	38 (6.6%)	31 (7.3%)	14 (6.7%)	22 (4.2%)	0.1251
Other	250 (14.5%)	84 (14.6%)	68 (16.0%)	30 (14.3%)	68 (13.0%)	0.5866
Need for bowel resection, *n* (%)	985 (57.2%)	321 (55.7%)	255 (60.1%)	115 (54.8%)	294 (56.2%)	0.6426
Peritoneal contamination, *n* (%)	504 (29.3%)	179 (31.1%)	130 (30.7%)	61 (29.0%)	134 (25.6%)	0.0824
Multiple deprivation index, median score (IQR)	785 (304–1531)	180 (93–306)	675 (579–813)	1193 (1129–1308)	1717 (1609–1815)	<0.0001
Domains of deprivation, median score (IQR)						
Income	765 (315–1452)	169 (97–315)	699 (580–811)	1127 (1030–1284)	1689 (1490–1823)	<0.0001
Employment	765 (340–1463)	183 (82–340)	672 (538–823)	1159 (974–1327)	1677 (1464–1798)	<0.0001
Health	741 (306–1406)	161 (84–309)	638 (536–815)	1058 (879–1238)	1663 (1407–1816)	<0.0001
Education	870 (380–1515)	223 (118–437)	694 (547–916)	1205 (1052–1520)	1713 (1511–1835)	<0.0001
Access to services	1210 (712–1571)	658 (519–898)	1221 (844–1517)	1351 (911–1515)	1653 (1449–1841)	<0.0001
Housing	923 (461–1445)	604 (250–1014)	567 (255–877)	947 (391–1257)	1639 (1383–1821)	<0.0001
Community safety	870 (509–1338)	482 (293–750)	754 (524–1092)	1020 (719–1301)	1502 (1145–1698)	<0.0001
Physical environment	511 (257–925)	526 (288–950)	459 (173–904)	464 (168–1007)	553 (313–914)	0.1214

Abbreviations: ASA, American Society of Anesthesiologists; IQR, interquartile range.

[a]The most deprived and least deprived groups were compared.

[b]Continuous variables were compared using Mann–Whitney test and dichotomous variables were compared using the chi-squared test.

TABLE 2 Risk of operative mortality for each socioeconomic deprivation quartile.

		Socioeconomic deprivation quartile				
	All patients	1 (most deprived)	2	3	4 (least deprived)	*p*-value[a,b]
30-day operative mortality, *n* (%)	182/1723 (10.6%)	76/576 (13.2%)	43/424 (10.1%)	22/210 (10.5%)	41/513 (7.9%)	0.0076

[a]The most deprived and least deprived groups were compared.

[b]Variables were compared using the chi-squared test.

TABLE 3 Comparison of operative mortality between socioeconomic deprivation quartiles.

	OR (95% CI)[a]	*p*-value[a]
Quartile 1 (most deprived) versus quartile 4 (least deprived)	1.75 (1.17–2.61)	0.006
Quartile 2 versus quartile 4 (least deprived)	1.30 (0.83–2.03)	0.253
Quartile 3 versus quartile 4 (least deprived)	1.35 (0.78–2.32)	0.284

Abbreviations: CI, confidence interval; OR, odds ratio.

[a]Binary logistic regression analysis using the least deprived quartile as reference.

TABLE 4 Results of stepwise multivariable binary logistic regression analysis for operative mortality.

	Thirty-day operative mortality		
Independent variables	Coefficient	Odds ratio (95% CI)	*p*-value
Age ≥80	0.42261	1.53 (1.05–2.22)	0.027
ASA status	1.27083	3.28 (2.60–4.13)	<0.001
Bowel resection	0.41887	1.54 (1.09–2.19)	0.018
Peritoneal contamination	0.68645	2.12 (1.50–3.00)	<0.001
Multiple socioeconomic deprivation	0.00032	1.03 (1.01–1.06)	0.023

Abbreviations: ASA, American Society of Anesthesiologists; CI, confidence interval.

0.58), housing (AUC: 0.54 and 95% CI 0.51–0.56), community safety (AUC: 0.52 and 95% CI 0.49–0.54), and physical environment (AUC: 0.53 and 95% CI 0.50–0.55).

3.5.1 | Tertiary center versus district general hospital

Risk of OM was lower in the tertiary center hospital compared with the DGH (7.9% vs. 14.5% and $p < 0.001$). The discriminatory value of deprivation in predicting OM was similar in both centers (AUC: 0.54 vs. 0.56 and $p = 0.674$).

4 | DISCUSSION

This is the first study to examine the relationship between deprivation and EL outcome in Wales, and the principal findings were that overall OM was relatively high, ranging from 7.9% to 14.5%. OM was related to deprivation, advanced age, ASA status, intestinal resection, and peritoneal contamination, in keeping with the primary hypothesis. Deprivation alone emerged as associated with a 1.75-fold greater risk of OM after EL. Among the domains of deprivation, income (OR 1.0017 and $p = 0.012$) and employment (OR 0.9986 and $p = 0.021$) were also predictors of OM, yet surprisingly, health, education, access to services, housing, community safety, and physical environment were not. OM was almost two-fold greater in a DGH setting when compared with a tertiary hospital setting, despite equivalent deprivation distributions in the populations served. This finding is again in keeping with Hart's inverse care law, which says that: "the availability of good medical care tends to vary inversely with the need for it in the population served. This inverse care law works more completely where medical care is most exposed to market forces and less so where exposure is reduced."[21]

Poulton et al.[22] has previously reported a retrospective cohort study of 58,790 patients undergoing EL in England and concluded that deprived patients have higher crude (11.2% vs. 9.8%) and risk-adjusted OM (OR 1.29 and 95% CI 1.16–1.44) after EL. This study represented an important contribution to the literature, not least because of its large sample size, and the results are in keeping with the findings of the present study, although close scrutiny reveals important differences. Specifically, granted that the most deprived quartile and least deprived quartile had similar baseline characteristics in the present study, Poulton's quartiles differed significantly related to ASA status, indications for laparotomy, and peritoneal contamination, raising the possibility of confounding bias. Hospital level data were examined in the present study, ensuring accurate data collection and processing, whereas Poulton used large administrative databases, including NELA and Hospital Episode Statistics, from 178 English hospitals, which are well recognized to carry limitations related to validity and accuracy of data collection, handling, and coding.[23–25] Cain et al.[26] analyzed 103,749 patients who underwent a wide range of emergency general surgery operations and concluded that deprivation was associated with increased OM (OR 1.30 and 95% CI 1.01–1.66) after high-risk emergency general surgery.[26] Similarly, Wohlgemut et al.[27] analyzed 1,477,810 emergency general surgery admissions and again concluded that deprivation was associated with increased risk of mortality (OR 1.36 and 95% CI 1.8–1.46) following hospital admission irrespective of whether the patients underwent emergency surgery.[27] However, neither study provided stratified data related to patients undergoing EL, and both populations were derived from large databases with the aforementioned associated limitations.

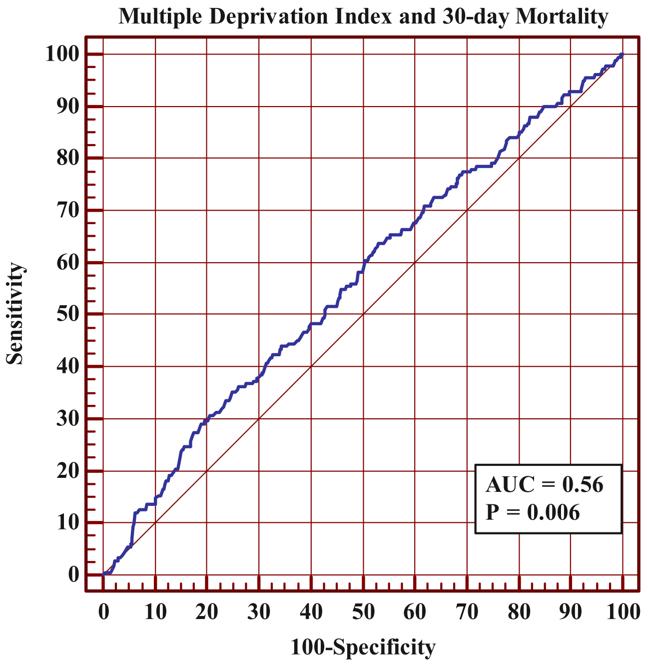

FIGURE 2 Receiver operating characteristic curves for performance of the multiple deprivation index in predicting 30-day operative mortality (AUC: 0.56 and 95% CI 0.54–0.59). [Colour figure can be viewed at wileyonlinelibrary.com]

The higher risk of postoperative mortality in the most deprived patients may be justified by findings of earlier studies. Krajewski et al.[13] reported that access to emergency operative care was affected by socioeconomic status; the results of the present study are in keeping with these findings as the most deprived patient cohort had significantly lower rank in terms of access to services in comparison with the least deprived patient cohort. On the other hand, McNeill et al.[8] and Hiscock et al.[9] reported that deprived patients were more likely to have high-risk lifestyle and noncompliant health-seeking behavior. Moreover, O'Kane et al.[10] reported that severe comorbidities with adverse prognostic significance were commoner in deprived patients.

While overall deprivation was an independent predictor of OM in patients undergoing EL, the individual domains of deprivation, expected income, and employment did not predict OM. Interestingly, regression analysis showed that all domains were correlated

TABLE 5 The performance of different domains of deprivation in predicting operative mortality.

Domains of deprivation	Coefficient	OR (95% CI)	*p*-value[a]	AUC (95% CI)[b]
Income	0.001697	1.0017 (1.0004, 1.0030)	0.012	0.56 (0.54–0.58)
Employment	−0.00136	0.9986 (0.9975, 0.9998)	0.021	0.57 (0.55–0.59)
Health	−0.000659	0.9993 (0.9983, 1.0003)	0.199	0.57 (0.55–0.59)
Education	−0.000211	0.9998 (0.9991, 1.0005)	0.542	0.56 (0.54–0.59)
Access to services	−0.000176	0.9998 (0.9994, 1.0003)	0.418	0.55 (0.53–0.58)
Housing	−0.00013	0.9999 (0.9995, 1.0002)	0.472	0.54 (0.51–0.56)
Community safety	0.000419	1.0004 (1.0000, 1.0009)	0.078	0.52 (0.49–0.54)
Physical environment	−0.000075	0.9999 (0.9995, 1.0003)	0.714	0.53 (0.50–0.55)

Abbreviations: AUC, area under the curve; CI, confidence interval; OR, odds ratio.

[a]Receiver operating characteristic curve analysis.

[b]Binary logistic regression analysis.

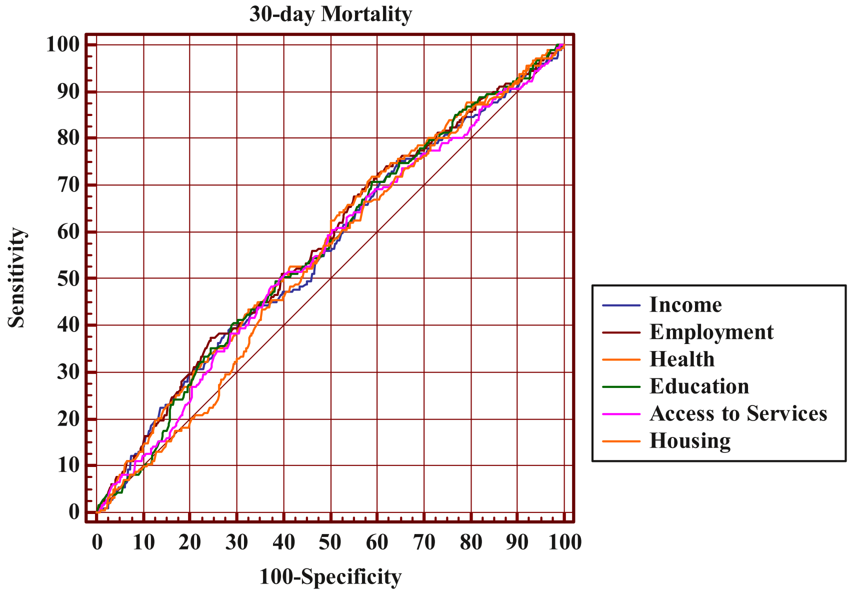

FIGURE 3 Receiver operating characteristic curves for performance of different domains of deprivation in predicting 30-day operative mortality. [Colour figure can be viewed at wileyonlinelibrary.com]

with overall deprivation (Table S1). Therefore, the possible explanation for the observation could be the fact that overall deprivation was by itself not a strong predictor of OM; hence, most of its domains were likely to be poor predictors. On the other hand, the emergency setting may be another possible reason for reducing the predictive significance of individual domains of deprivation. In fact, the severity and rapid deterioration of an acute abdominal pathology indicating EL are alarming enough to convince any individual to seek emergency advice regardless of their socioeconomic status. On the other hand, emergency general surgery service is free and accessible for almost all individuals in the United Kingdom and unlike many countries,[13] the concern over the ability to pay medical bills or the lack of a stable relationship with a primary care provider may not be a barrier against seeking medical advice in the United Kingdom, which may downgrade the negative impact of deprivation and its domains in terms of short-term outcomes.

The negative impact of deprivation may be less in an emergency setting in comparison with an elective setting. In an elective setting, patients are not necessarily acutely unwell and are required to attend preoperative clinic appointments and investigations before their operations. Moreover, they are required to attend several postoperative clinic appointments and surveillance investigations. Consequently, the high-risk lifestyle and noncompliant health-seeking behaviors associated with socioeconomic deprivation are more likely to interfere with preoperative and postoperative care, which can negatively affect the short-term and long-term outcomes. However, in an emergency setting, the severity of underlying pathology would minimize the delay in seeking medical advice in acutely unwell patients, specifically when the healthcare system is free. Considering that deprivation may not be a strong predictor of OM following EL, it remains unknown whether the incorporation of socioeconomic deprivation as a variable into preoperative risk assessment tools would improve their predictive performance; therefore, future studies should investigate the potential prognostic value of incorporating deprivation into the commonly used preoperative risk assessment algorithms. The results of future studies would determine whether or not spending the already limited healthcare funding on addressing socioeconomic deprivation in order to improve EL outcomes is justified.

Prevention is better than cure! A synonym for deprivation is rob of and the best target to focus on is that the deprived should not be robbed of in the first place. While addressing deprivation, it is beyond the scope of the current study, and identifying the areas of deprivation and reducing the gaps in terms of income, employment, health, education, access to services, housing, community safety, and physical environment would improve lifestyle, would reduce the number of comorbidities, would improve health-seeking behavior, would improve compliance with medical advice, and would improve the outcomes of medical interventions.

There are several potential limitations to this study. There was an apparently paradoxical finding in the current study. While it is well known that socioeconomically deprived patients are likely to have more severe comorbidities,[10] the included populations in the most- and least-deprived cohorts were comparable in terms of ASA status and frailty. There are two possible explanations for this apparent paradox. Firstly, the included patients in the most deprived cohort were younger and the number of octogenarians was smaller in the most deprived cohort. This would mean that the younger deprived patients were as comorbid as the older non-deprived patients, which highlights the consistency with previous literature and confirms the difference in age as a potential confounding factor in this study. Another possible explanation for comparable baseline comorbidities in both cohorts may be the use of such area-based deprivation scores as opposed to individual-based scores, calculated on individuals' incomes or occupations, does introduce potential bias, given that it is unlikely that all residents of a specific postcode will have the attributes of that community, but WIMD is the only validated tool for the assessment of deprivation within Wales. Deprivation exists in several forms and such multimodal complexity makes quantification challenging. Important discrepancies in outcome and duration of survival between patients from different socioeconomic backgrounds were shown, but no explanation appeared as to why this should be so. This study used deprivation scores measured at the area level, that is, every patient was given a score based on the degree of deprivation of their local community. Survival was calculated using all-cause mortality and this is of relevance when considering deprivation, as patients from more deprived areas have a higher proportion of many chronic diseases, and their mortality is therefore higher than that of patients from more socioeconomically advantaged areas. However, this latter point is controversial as it has previously been reported that disease-specific mortality provides the most correct measure of survival, when no information about comorbidity is available.[28] The study was conducted in two centers in Wales, which may affect the generalizability of the findings; however, conducting the study in two different hospital settings (tertiary and secondary care general surgery centers) and the consistency of the findings with reports of studies from England,[22] Scotland,[27] and the USA[26] should minimize this concern.

5 | CONCLUSIONS

Deprivation is an independent but modest predictor of OM after EL. The potential prognostic value of incorporating deprivation into preoperative risk assessment algorithms deserves further examination.

AUTHOR CONTRIBUTIONS

Shahab Hajibandeh: Conceptualization; data curation; formal analysis; investigation; methodology; project administration; supervision; validation; visualization; writing—original draft; writing—review & editing. **Anastasia Efstathiou**: Data curation; writing—original draft; writing—review & editing. **Shahin Hajibandeh**: Data curation; formal analysis; methodology; writing—original draft; writing—review & editing. **Ahmad Al-Sarireh**: Data curation; writing—original draft; writing—review & editing. **Hashim Al-Sarireh**: Data curation; writing—original draft; writing—review & editing. **Hamza Duffaydar**: Data curation; writing—original draft; writing—review & editing. **Michael Stechman**: Validation; visualization; writing—original draft; writing—review & editing. **Richard John Egan**: Conceptualization; supervision; validation; visualization; writing—original draft; writing—review & editing. **Wyn G. Lewis**: Conceptualization; supervision; validation; visualization; writing—original draft; writing—review & editing.

ACKNOWLEDGMENTS

There were no funding resources for this study.

CONFLICT OF INTEREST STATEMENT

The authors declare that they have no conflicts of interest.

ETHICS STATEMENT

Due to the retrospective nature of the study, use of non-identifiable hospital data and indirect involvement of patients in the study, ethical approval and patient consent were not needed. However, the study was compliant with the Helsinki medical research ethical principles and the policies recommended by the local Clinical Governance Unit.

ORCID

Shahab Hajibandeh https://orcid.org/0000-0002-3294-4335

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SUPPORTING INFORMATION

Additional supporting information can be found online in the Supporting Information section at the end of this article.

Full text 8

Article 8. Socioeconomic Deprivation and Risk of Operative Mortality After Emergency Laparotomy: A Systematic Review and Meta-Analysis

Citation: Ambler O, Hajibandeh S, **Hajibandeh S**. Socioeconomic Deprivation and Risk of Operative Mortality After Emergency Laparotomy: A Systematic Review and Meta-Analysis. Am Surg. 2025 Apr;91(4):644-652. doi: 10.1177/00031348251314151.

Contribution: Conception, design, data collection, data analysis, write up, and critical revision

Review Article

The American Surgeon™
2025, Vol. 91(4) 644–652

DOI: 10.1177/00031348251314151
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Socioeconomic Deprivation and Risk of Operative Mortality After Emergency Laparotomy: A Systematic Review and Meta-Analysis

Olivia Ambler, MRCS[1], Shahin Hajibandeh, FRCS[2], and Shahab Hajibandeh, FRCS[1]

Abstract

Aims: The aim was to determine the effect of socioeconomic deprivation on operative mortality after emergency laparotomy.

Methods: A PRISMA-compliant systematic review and meta-analysis (random-effects modeling) was performed searching for studies comparing operative mortality between the least and the most socioeconomically deprived patients undergoing emergency laparotomy. Both unadjusted and adjusted odds ratio (OR) were calculated as summary measure. Risk of bias was assessed using the Quality In Prognosis Studies tool, and certainty of evidence was assessed using the GRADE system.

Results: Four studies comprising 87,690 patients were included. There was no difference in the risk of operative mortality between the most and least deprived groups (unadjusted OR: 1.57, 95% CI .92, 2.68, *P* = .100) and when adjusted for other predictors (adjusted OR: 1.11, 95% CI .93, 1.32, *P* = .230). Subgroup analysis showed consistency of the findings in the United Kingdom (unadjusted OR: 1.36, 95% CI .92, 2.01, *P* = .130; adjusted OR: 1.15, 95% CI .92, 1.43, *P* = .230) and in the United States (unadjusted OR: 1.75, 95% CI .75, 4.06, *P* = .190; adjusted OR: 1.01, 95% CI .79, 1.29, *P* = .940). Sensitivity analyses showed inconsistency in favor of higher mortality risk in the most deprived patients. The GRADE certainty was moderate.

Conclusions: Socioeconomic deprivation may have minor effect on operative mortality after emergency laparotomy; however, such effect fades away once adjusted for other predictors of mortality. Although independent research is required, it may be reasonable to predict that incorporation of socioeconomic deprivation into preoperative risk assessment tools may not improve their predictive performance.

Keywords
socioeconomic deprivation, laparotomy, mortality

Introduction

Emergency laparotomy accounts for over 30,000 operations performed annually in the United Kingdom,[1] but it still carries a high risk of mortality despite recent improvements.[2] Therefore, decisions around emergency laparotomy require multidisciplinary peri-operative consideration and planning which are heavily dependent on detailed knowledge about predictors of mortality in patients undergoing such high-risk procedures. Our understanding of predictors of mortality after emergency laparotomy has evolved extensively over recent years, and the modern predictors include objective measures of age-related physiological decline such as sarcopenia, the clinical frailty scale and American Society of Anesthesiologists (ASA) status, and also objective measures of severity of underlying pathology such as a peritoneal contamination index (Hajibandeh index), and the need for bowel resection.[3]

Whilst the predictors of mortality related to patient's underlying abdominal pathology and patient's physiological physical fitness have been the interest of recent literature, evaluation of prognostic significance of

[1]Department of General Surgery, Morriston Hospital, Swansea, UK
[2]Department of General Surgery, Royal Stoke University Hospital, Stoke-on-Trent, UK

Corresponding Author:
Shahab Hajibandeh, FRCS, Department of General Surgery, Morriston Hospital, Swansea SA6 6NL, UK.
Email: [redacted]

patients' socioeconomic status has also gained popularity.[4] Socioeconomic status can affect individuals' exposure to lifestyle-related risk factors, individuals' health-seeking behavior and access to health care, and individuals' comorbidities,[5-9] which may negatively impact postoperative mortality. The prognostic significance of socioeconomic status in emergency laparotomy setting has been evaluated in several observational studies providing a rationale for evidence synthesis via a systematic review. We aimed to conduct a systematic review and meta-analysis to determine the effect of socioeconomic deprivation on operative mortality after emergency laparotomy.

Methods

Methodological and Reporting Compliance

The study was conducted and reported in compliance with the Cochrane Handbook for Systematic Reviews (version 6.4)[10] and the Preferred Reporting Items for Systematic reviews and Meta-Analyses (PRISMA) 2020 statement standards,[11] respectively.

Registration and Protocol

The study followed a predefined protocol which was prospectively registered in PROSPERO which is a publicly available international database of prospectively registered systematic reviews (PROSPERO registration number: CRD42024603033).

Eligibility Criteria

Study Design. All comparative observational studies were considered eligible for inclusion in this study. Systematic reviews, meta-analyses, scoping reviews, review articles, single-arm studies, retrospective studies, case series, case reports, and correspondence articles were excluded.

Population. All adult patients aged 18 or over with acute non-traumatic abdominal pathology who underwent emergency laparotomy were eligible. The non-traumatic abdominal pathologies of interest included visceral perforation, intestinal obstruction, intestinal ischemia, intra-abdominal bleeding, and intra-abdominal sepsis of any source (intra-abdominal collection, colitis, anastomotic leak, and intestinal fistula).

Prognostic Factor. Socioeconomic deprivation was defined based on a recognized multiple deprivation index. The most deprived population (as determined by multiple deprivation index) was compared with the least deprived population.

Outcomes. Operative mortality defined as death due to any cause within 30 days of emergency laparotomy or during postoperative inpatient stay was the outcome of interest.

Information Sources and Search Strategy

A comprehensive search strategy consisting of proper search keywords, limits, thesaurus headings, and operators was created, adopted, and applied on the following electronic sources: Scopus®, MEDLINE®, the Cochrane Central Register of Controlled Trials, the Cumulative Index to Nursing and Allied Health Literature, the International Standard Randomised Controlled Trial Number Registry, the International Clinical Trials Registry Platform, ClinicalTrials.gov, and the Grey Literature Network Service (Appendix I). Two authors with expertise in evidence synthesis designed and applied the search strategy on 11 October 2024 with no language restrictions.

Study Selection, Data Collection, and Data Items

Two authors independently screened the identified articles through titles and abstracts against the aforementioned eligibility criteria and retrieved the full-text of potentially eligible articles. The articles that met the eligibility criteria were selected for inclusion. If there was discrepancy in findings of the first two authors, a third author provided opinion on eligibility. The data items were determined at protocol development stage by the authors with expertise on the field and after selection of eligible studies by the authors with expertise in evidence synthesis using pilot-testing technique of randomly selected studies. Data items were collected in an electronic data collection sheet by two independent authors. These included information about the bibliometric parameters, study design, included population, the multiple deprivation index used, and operative mortality.

Study Risk of Bias Assessment

The risk of bias in study participation, study attrition, prognostic factor measurement, outcome measurement, study confounding, and statistical analysis were judged using the QUIPS (Quality In Prognosis Studies) tool.[12] The risk of bias in the included studies was assessed by two independent authors. If there was discrepancy in assessment by the first two authors, a third author provided opinion.

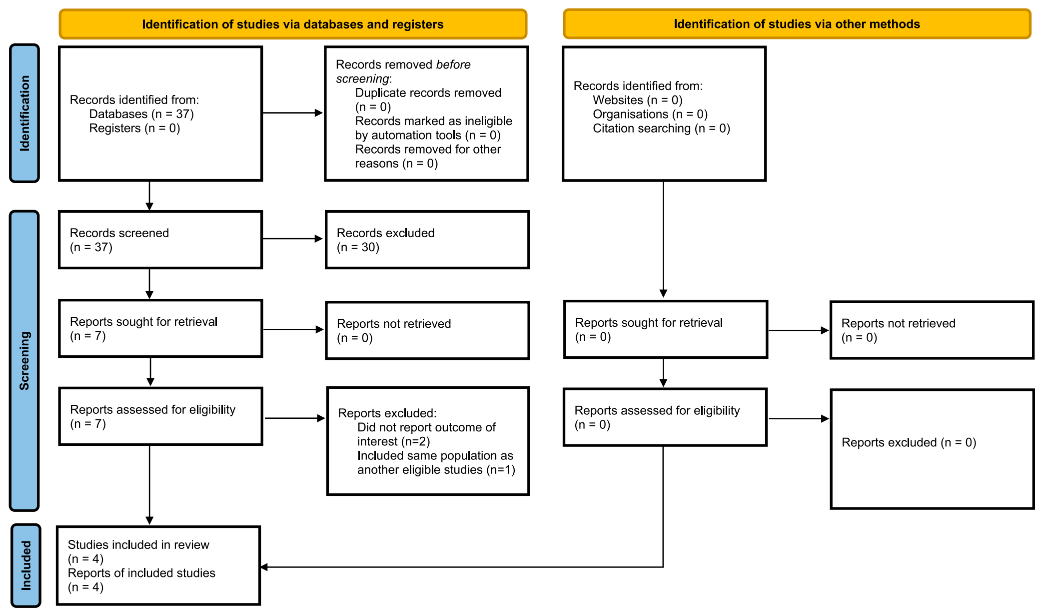

Figure 1. Study PRISMA flow diagram.

Effect Measures and Synthesis Methods

Because the outcome of this study was a dichotomous variable, unadjusted and where possible adjusted odds ratio (OR) were calculated as summary effect measure. Individual patients were considered a unit of analysis. Random-effects modeling was used for analyses, and forest plots with 95% confidence intervals (CIs) were constructed to present the results. Statistical heterogeneity was measured as I^2 using Cochran's Q test ($\chi 2$), and heterogeneity was classified as low when I^2 was 0-25%, moderate when I^2 was 25-75%, and high when I^2 was 75-100%. RevMan 5.4 software (Nordic Cochrane Centre, Copenhagen, Denmark) was employed for meta-analysis. Sensitivity analyses (leave-one-out analysis and separate analysis for studies with low overall risk of bias) were performed if the outcome was reported by a minimum of four studies. Moreover, subgroup analyses were performed based on the country of the included studies.

Reporting Bias Assessment

The protocol planned to evaluate the risk of reporting bias by constructing funnel plot if the outcome was reported by at least ten studies; however, because the outcome was reported by less than ten studies, reporting bias could not be evaluated.

Certainty Assessment

The GRADE (Grading of Recommendations Assessment, Development and Evaluation) system was used for assessment of the certainty of evidence for operative mortality.[13]

Deviation from the Registered Protocol

The study remained compliant with the registered protocol with no deviations.

Results

Study Selection and Study Characteristics

Search of the information sources resulted in 37 articles; 30 articles were excluded directly by screening their titles and abstracts. The full-text of the remaining seven articles was reviewed which resulted in exclusion of three articles (two studies did not report 30-day mortality; one study included the same population as another eligible article). Consequently, four comparative retrospective cohort studies[14-17] comprising 87,690 patients were included; 22,926 patients were classified as most socioeconomically deprived and 64,764 patients were classified as least socioeconomically deprived. The study PRISMA flow diagram is shown in Figure 1, and baseline characteristics of the included studies are shown in Table 1.

Risk of Bias in Studies

Figure 2 shows overall risk of bias graph, and Figure 3 demonstrates the risk of bias judgement for each domain of QUIPS tool for each study. All of the included studies

Table 1. Characteristics of Included Studies at Baseline.

Authors and year	Country	Journal	Design	Assessment Tool for Deprivation	Domains of Deprivation Evaluated	Sample Size: Total	Sample Size: Most Deprived	Sample Size: Least Deprived	Operative Mortality (Most Deprived vs Least Deprived): Crude Risk % (Event/Total)	Operative Mortality: Unadjusted OR (95% CI)	Operative Mortality: Adjusted OR (95% CI)	Variables Used in Multivariable Analysis for Adjusted OR
Hajibandeh et al (2024)	UK	World J Surg	Retrospective cohort	Welsh Index of Multiple Deprivation including the following domains:	Income, employment, health, education, access to services, housing, community safety, and physical environment	1089	576	513	13.2% (76/576) vs 7.9% (41/513)	1.75 (1.17-2.61)	1.03 (1.01-1.06)	Age≥80, ASA status, bowel resection, and peritoneal contamination
Sakowitz et al (2024)	USA	Surgery	Retrospective cohort	International Classification of Diseases, Tenth Revision	Economic, education, social, health care, and environmental	54190	7466	46724	10% (747/7466) vs 4% (1869/46724)	2.67 (2.44-2.92)	NR	Not applicable
Cain et al (2022)	USA	J Trauma Acute Care Surg	Retrospective cohort	Area Deprivation Index	Income, education, employment, and housing quality	9332	2988	6344	4.7% (143/2988) vs 4.3% (271/6344)	1.13 (0.91-1.38)	1.30 (1.01-1.66)	Comorbidities, race, age, sex, primary payer status, state, and hospital setting
Poulton et al (2020)	UK	Br J Anaesth	Retrospective cohort	Index of Multiple Deprivation	Income, employment, health deprivation and disability, education, skills training, crime, barriers to housing and services, and living environment	23079	11896	11183	11.2 % (1333/11896) vs 9.8 % (1093/ 11183)	1.16 (1.07-1.27)	1.29 (1.16-1.44)	Age, sex, ethnicity, ASA status, comorbidities, physiological status, mental status, timing, type, urgency and severity of operation, peritoneal contamination, and malignancy

OR, odds ratio; CI, confidence intervals; ASA, American Society of Anesthesiologists

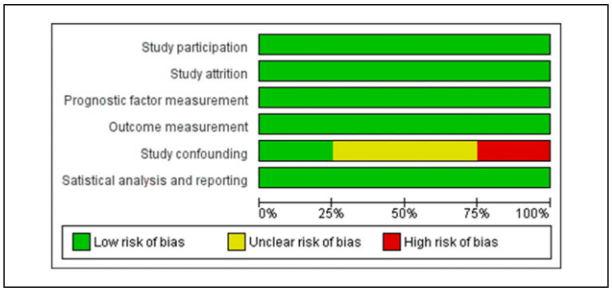

Figure 2. Overall risk of bias graph based on domains of the Quality In Prognosis Studies tool.

were judged to be of low risk of selection bias in study participation, study attrition, prognostic factor measurement, outcome measurement, and statistical analysis. The risk of bias due to study confounding was judged to be low in one study, unclear in two studies, and high in one study.

Results of Outcome Syntheses for Operative Mortality

Unadjusted Operative Mortality Risk. Unadjusted operative mortality risk was reported in four studies including 87,690 patients. There was no difference in the risk of operative mortality between the most and least deprived groups (unadjusted OR: 1.57, 95% CI .92, 2.68, $P = .100$) (Figure 3). The level of between-study heterogeneity was high ($I^2 = 98\%$, $P < .00001$), and the GRADE certainty of evidence was moderate (Table 2).

Adjusted Operative Mortality Risk. Adjusted operative mortality risk was reported in three studies including 33,500 patients. There was no difference in the risk of operative mortality between the most and least deprived groups (adjusted OR: 1.11, 95% CI .93, 1.32, $P = .230$) (Figure 3). The level of between-study heterogeneity was high ($I^2 = 87\%$, $P = .0003$), and the GRADE certainty of evidence was moderate (Table 2).

Sensitivity Analyses

Sensitivity analyses were performed for unadjusted operative mortality risk which was reported by four studies. Separate analysis for studies with low overall risk of bias moved the direction of effect size in favor of least deprived group. Moreover, leave-one-out analysis changed the direction of the effect size in favor of least deprived group.

Subgroup Analyses

UK Population. Subgroup analysis of 24,168 patients from the United Kingdom showed no difference in the risk of operative mortality between the most and least deprived groups (unadjusted OR: 1.36, 95% CI .92, 2.01, $P = .130$; adjusted OR: 1.15, 95% CI .92, 1.43, $P = .230$) (Figure 4, Figure 5).

USA Population. Subgroup analysis of 63,522 patients from the United States showed no difference in the risk of operative mortality between the most and least deprived groups (unadjusted OR: 1.75, 95% CI .75, 4.06, $P = .190$; adjusted OR: 1.01, 95% CI .79, 1.29, $P = .940$) (Figure 4, Figure 5).

Discussion

In view of the popularity of socioeconomic status in the recent literature as a prognostic factor in patients undergoing emergency laparotomy, we conducted a systematic review and meta-analysis of 87,690 patients from four studies which showed no significant difference in operative mortality between the least and most socioeconomically deprived patients undergoing emergency laparotomy. The GRADE certainty was moderate, and subgroup analyses confirmed consistency of the findings in the United Kingdom and United States.

This study is the first meta-analysis evaluating the effect of socioeconomic deprivation on mortality after emergency laparotomy. Consequently, the results cannot be compared with another similar systematic review; nevertheless, the pooled findings can be compared with the findings of individual studies. All of the included studies identified socioeconomic deprivation as an independent predictor of operative mortality[14-17]; however, the magnitude of the effect size was very small in all of the included studies; hence when the results were pooled under random effects, the pooled OR was not significant. This may explain why sensitivity analyses showed inconsistency of the findings for unadjusted mortality risk. Nevertheless, the above inconsistencies suggest that even if socioeconomic deprivation may be an independent predictor of operative mortality, it would be a very weak predictor. Consistent with this, Hajibandeh et al[14] showed that deprivation and its domains are weak predictors of mortality as demonstrated by the results of receiver operating characteristic (ROC) curve analysis.[14] Similarly, Pouke et al[18] showed no difference in mortality between patients from rural areas and urban areas undergoing emergency laparotomy.

Poor predictive significance of socioeconomic deprivation in the emergency laparotomy setting may be explained by the nature of the emergency setting itself. In fact, almost all individuals, regardless of

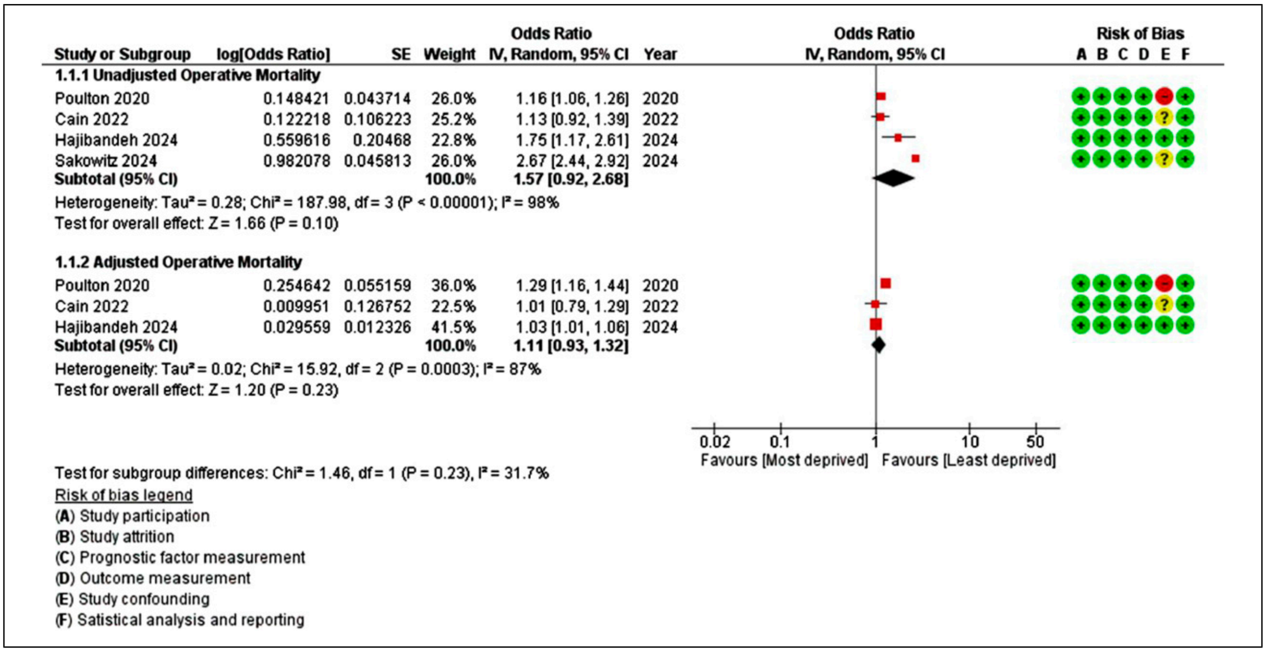

Figure 3. Forest plot for comparison of operative mortality between the most and least deprived patients.

their socioeconomic status, seek medical help on an emergent basis when they face the severity and rapid deterioration of an acute abdominal pathology indicating emergency laparotomy.[14] This is indeed reflected by the fact that unlike in the emergency setting, socioeconomic deprivation has a strong negative impact on mortality in the elective surgery setting when patients are not necessarily acutely unwell.[19] In fact, deprivation-related non-compliant health-seeking behaviors and high-risk lifestyles may prevent the deprived individuals from attending the required preoperative clinic appointments and investigations before their elective surgery, resulting in less favorable short-term and long-term outcomes.

Evidence synthesis on effect of socioeconomic deprivation on mortality is challenging. This is due to the fact that deprivation exists in several forms and quantification of such multimodal complexity is difficult. Furthermore, deprivation indices used for quantifying deprivation in different countries are different in terms of the domains of deprivation. On the other hand, a specific domain of deprivation may have different significance among different countries. In addition, most of the available deprivation indices are area-based rather than individual-based and may not reflect patients' socioeconomic status accurately. Consequently, due to the above limitations, the results of studies evaluating the prognostic significance of socioeconomic deprivation should be interpreted with caution.

The current study has the following limitations: although the sample size was very large in terms of the number of patients, the number of studies was small so type 2 error cannot be excluded. The statistical between-study heterogeneity was high and it can be explained by the fact that the included studies used a different multiple deprivation index for assessment of socioeconomic status—however we did downgrade the certainty of the evidence to compensate for this limitation. The retrospective nature of the included studies would subject the findings to selection bias. Finally, the publication bias could not be assessed formally due to not having more than 10 studies reporting operative mortality.

Conclusions

Socioeconomic deprivation may have minor effect on operative mortality after emergency laparotomy; however, such effect fades away once adjusted for other predictors of mortality. Although independent research is required, it may be reasonable to predict that incorporation of socioeconomic deprivation into preoperative risk assessment tools may not improve their predictive performance.

Table 2. Summary of Finding Table for Comparison of Operative Mortality Between the Most and Least Deprived Patients.

Certainty Assessment							Summary of Findings				
							Study Event Rates (%)			Anticipated Absolute Effects	
Participants (studies) Follow-up	Risk of Bias	Inconsistency	Indirectness	Imprecision	Publication Bias	Overall Certainty of Evidence	With Least Deprived	With Most Deprived	Relative Effect (95% CI)	Risk With Least Deprived	Risk Difference With Most Deprived
Operative mortality—unadjusted operative mortality											
87690 (4 non-randomized studies)	Not serious	Serious[a]	Not serious	Not serious	None	⨁⨁⨁◯ Moderate[a]	3274/64764 (5.1%)	2299/22926 (10.0%)	**OR 1.57** (0.92 to 2.68)	3274/64764 (5.1%)	**27 more per 1000** (from 4 fewer to 74 more)
Operative mortality—adjusted operative mortality											
33500 (3 non-randomized studies)	Not serious	Serious[a]	Not serious	Not serious	None	⨁⨁⨁◯ Moderate[a]	1405/18040 (7.8%)	1552/15460 (10.0%)	**OR 1.11** (0.93 to 1.32)	1405/18040 (7.8%)	**8 more per 1000** (from 5 fewer to 22 more)

CI, confidence interval; **OR,** odds ratio.
[a]High between-study heterogeneity.

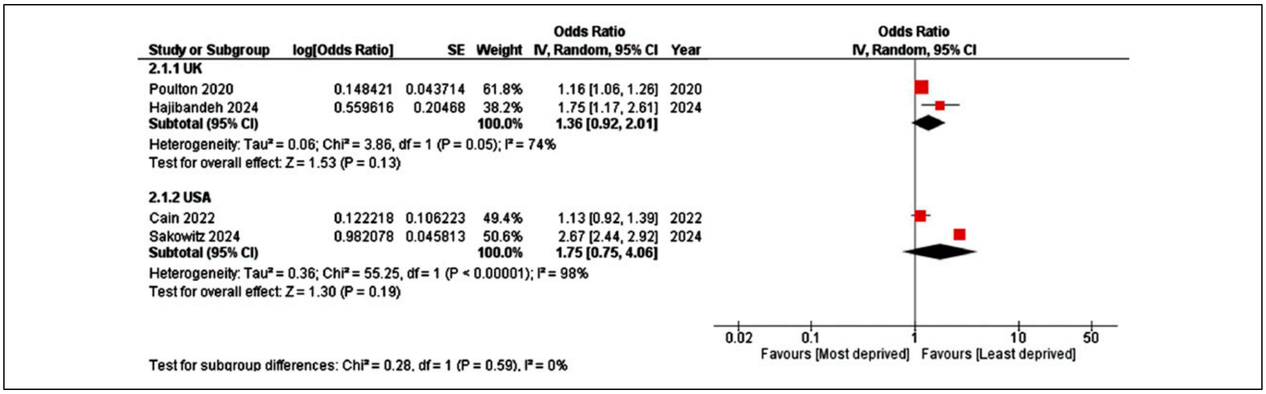

Figure 4. Subgroup analysis based on country of the included studies for unadjusted operative mortality risk.

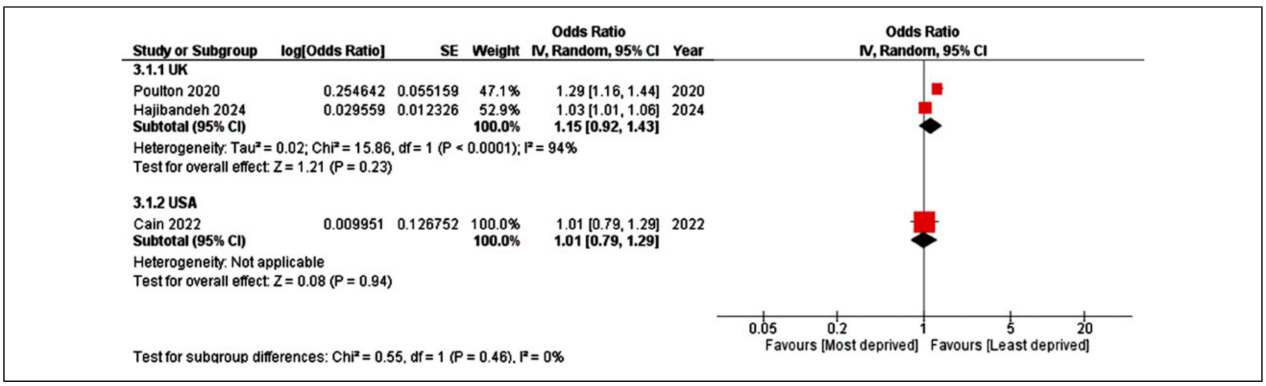

Figure 5. Subgroup analysis based on country of the included studies for adjusted operative mortality risk.

Appendix I

Literature Search Strategy

Search Number	Search Description	Action
Number 1	Socioeconomic near2 deprivation	Titles, abstracts, and keywords
Number 2	Socio-economic near2 deprivation	Ttitles, abstracts, and keywords
Number 3	Number 1 OR Number 2	Combined with OR
Number 4	Emergency near 2 laparotomy	Titles, abstracts, and keywords
Number 5	Laparotomy	Titles, abstracts, and keywords
Number 6	Number 4 OR Number 5	Combined with OR
Number 7	Number 3 AND Number 6	Combined with AND

Author Contributions

Conception and design: Shahab H. Data collection: OA, Shahab H, and Shahin H. Analysis and interpretation: OA, Shahab H, and Shahin H. Writing the article: OA, Shahab H, and Shahin H. Critical revision for important intellectual content: OA, Shahab H, and Shahin H. Final approval of the article: OA, Shahab H, and Shahin H.

Declaration of Conflicting Interests

The author(s) declared no potential conflicts of interest with respect to the research, authorship, and/or publication of this article.

Funding

The author(s) received no financial support for the research, authorship, and/or publication of this article.

Human and Animal Rights

This study is a systematic review with meta-analysis of outcomes which does not include research directly involving human or animal participation.

PROSPERO protocol registration number

CRD42024603033.

ORCID iDs

Shahin Hajibandeh https://orcid.org/0000-0001-6159-1068
Shahab Hajibandeh https://orcid.org/0000-0002-3294-4335

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Full text 9

Article 9. Meta-analysis of Enhanced Recovery After Surgery (ERAS) Protocols in Emergency Abdominal Surgery

Citation: Hajibandeh S, Hajibandeh S, Bill V, Satyadas T. Meta-analysis of Enhanced Recovery After Surgery (ERAS) Protocols in Emergency Abdominal Surgery. World J Surg. 2020 May;44(5):1336-1348. doi: 10.1007/s00268-019-05357-5.

Contribution: Conception, design, data collection, data analysis, write up, and critical revision

World J Surg (2020) 44:1336–1348
https://doi.org/10.1007/s00268-019-05357-5

SCIENTIFIC REVIEW

Meta-analysis of Enhanced Recovery After Surgery (ERAS) Protocols in Emergency Abdominal Surgery

Shahab Hajibandeh[1] · Shahin Hajibandeh[2] · Victor Bill[3] · Thomas Satyadas[4]

Published online: 2 January 2020

Abstract

Objectives To evaluate enhanced recovery after surgery (ERAS) protocols in emergency abdominal surgery.

Methods The electronic data sources were explored to capture all studies that evaluated the impact of ERAS protocols in patients who underwent emergency abdominal surgery. The quality of randomised and non-randomised studies was evaluated by the Cochrane tool and the Newcastle–Ottawa scale, respectively. Random or fixed effects modelling were utilised as indicated.

Results Six comparative studies, enrolling 1334 patients, were eligible. ERAS protocols resulted in shorter post-operative time to first flatus (mean difference: −1.40, $P < 0.00001$), time to first defecation (mean difference: −1.21, $P = 0.02$), time to first oral liquid diet (mean difference: −2.30, $P < 0.00001$), time to first oral solid diet (mean difference: −2.40, $P < 0.00001$) and length of hospital stay (mean difference: −3.09, −2.80, $P < 0.00001$). ERAS protocols also resulted in lower risks of total complications (odds ratio: 0.50, $P < 0.00001$), major complications (odds ratio: 0.60, $P = 0.0008$), pulmonary complications (odds ratio: 0.38, $P = 0.0003$), paralytic ileus (odds ratio: 0.53, 0.88, $P = 0.01$) and surgical site infection (odds ratio: 0.39, $P = 0.0001$). Both ERAS and non-ERAS protocols resulted in similar risk of 30-day mortality (risk difference: −0.00, $P = 0.94$), need for re-admission (risk difference: −0.01, $P = 0.50$) and need for re-operation (odds ratio: 0.83, $P = 0.50$).

Conclusions Although ERAS protocols are commonly used in elective settings, they are associated with favourable outcomes in emergency settings as indicated by reduced post-operative complications, accelerated recovery of bowel function and shorter post-operative hospital stay without increasing need for re-admission or re-operation. There should be an effort to incorporate ERAS protocols into emergency abdominal surgery settings.

Shahab Hajibandeh and Shahin Hajibandeh had equal contributions in this study proposing joined first authorship.

✉ Shahab Hajibandeh
[redacted]

1 Glan Clwyd Hospital, Rhyl, Denbighshire, UK

2 Sandwell and West, Birmingham Hospitals NHS Trust, Birmingham, UK

3 North Manchester General Hospital, Manchester, UK

4 Manchester Royal Infirmary Hospital, Manchester, UK

Introduction

Enhanced recovery after surgery (ERAS) protocols via a multidisciplinary team approach aim to decrease perioperative surgical stress, sustain post-operative physiological function and facilitate recovery in surgical patients [1]. ERAS protocols comprise preoperative (consultations before procedure, use of carbohydrate drinks before the procedure, preparation of bowel when indicated), intraoperative (prevention of venous thromboembolism, prophylactic use of antibiotics, maintaining temperature during procedure, objective fluid replacement, use of the best possible surgical approach and incision) and post-operative (appropriate pain control following procedure, early removal of tubes including nasogastric tube, urinary catheter and drains, early mobilisation and commencement of enteral feeding) components [2].

ERAS protocols were originally applied in colorectal surgical setting and were found to be successful in decreasing duration of hospital stay and improving post-operative outcomes [3]. ERAS approach is regarded as the standard of care in various elective surgical settings [4–9]. Although the significance of ERAS protocols in terms of post-operative outcomes has been investigated extensively in elective settings, the effectiveness of these protocols in emergency abdominal surgical settings is not established. Hence, our main purpose was to complete a systematic review and meta-analysis of outcomes to evaluate the impact of ERAS protocols in emergency abdominal surgical settings.

Methods

This study was designed according to an agreed protocol which was in compliance with PRISMA statement standards [10].

Eligibility criteria

All comparative studies (randomised or non-randomised) comparing ERAS protocols with standard protocols in patients undergoing emergency abdominal surgery were considered qualified for inclusion. All adult patients who underwent emergency abdominal procedures (emergency resection of small bowel, segmental colectomy, total colectomy, operation for perforated viscus, adhesiolysis or laparotomy) were regarded as the participants of interest. ERAS protocols, comprising components recommended by ERAS group [11], were regarded as intervention of interest, and non-ERAS (standard or conventional) perioperative protocols were regarded as comparison of interest.

Primary outcomes

- Length of hospital stay
- Total post-operative complications.

Secondary outcomes

- Post-operative time to first flatus
- Post-operative time to first defecation
- Post-operative time to first oral liquid diet
- Post-operative time to first oral solid diet
- Major complications
- Pulmonary complications
- Paralytic ileus
- Surgical site infection
- 30-Day mortality
- Need for re-admission
- Need for re-operation.

Search methods

Two separate authors explored the following sources:

- CINAHL
- EMBASE
- MEDLINE
- The Cochrane Central Register of Controlled Trials
- ClinicalTrials.gov
- WHO International Clinical Trials Registry
- SRCTN Register.

The date for the last literature search was 15 April 2019. Moreover, in order to identify more eligible studies, the references mentioned within full-text of relevant papers were searched. There were no language limitations in the search strategies. "Appendix" demonstrates the main literature search strategy which was modified according to each database.

Study selection and data extraction

The title and abstract of the articles found after running the search strategy in the aforementioned databases were reviewed. This was followed by obtaining the full texts of the identified studies and selecting the appropriate studies meeting the eligibility criteria. A data collection proforma was then designed and tested in randomly chosen studies. This was in compliance with Cochrane's guidelines. As outlined in the tables and figures, the data collection proforma contained information on:

- Bibliometric parameters of the eligible studies
- Characteristics of the eligible patients at baseline
- Outcome measures.

The study selection and data extraction steps were done by two separate reviewers. Any disagreements during selection of the included studies or data extraction process were discussed between the first two authors, and a separate author was involved when required.

Risk of bias assessment

The methodological quality of RCTs was evaluated using the Cochrane tool that examines the quality of the study design in terms of selection, performance, detection, attrition, reporting and other sources of bias. The methodological quality of non-randomised comparative studies was evaluated using the Newcastle–Ottawa scale [12] that examines the quality of the study design in terms of selection of the eligible patients, comparability of the intervention and comparison groups within the study and outcome assessments. This process was done by two separate reviewers. Any disagreements were discussed between the first two authors, and a separate author was involved when required.

Data analysis

In terms of summary measures, odds ratio (OR) was computed for dichotomous outcomes and mean difference (MD) for continuous outcomes; risk difference (RD) was computed in the case of no occurrence of the outcome of interest (zero event) in either groups in more than a third of the studies. The unit of analysis was an individual patient, and the analyses were according to intention to treat information. The Review Manager (RevMan, version 5.3. Copenhagen, 2014) software was used for data synthesis. Random or fixed effects modelling was utilised as indicated; when between-study heterogeneity was conspicuous, random effects models were applied. The heterogeneity was quantified and reported as I^2 using Cochran Q test (χ^2). We interpreted I^2 as below:

- 0–50% means low heterogeneity
- 50–75% means moderate heterogeneity
- 75–100% means high heterogeneity.

For the outcomes reported by at least 10 studies, we aimed to generate funnel plots and planned to examine the possibility of publication bias by assessing the symmetry of the funnel plots.

Additional analyses

The robustness of the analyses was examined by performing sensitivity analyses for the outcomes reported by a minimum number of four comparative studies. The first set of analyses included separate calculation of risk ratio, OR and RD for dichotomous outcomes. The second set of analyses aimed to examine the impact of each study on the total effect size and heterogeneity. This involved elimination of one study at a time followed by repeating the analyses. The third set of analyses involved independent analyses using random effects and fixed effect models. Furthermore, where applicable, we did subgroup analysis according to design of the studies (RCTs and observational studies) and reason for emergency operation (visceral perforation and bowel obstruction).

Results

Results of the search

Overall, 300 articles were identified after applying the search strategy in the aforementioned databases. Among these, 6 studies [13–18] were qualified for inclusion (Fig. 1). These were 2 RCTs [14, 17] and 4 observational studies [13, 15, 16, 18], including 1334 patients. Among the eligible patients, 690 patients were treated according to the ERAS protocols and 644 patients were treated according to standard non-ERAS protocols. Both ERAS and non-ERAS groups were similar in terms of mean age (57.9 versus 57.4, $P = 0.95$) and gender (male: 59% versus 62%, $P = 0.25$; female: 41% versus 38%, $P = 0.25$). Three studies [13, 15, 18] included patients with bowel

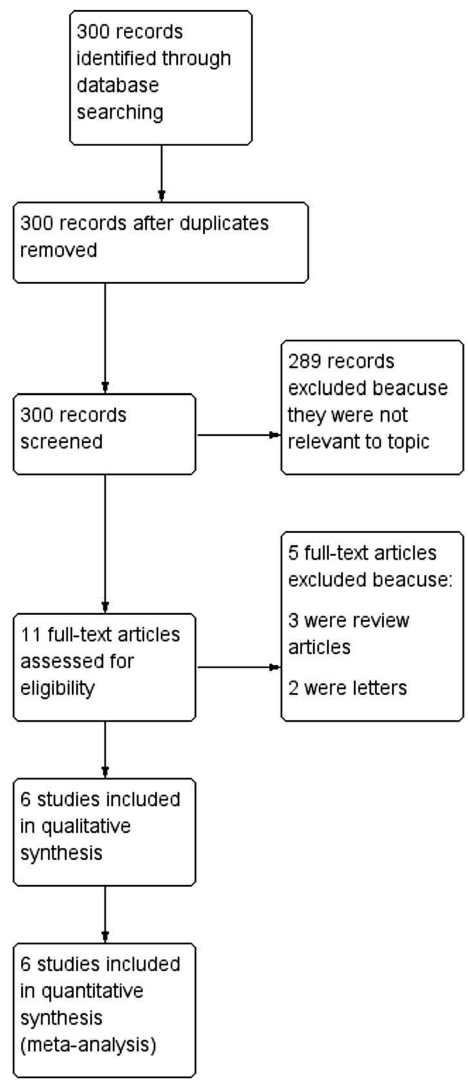


Fig. 1 Study flow diagram

obstruction; two studies [14, 17] included patients with perforated duodenal ulcer; one study [16] included patients with abdominal pathology requiring major abdominal procedure (Tables 1, 2). Table 3 highlights the ERAS components considered as part of ERAS protocols in each of the eligible studies.

Risk of bias in included studies

Figure 2 highlights the outcomes of methodological quality assessment based on the Cochrane tool and Newcastle–Ottawa scale.

Outcome synthesis (Fig. 3)

Length of hospital stay

Analysis of 964 patients from five studies [13–15, 17, 18] showed that ERAS protocols resulted in shorter length of hospital stay compared with non-ERAS protocols (mean difference: −3.09, 95% CI −3.37, −2.80, $P < 0.00001$). The reported between-study heterogeneity was judged to be low ($I^2 = 14\%$, $P = 0.32$).

Total post-operative complications

Analysis of 964 patients from five studies [13–15, 17, 18] showed that ERAS protocols resulted in lower risk of total post-operative complications compared with non-ERAS protocols (odds ratio: 0.50, 95% CI 0.38, 0.66, $P < 0.00001$). The reported between-study heterogeneity was judged to be moderate ($I^2 = 69\%$, $P = 0.01$).

Time to first flatus

Analysis of 795 patients from three studies [13, 14, 18] showed that ERAS protocols resulted in shorter time to first flatus compared with non-ERAS protocols (mean difference: −1.40, 95% CI −1.52, −1.27, $P < 0.00001$). The reported between-study heterogeneity was judged to be low ($I^2 = 0\%$, $P = 0.69$).

Time to first defecation

Analysis of 795 patients from three studies [13, 14, 18] showed that ERAS protocols resulted in shorter time to first defecation compared with non-ERAS protocols (mean difference: −1.21, 95% CI −2.19, − 0.23, $P = 0.02$). The reported between-study heterogeneity was judged to be high ($I^2 = 94\%$, $P < 0.00001$).

Time to first oral liquid diet

Analysis of 735 patients from two studies [13, 14] showed that ERAS protocols resulted in shorter time to first oral liquid diet compared with non-ERAS protocols (mean difference: −2.30, 95% CI −2.37, −2.23, $P < 0.00001$). The reported between-study heterogeneity was judged to be low ($I^2 = 12\%$, $P = 0.29$).

Table 1 Baseline characteristics of the included studies

References	Country	Journal	Design	Included populations	Sample size		
					Total	ERAS	Non-ERAS
Shang et al. [13]	China	Medicine	Retrospective observational	Patients with obstructive colorectal cancer undergoing the unplanned emergency operation	636	318	318
Mohsina et al. [14]	India	J Gastrointest Surg	Randomised controlled trial	Patients undergoing emergency operation for perforated duodenal ulcer	99	50	49
Shida et al. [15]	Japan	BMC Surgery	Retrospective observational	Patients undergoing emergency operation for obstructive colorectal cancer	122	80	42
Wisely et al. [16]	Australia	ANZ J Surg	Retrospective observational	Patients undergoing major emergency abdominal surgery	370	201	169
Gonenc et al. [17]	Turkey	Am J Surg	Randomised controlled trial	Patients undergoing emergency operation for perforated duodenal ulcer	47	21	26
Lohsiriwat et al. [18]	Thailand	World J Gastroenterol	Retrospective observational	Patients undergoing emergency operation for obstructing colorectal adenocarcinoma	60	20	40

ERAS enhanced recovery after surgery

Table 2 Baseline characteristics of the included population

	Age ERAS versus non-ERAS	Male ERAS versus non-ERAS	Female ERAS versus non-ERAS	BMI (kg/m^2) ERAS versus non-ERAS	ASA1–2 ERAS versus non-ERAS	ASA3–4 ERAS versus non-ERAS
Shang et al. [13]	Median 66 versus 65	192/318 versus 201/318	126/318 versus 117/318	25.1 ± 2.6 versus 24.9 ± 2.5	216/318 versus 220/318	102/318 versus 98/318
Mohsina et al. [14]	Mean: 46 versus 44	44/50 versus 44/49	6/50 versus 5/49	24.82 ± 0.35 versus 24.6 ± 0.34	50/50 versus 49/49	0/50 versus 0/49
Shida et al. [15]	Mean: 69 versus 68	52/80 versus 25/42	28/80 versus 17/42	NR	NR	NR
Wisely et al. [16]	Median 68 versus 68	87/201 versus 85/169	114/201 versus 84/169	NR	71/201 versus 74/169	130/201 versus 95/169
Gonenc et al. [17]	Mean 35 versus 38	16/21 versus 20/26	5/21 versus 6/26	NR	NR	NR
Lohsiriwat et al. [18]	Mean 58 versus 62	14/20 versus 24/40	6/20 versus 16/40	21.7 ± 3.3 versus 22.8 ± 3.4	16/20 versus 36/40	4/20 versus 4/20

NR not reported, *ERAS* enhanced recovery after surgery, *BMI* body mass index, *ASA* American Society of Anaesthesiologists

Table 3 Enhanced recovery after surgery components considered in the included studies

ERAS component	Shang et al. [13]	Mohsina et al. [14]	Shida et al. [15]	Wisely et al. [16]	Gonenc et al. [17]	Lohsiriwat et al. [18]
Preoperative counselling	Yes	Yes	Yes	Yes	Yes	Yes
Preoperative fasting and carbohydrate loading	Yes	NR	Yes	Yes	Yes	Yes
Mechanical bowel preparation	Yes	NR	NR	Yes	Yes	NR
Thromboprophylaxis	Yes	NR	NR	NR	Yes	NR
Antibiotic prophylaxis	NR	Yes	NR	NR	Yes	NR
Maintenance of intraoperative normothermia	Yes	NR	Yes	NR	Yes	Yes
Goal-directed fluid therapy	Yes	NR	Yes	Yes	Yes	Yes
Surgical incision and approach	Yes	Yes	NR	Yes	Yes	Yes
Avoidance of nasogastric tubes	Yes	Yes	Yes	Yes	Yes	Yes
Post-operative analgesia	Yes	Yes	Yes	Yes	Yes	Yes
Prevention of post-operative ileus	Yes	Yes	Yes	Yes	Yes	Yes
Avoidance of peritoneal drains	Yes	Yes	NR	Yes	Yes	Yes
Early removal of urinary catheter	Yes	Yes	Yes	Yes	Yes	Yes
Early post-operative enteral nutrition	Yes	Yes	Yes	Yes	Yes	Yes
Early mobilisation patients should	Yes	Yes	Yes	Yes	Yes	Yes

ERAS enhanced recovery after surgery, *NR* not reported

Time to first oral solid diet

Analysis of 842 patients from four studies [13, 14, 17, 18] showed that ERAS protocols resulted in shorter time to first oral solid diet compared with non-ERAS protocols (mean difference: −2.40, 95% CI −2.62, −2.19, $P < 0.00001$). The reported between-study heterogeneity was judged to be moderate ($I^2 = 69\%$, $P = 0.02$).

Major complications

Analysis of 818 patients from three studies [13, 15, 18] showed that ERAS protocols resulted in lower risk of major post-operative complications compared with non-ERAS protocols (odds ratio: 0.60, 95% CI 0.45, 0.81, $P = 0.0008$). The reported between-study heterogeneity was judged to be low ($I^2 = 0\%$, $P = 0.70$).

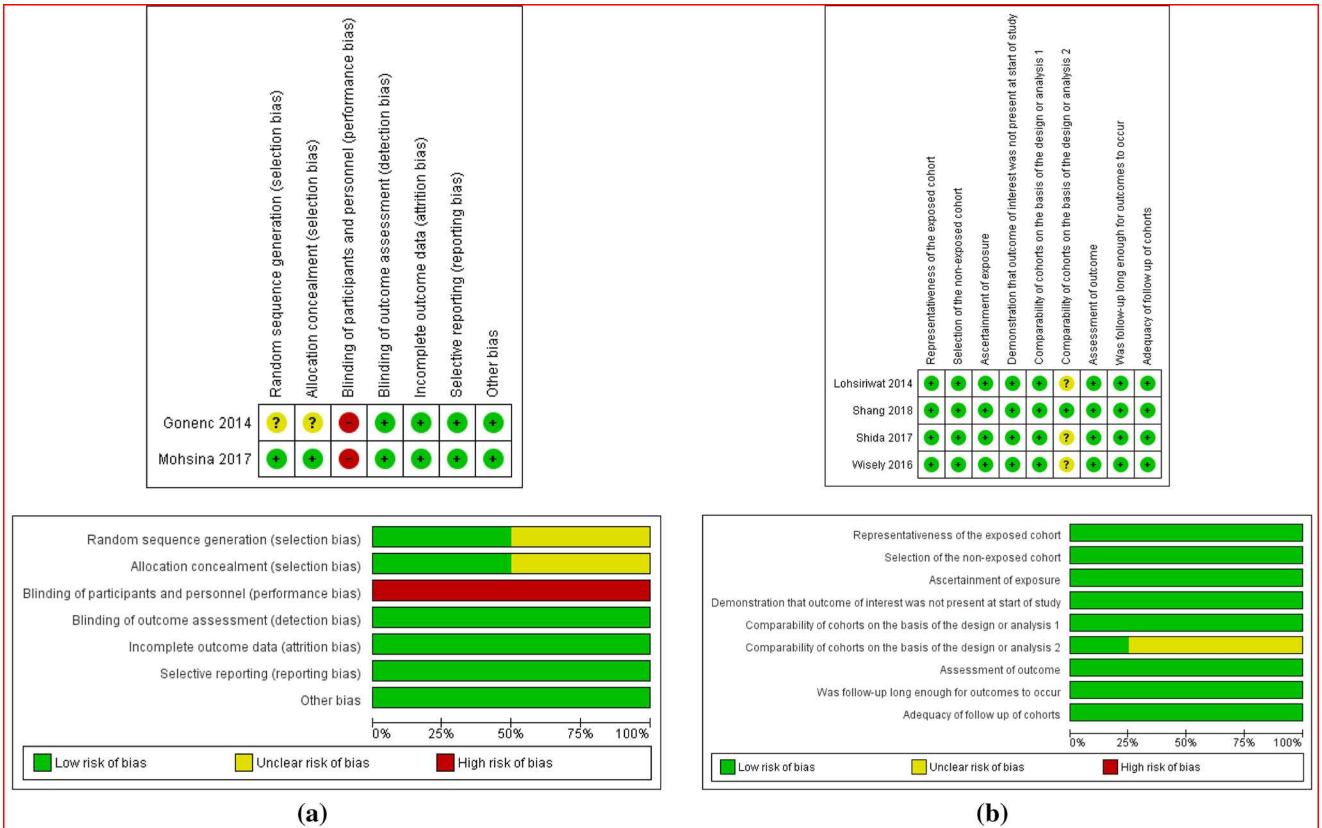


Fig. 2 Risk of bias summary and graph showing authors' judgements about each risk of bias item for: **a** randomised trials, **b** observational studies

Pulmonary complications

Analysis of 638 patients from four studies [14–17] showed that ERAS protocols resulted in lower risk of pulmonary complications compared with non-ERAS protocols (odds ratio: 0.38, 95% CI 0.22, 0.64, $P = 0.0003$). The reported between-study heterogeneity was judged to be low ($I^2 = 0\%$, $P = 0.65$).

Paralytic ileus

Analysis of 904 patients from four studies showed that ERAS protocols resulted in lower risk of paralytic ileus compared with non-ERAS protocols (odds ratio: 0.53, 95% CI 0.32, 0.88, $P = 0.01$). The reported between-study heterogeneity was judged to be low ($I^2 = 0\%$, $P = 0.97$).

Surgical site infection

Analysis of 516 patients from three studies [14, 16, 17] showed that ERAS protocols resulted in lower risk of surgical site infection compared with non-ERAS protocols (odds ratio: 0.39, 95% CI 0.24, 0.64, $P = 0.0001$). The reported between-study heterogeneity was judged to be low ($I^2 = 0\%$, $P = 0.61$).

30-Day mortality

Analysis of 1334 patients from six studies [13–18] showed that ERAS protocols and non-ERAS protocols were similar in terms of 30-day mortality risk (risk difference: −0.00, 95% CI − 0.02, 0.02, $P = 0.94$). The reported between-study heterogeneity was judged to be low ($I^2 = 0\%$, $P = 0.92$).

Need for re-admission

Analysis of 1334 patients from six studies [13–18] showed that ERAS protocols and non-ERAS protocols were similar in terms of need for re-admission (risk difference: −0.01, 95% CI − 0.04, 0.02, $P = 0.50$). The reported between-study heterogeneity was judged to be low ($I^2 = 7\%$, $P = 0.37$).

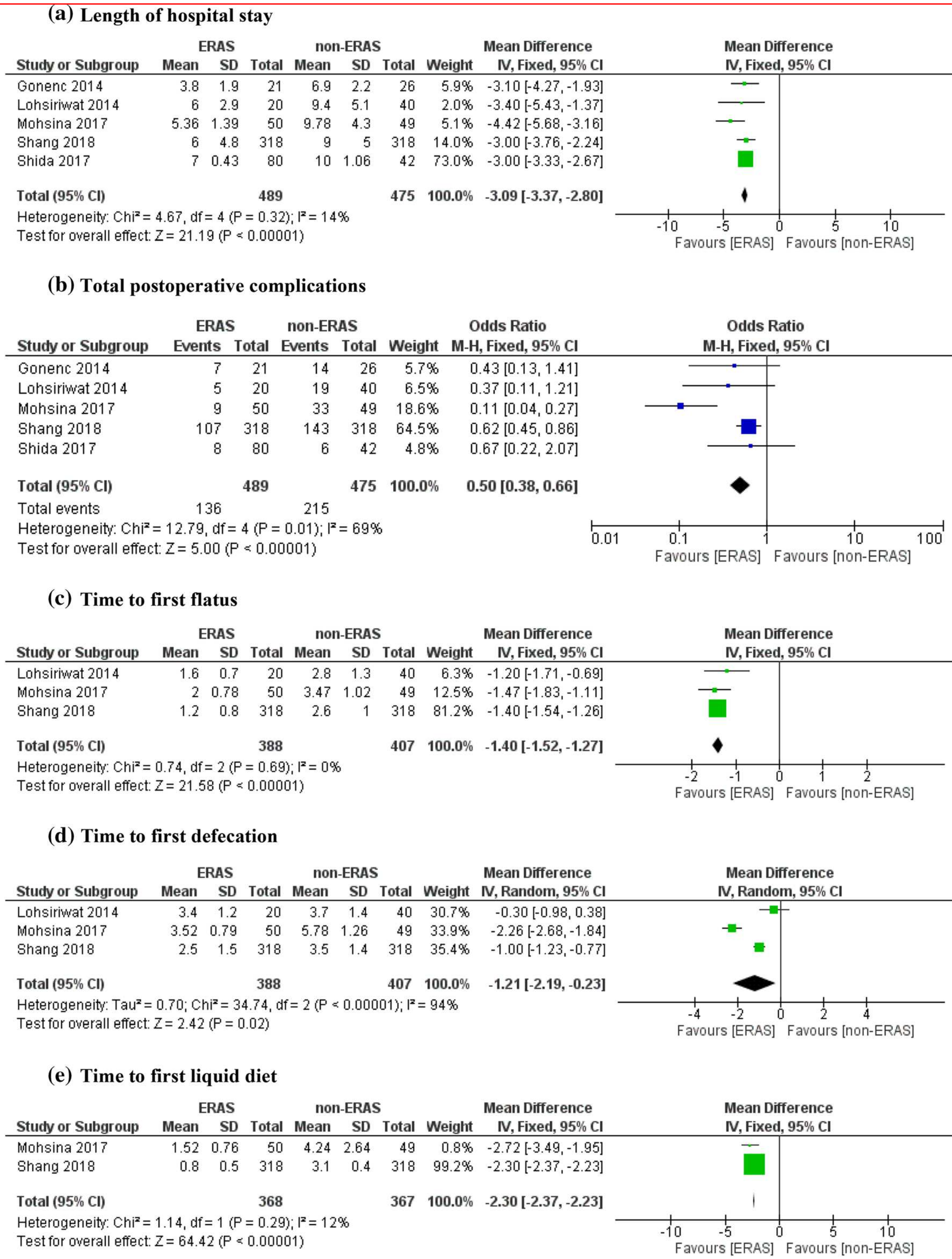
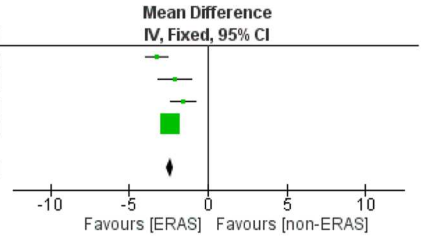


Fig. 3 Forest plots of the comparisons of outcomes between the ERAS and non-ERAS groups: **a** length of hospital stay; **b** total post-operative complications; **c** time to first flatus; **d** time to first defecation; **e** time to first liquid diet; **f** time to first solid diet; **g** major complications; **h** pulmonary complications; **i** paralytic ileus; **j** surgical site infection; **k** 30-day mortality; **l** need for re-admission; **m** need for re-operation

(f) Time to first solid diet

Study or Subgroup	ERAS Mean	ERAS SD	ERAS Total	non-ERAS Mean	non-ERAS SD	non-ERAS Total	Weight	Mean Difference IV, Fixed, 95% CI
Gonenc 2014	1.55	1.27	21	4.82	1.28	26	8.6%	-3.27 [-4.00, -2.54]
Lohsiriwat 2014	3.4	1.7	20	5.5	2.4	40	4.2%	-2.10 [-3.15, -1.05]
Mohsina 2017	2.64	1.08	50	4.24	2.64	49	7.3%	-1.60 [-2.40, -0.80]
Shang 2018	3.2	1.5	318	5.6	1.6	318	79.9%	-2.40 [-2.64, -2.16]
Total (95% CI)			**409**			**433**	**100.0%**	**-2.40 [-2.62, -2.19]**

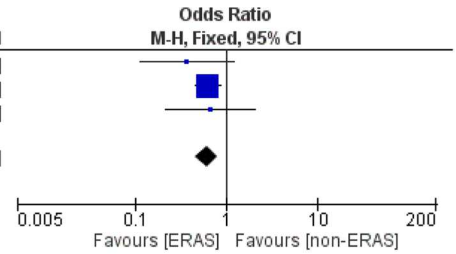
Heterogeneity: Chi² = 9.59, df = 3 (P = 0.02); I² = 69%
Test for overall effect: Z = 21.87 (P < 0.00001)



(g) Major complications

Study or Subgroup	ERAS Events	ERAS Total	non-ERAS Events	non-ERAS Total	Weight	Odds Ratio M-H, Fixed, 95% CI
Lohsiriwat 2014	5	20	19	40	8.5%	0.37 [0.11, 1.21]
Shang 2018	107	318	143	318	85.1%	0.62 [0.45, 0.86]
Shida 2017	8	80	6	42	6.4%	0.67 [0.22, 2.07]
Total (95% CI)		**418**		**400**	**100.0%**	**0.60 [0.45, 0.81]**
Total events	120		168			

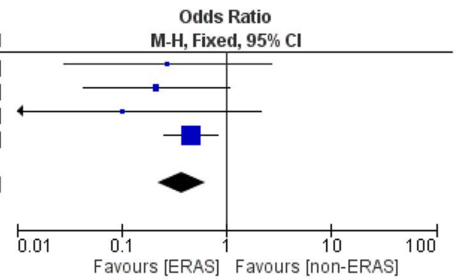
Heterogeneity: Chi² = 0.72, df = 2 (P = 0.70); I² = 0%
Test for overall effect: Z = 3.34 (P = 0.0008)



(h) Pulmonary complications

Study or Subgroup	ERAS Events	ERAS Total	non-ERAS Events	non-ERAS Total	Weight	Odds Ratio M-H, Fixed, 95% CI
Gonenc 2014	1	21	4	26	7.3%	0.28 [0.03, 2.67]
Mohsina 2017	2	50	8	49	16.6%	0.21 [0.04, 1.06]
Shida 2017	0	80	2	42	7.0%	0.10 [0.00, 2.15]
Wisely 2016	20	201	33	169	69.1%	0.46 [0.25, 0.83]
Total (95% CI)		**352**		**286**	**100.0%**	**0.38 [0.22, 0.64]**
Total events	23		47			

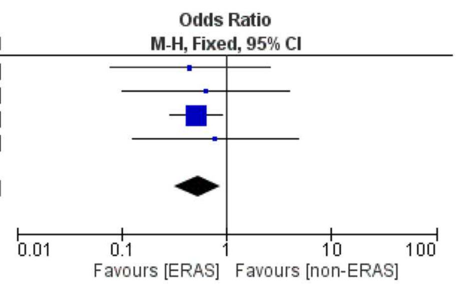
Heterogeneity: Chi² = 1.65, df = 3 (P = 0.65); I² = 0%
Test for overall effect: Z = 3.61 (P = 0.0003)



(i) Paralytic ileus

Study or Subgroup	ERAS Events	ERAS Total	non-ERAS Events	non-ERAS Total	Weight	Odds Ratio M-H, Fixed, 95% CI
Gonenc 2014	2	21	5	26	9.5%	0.44 [0.08, 2.55]
Mohsina 2017	2	50	3	49	6.9%	0.64 [0.10, 4.00]
Shang 2018	19	318	35	318	77.6%	0.51 [0.29, 0.92]
Shida 2017	3	80	2	42	6.0%	0.78 [0.13, 4.86]
Total (95% CI)		**469**		**435**	**100.0%**	**0.53 [0.32, 0.88]**
Total events	26		45			

Heterogeneity: Chi² = 0.26, df = 3 (P = 0.97); I² = 0%
Test for overall effect: Z = 2.45 (P = 0.01)



(j) Surgical site infection

Study or Subgroup	ERAS Events	ERAS Total	non-ERAS Events	non-ERAS Total	Weight	Odds Ratio M-H, Fixed, 95% CI
Gonenc 2014	2	21	3	26	4.5%	0.81 [0.12, 5.34]
Mohsina 2017	6	50	16	49	26.2%	0.28 [0.10, 0.80]
Wisely 2016	22	201	39	169	69.4%	0.41 [0.23, 0.72]
Total (95% CI)		**272**		**244**	**100.0%**	**0.39 [0.24, 0.64]**
Total events	30		58			

Heterogeneity: Chi² = 0.97, df = 2 (P = 0.61); I² = 0%
Test for overall effect: Z = 3.80 (P = 0.0001)

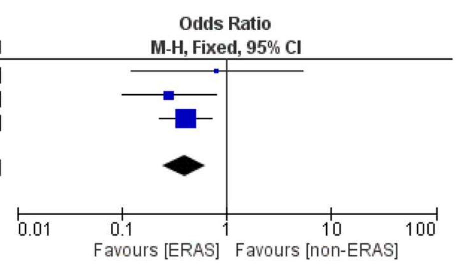


Fig. 3 continued

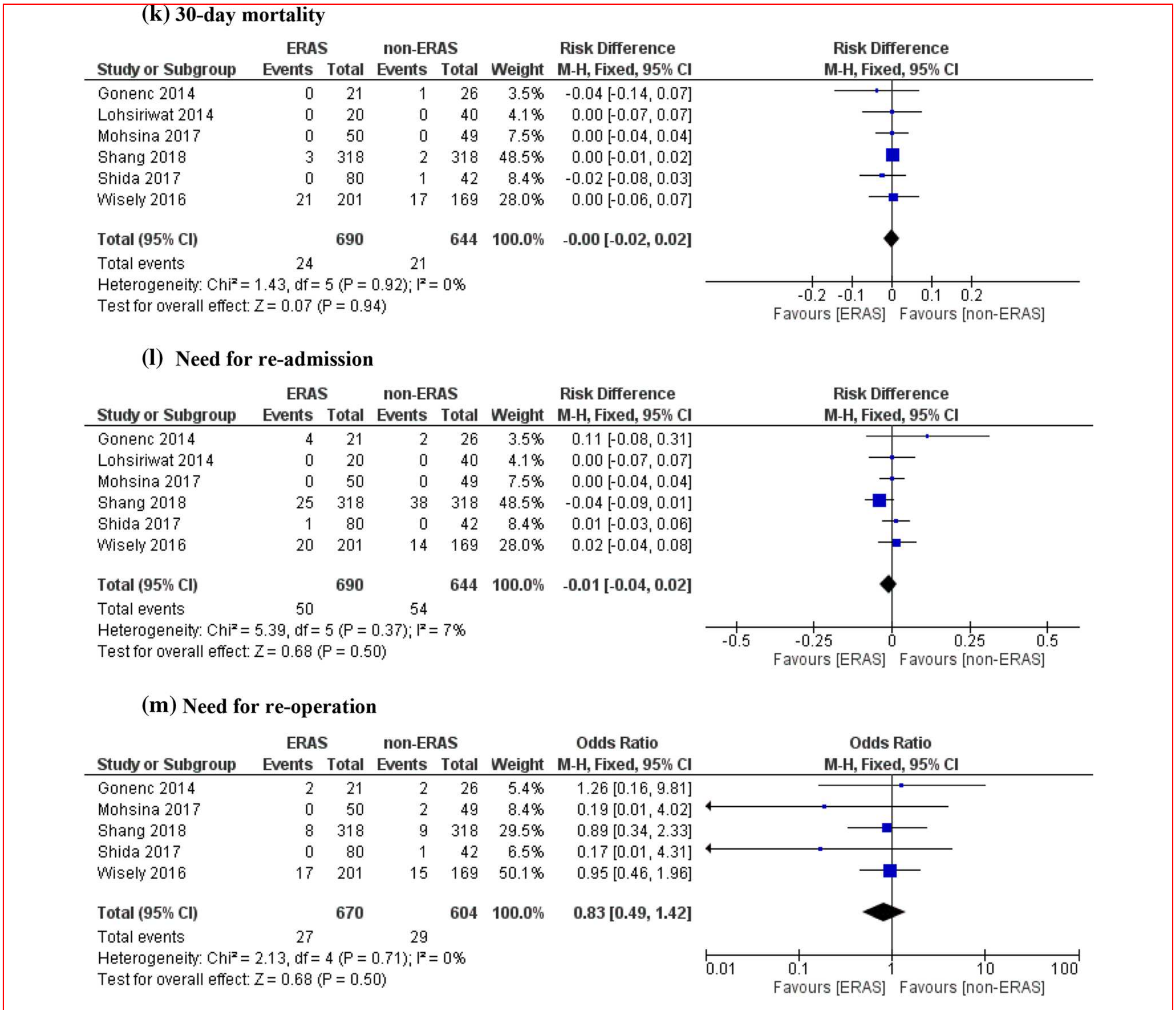


Fig. 3 continued

Need for re-operation

Analysis of 1274 patients from five studies [13–17] showed that ERAS protocols and non-ERAS protocols were similar in terms of need for re-operation (odds ratio: 0.83, 95% CI 0.49, 1.42, $P = 0.50$). The reported between-study heterogeneity was judged to be low ($I^2 = 0\%$, $P = 0.71$).

Additional analyses

Sensitivity analyses

The outcomes presented by a minimum number of four comparative studies were qualified for sensitivity analyses. First set of analysis showed that the results stayed unaffected when RRs, ORs and RDs were computed independently. Eliminating one study at a time in the second set of analyses did not affect the results. Application of fixed effect and random effects modelling in the third set of analyses did not affect the results.

Randomised controlled trials

Analysis of 146 patients from two RCTs [14, 17] showed that ERAS protocols resulted in shorter post-operative time to first flatus (mean difference: −1.47, 95% CI −1.83, −1.11, $P < 0.00001$), time to first defecation (mean difference: −2.26, 95% CI −2.68, −1.84, $P < 0.00001$), time to first oral liquid diet (mean difference: −2.72, 95% CI −3.49, −1.95, $P < 0.00001$), time to first oral solid diet (mean difference: −2.51, 95% CI −3.05, −1.97, $P < 0.00001$) and length of hospital stay (mean difference: −3.71, 95% CI −4.57, −2.85, $P < 0.00001$). ERAS protocols resulted in lower risks of total complications (odds ratio: 0.18, 95% CI 0.09, 0.37, $P < 0.00001$), pulmonary complications (odds ratio: 0.23, 95% CI 0.06, 0.86, $P = 0.03$) and surgical site infection (odds ratio: 0.36, 95% CI 0.15, 0.88, $P = 0.03$). Both ERAS and non-ERAS protocols resulted in similar risk of paralytic ileus (odds ratio: 0.52, 95% CI 0.15, 1.85, $P = 0.32$), risk of 30-day mortality (risk difference: −0.01, 95% CI − 0.06, 0.03, $P = 0.59$), need for re-admission (risk difference: 0.04, 95% CI − 0.03, 0.10, $P = 0.30$) and need for re-operation (odds ratio: 0.61, 95% CI 0.13, 2.96, $P = 0.54$).

Observational studies

Analysis of 1188 patients from four observational studies [13, 15, 16, 18] showed that ERAS protocols resulted in shorter post-operative time to first flatus (mean difference: −1.39, 95% CI −1.52, −1.25, $P < 0.00001$), time to first defecation (mean difference: −0.73, 95% CI −1.40, − 0.06, $P = 0.03$), time to first oral liquid diet (mean difference: −2.30, 95% CI −2.37, −2.23, $P < 0.00001$), time to first oral solid diet (mean difference: 2.39, 95% CI −2.62, −2.15, $P < 0.00001$) and length of hospital stay (mean difference: −3.01, 95% CI −3.31, −2.71, $P < 0.00001$). ERAS protocols resulted in lower risks of total complications (odds ratio: 0.60, 95% CI 0.45, 0.81, $P = 0.0008$), major complications (odds ratio: 0.60, 95% CI 0.45, 0.81, $P = 0.0008$), pulmonary complications (odds ratio: 0.42, 95% CI 0.24, 0.76, $P = 0.004$), paralytic ileus (odds ratio: 0.53, 95% CI 0.31, 0.93, $P = 0.03$) and surgical site infection (odds ratio: 0.41, 95% CI 0.23, 0.72, $P = 0.002$). Both ERAS and non-ERAS protocols resulted in similar risk of 30-day mortality (risk difference: 0.00, 95% CI − 0.02, 0.02, $P = 0.95$), need for re-admission (risk difference: −0.02, 95% CI − 0.05, 0.02, $P = 0.33$) and need for re-operation (odds ratio: 0.87, 95% CI 0.49, 1.53, $P = 0.62$).

Subgroup analyses (Table 4)

Emergency operation for visceral perforation Overall, 146 patients underwent emergency operation for visceral perforation. ERAS protocols resulted in shorter post-operative time to first flatus (mean difference: −1.47, 95% CI −1.83, −1.11, $P < 0.00001$), time to first defecation (mean difference: −2.26, 95% CI −2.68, −1.84, $P < 0.00001$), time to first oral liquid diet (mean difference: −2.72, 95% CI −3.49, −1.95, $P < 0.00001$), time to first oral solid diet (mean difference: −2.51, 95% CI −3.05, −1.97, $P < 0.00001$) and length of hospital stay (mean difference: −3.71, 95% CI −4.57, −2.85, $P < 0.00001$). ERAS protocols resulted in lower risks of total complications (odds ratio: 0.18, 95% CI 0.09, 0.37, $P < 0.00001$), pulmonary complications (odds ratio: 0.23, 95% CI 0.06, 0.86, $P = 0.03$) and surgical site infection (odds ratio: 0.36, 95% CI 0.15, 0.88, $P = 0.03$). Both ERAS and non-ERAS protocols resulted in similar risk of paralytic ileus (odds ratio: 0.52, 95% CI 0.15, 1.85, $P = 0.32$), risk of 30-day mortality (risk difference: −0.01, 95% CI − 0.06, 0.03, $P = 0.59$), need for re-admission (risk difference: 0.04, 95% CI − 0.03, 0.10, $P = 0.30$) and need for re-operation (odds ratio: 0.61, 95% CI 0.13, 2.96, $P = 0.54$).

Emergency operation for bowel obstruction Overall, 818 patients underwent emergency operation for bowel obstruction. ERAS protocols resulted in shorter post-operative time to first flatus (mean difference: −1.39, 95% CI −1.52, −1.25, $P < 0.00001$), time to first defecation (mean difference: −0.73, 95% CI −1.40, − 0.06, $P = 0.03$), time to first oral liquid diet (mean difference: −2.30, 95% CI −2.37, −2.23, $P < 0.00001$), time to first oral solid diet (mean difference: 2.39, 95% CI −2.62, −2.15, $P < 0.00001$) and length of hospital stay (mean difference: −3.01, 95% CI −3.31, −2.71, $P < 0.00001$). ERAS protocols resulted in lower risks of total complications (odds ratio: 0.60, 95% CI 0.45, 0.81, $P = 0.0008$), major complications (odds ratio: 0.60, 95% CI 0.45, 0.81, $P = 0.0008$) and paralytic ileus (odds ratio: 0.53, 95% CI 0.31, 0.93, $P = 0.03$). Both ERAS and non-ERAS protocols resulted in similar risk of pulmonary complications (odds ratio: 0.10, 95% CI 0.00, 2.15, $P = 0.14$), risk of 30-day mortality (risk difference: −0.00, 95% CI − 0.02, 0.01, $P = 0.92$), need for re-admission (risk difference: −0.03, 95% CI − 0.07, 0.01, $P = 0.11$) and need for re-operation (odds ratio: 0.76, 95% CI 0.30, 1.88, $P = 0.55$).

Discussion

In this study, analysis of the outcomes related to 1334 patients from six comparative studies showed that ERAS protocols resulted in favourable outcomes in emergency settings as indicated by reduced post-operative complications, accelerated recovery of bowel function, and shorter length of hospital stay without increasing the need for re-admission or re-operation. The sensitivity and subgroup analyses confirmed the consistency of the results.

Although the impact of ERAS protocols on post-operative outcomes in elective settings has been investigated by previous meta-analyses, this is the first meta-analysis in the literature evaluating ERAS protocols in emergency settings. Our results are comparable with the evidence provided by previously published studies in elective settings.

Table 4 Results of subgroup analyses

Outcomes	Randomised controlled trials		Observational studies		Visceral perforation		Bowel obstruction	
	Summary measure (95% CI)	*P* value	Summary measure (95% CI)	*P* value	Summary measure (95% CI)	*P* value	Summary measure (95% CI)	*P* value
Length of hospital stay	MD: −3.71 (4.57, − 2.85)	<0.00001	MD: −3.01 (− 3.31, − 2.71)	<0.00001	MD: −3.71 (4.57, − 2.85)	<0.00001	MD: −3.01 (− 3.31, − 2.71)	<0.00001
Total post-operative complications	OR: 0.18 (0.09, 0.37)	<0.00001	OR: 0.60 (0.45, 0.81)	0.0008	OR: 0.18 (0.09, 0.37)	<0.00001	OR: 0.60 (0.45, 0.81)	0.0008
Time to first flatus	MD: −1.47 (− 1.83, − 1.11)	<0.00001	MD: −1.39 (− 1.52, − 1.25)	<0.00001	MD: −1.47 (− 1.83, − 1.11)	<0.00001	MD: −1.39 (− 1.52, − 1.25)	<0.00001
Time to first defecation	MD: −2.26 (− 2.68, − 1.84)	<0.00001	MD: −0.73 (− 1.40, − 0.06)	0.03	MD: −2.26 (− 2.68, − 1.84)	<0.00001	MD: −0.73 (− 1.40, − 0.06)	0.03
Time to first oral liquid diet	MD: −2.72 (− 3.49, − 1.95)	<0.00001	MD: −2.30 (− 2.37, − 2.23)	<0.00001	MD: −2.72 (− 3.49, − 1.95)	<0.00001	MD: −2.30 (− 2.37, − 2.23)	<0.00001
Time to first oral solid diet	MD: −2.51 (− 3.05, − 1.97)	<0.00001	MD: 2.39 (− 2.62, − 2.15)	<0.00001	MD: −2.51 (− 3.05, − 1.97)	<0.00001	MD: 2.39 (− 2.62, − 2.15)	<0.00001
Major complications	NR	NR	OR: 0.60 (0.45, 0.81)	0.0008	NR	NR	OR: 0.60 (0.45, 0.81)	0.0008
Pulmonary complications	OR: 0.23 (0.06, 0.86)	0.03	OR: 0.42 (0.24, 0.76)	0.004	OR: 0.23 (0.06, 0.86)	0.03	OR: 0.10 (0.00, 2.15)	0.14
Paralytic ileus	OR: 0.52 (0.15, 1.85)	0.32	OR: 0.53 (0.31, 0.93)	0.03	OR: 0.52 (0.15, 1.85)	0.32	OR: 0.53 (0.31, 0.93)	0.03
Surgical site infection	OR: 0.36 (0.15, 0.88)	0.03	OR: 0.41 (0.23, 0.72)	0.002	OR: 0.36 (0.15, 0.88)	0.03	NR	NR
30-Day mortality	RD: −0.01 (− 0.06, 0.03)	0.59	RD: 0.00 (− 0.02, 0.02)	0.95	RD: −0.01 (− 0.06, 0.03)	0.59	RD: −0.00 (− 0.02, 0.01)	0.92
Need for re-admission	RD: 0.04 (− 0.03, 0.10)	0.3	RD: −0.02 (− 0.05, 0.02)	0.33	RD: 0.04 (− 0.03, 0.10)	0.3	RD: −0.03 (− 0.07, 0.01)	0.11
Need for re-operation	OR: 0.61 (0.13, 2.96)	0.54	OR: 0.87 (0.49, 1.53)	0.62	OR: 0.61 (0.13, 2.96)	0.54	OR: 0.76 (0.30, 1.88)	0.55

MD mean difference, *OR* odds ratio, *RD* risk difference, *CI* confidence interval, *NR* not reported

Ji et al. [19] completed a meta-analysis of 3694 patients from twenty comparative studies and concluded that ERAS protocols resulted in improved complication rates, better post-operative recovery and shorter hospital stay in elective pancreatic surgery. Wang et al., in another meta-analysis [20], reached similar conclusions in elective gastric cancer surgery. Other studies have reported comparable findings in patients undergoing hepatectomy [21], oesophageal cancer surgery [22] and colorectal surgery [23].

Although some of the preoperative components of ERAS protocols (e.g. nutritional support and carbohydrate loading) cannot be achieved in emergency setting, most components of ERAS protocols are considered applicable and appropriate in emergency setting. Full preoperative counselling, which is known to reduce post-operative stress, pain and anxiety [24], may not be possible in emergency setting; nevertheless, information such as details of procedure, possible perioperative complications, need for creation of stoma and length of hospitalisation can be communicated with patients and their family before the procedure. On the other hand, although complete optimisation of medical conditions cannot be achieved in emergency setting, objective intravenous fluid and antibiotic resuscitation in emergency major abdominal surgery are crucial and feasible [25]. Apart from these, the rest of intraoperative and post-operative components of ERAS protocols [26–31] are achievable in emergency settings. Consistent with the above, our results also support the applicability of the above components of ERAS protocols in emergency general surgery setting.

Use of ERAS protocols in emergency setting may face some barriers postoperatively. The critically unwell patients undergoing emergency abdominal procedures may require longer period of post-operative ventilation and circulation supports in intensive care unit compared to those undergoing minor emergency abdominal procedures. This would limit early mobilisation, early removal of drains or catheters and early enteral nutrition. Although the available data from the included studies do not support this argument as almost all studies demonstrated feasibility of the above components of ERAS protocols, we could not perform subgroup analysis for patients who were critically unwell postoperatively requiring high level of ventilation and circulation supports. Therefore, applicability of ERAS protocols in this subgroup needs further evaluation in future studies.

In the current study, an objective approach was followed to report the best available comparative evidence and to examine the possibility of bias in the current evidence. Our findings stayed unaffected during sensitivity analyses, separate analyses of randomised and non-randomised studies and subgroup analyses. These would strongly support our conclusions of the published evidence. However, this study was associated with some limitations. Only six eligible studies were found after applying the search strategy in the aforementioned databases of which four were non-randomised observational studies, and their results may be associated with inevitable selection bias. Finally, because less than 10 comparative studies were qualified for inclusion; publication bias could not be examined.

Conclusions

Although ERAS protocols are commonly used in elective settings, they are associated with favourable outcomes in emergency settings as indicated by reduced post-operative complications, accelerated recovery of bowel function and shorter hospital stay without increasing need for re-admission or re-operation. There should be an effort to incorporate ERAS protocols into emergency abdominal surgery settings.

Author contributions SH was the lead of the project and designed the study. SH and SH performed the statistical analyses required in this study and wrote the first draft of the article. All authors contributed to collection of data, revision of the first draft and approving the final version of the article

Funding There were no funding resources for this study

Compliance with ethical standards

Conflict of interest All authors confirmed that they had no conflict of interest.

Ethical approval Ethical approval was not required for this study.

Appendix

Search	Search description	
Search #1	enhance* near2 recovery	T, A, K
Search #2	ERAS	T, A, K
Search #3	Search #1 OR Search #2	Combined with OR
Search #4	emergency near2 surgery	T, A, K
Search #5	MeSH term: [laparotomy]	explode all trees
Search #6	emergency near2 laparotomy	T, A, K
Search #7	Search #4 OR Search #5 OR Search #6	Combined with OR
Search #8	Search #3 AND Search #7	Combined with AND

T, A, K: titles, abstracts, keywords

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Full text 10

Article 10. Impact of weekend effect on postoperative mortality in patients undergoing emergency General surgery procedures: Meta-analysis of prospectively maintained national databases across the world

Citation: **Hajibandeh S**, Hajibandeh S, Satyadas T. Impact of weekend effect on postoperative mortality in patients undergoing emergency General surgery procedures: Meta-analysis of prospectively maintained national databases across the world. Surgeon. 2020 Aug;18(4):231-240. doi: 10.1016/j.surge.2019.09.006.

Contribution: Conception, design, data collection, data analysis, write up, and critical revision

Impact of weekend effect on postoperative mortality in patients undergoing emergency General surgery procedures: Meta-analysis of prospectively maintained national databases across the world

Shahab Hajibandeh [a,*,1], *Shahin Hajibandeh* [b,1], *Thomas Satyadas* [c]

[a] *Department of General Surgery, Glan Clwyd Hospital, Rhyl, Denbighshire, UK*
[b] *Department of General Surgery, Sandwell and West Birmingham Hospitals NHS Trust, Birmingham, UK*
[c] *Department of Hepatobiliary and Pancreatic Surgery, Manchester Royal Infirmary Hospital, Manchester, UK*

ARTICLE INFO

Article history:
Received 28 July 2019
Received in revised form
8 September 2019
Accepted 14 September 2019
Available online 18 October 2019

Keywords:
Weekend
General surgery
Emergency surgery
Mortality

ABSTRACT

Objectives: to investigate the impact of weekend effect on postoperative mortality in patients undergoing emergency General Surgery operations across the world.
Methods: A search of electronic information sources was conducted to identify all studies investigating the weekend effect in patients undergoing emergency General Surgery operations. Emergency operation during weekend was considered as exposure of interest, emergency operation during weekdays as comparison of interest, and postoperative mortality as the outcome of interest. Random or fixed effects modelling were applied to calculate pooled outcome data.
Results: Overall, 10 studies, enrolling 394,646 patients, were included. Worldwide, emergency General surgery operation during weekend was associated with a higher risk of postoperative mortality compared to weekdays (OR: 1.08, 95% CI 1.02, 1.14, P = 0.008, moderate quality evidence). The weekend effect was variable across the world. Although emergency operation during weekend was associated with a higher risk of postoperative mortality in the USA (OR: 1.12, 95% CI 1.01, 1.24, P = 0.03, moderate quality evidence) and Europe (OR: 1.37, 95% CI 1.11, 1.69, P = 0.003, moderate quality evidence), there was no difference in postoperative mortality between weekend and weekday groups in the UK (OR: 1.04, 95% CI 0.97, 1.11, P = 0.30, moderate quality evidence) and South Africa (OR: 0.79, 95% CI 0.44, 1.42, P = 0.43, moderate quality evidence).
Conclusions: The weekend effect in emergency General Surgery is variable across the world. Although it seems to be significant in the USA and Europe, it does not increase the risk of postoperative mortality in the UK. Future studies should focus on differences in staffing levels and available resources at weekends in emergency General surgery settings across the world.

Introduction

The ‘weekend effect’ refers to variation in clinical outcomes for patients admitted to hospital during weekends when compared with weekdays. It has been shown that admission on a weekend is associated with increased risk of mortality compared with a weekday.[1,2] This weekend effect has been demonstrated for a wide range of medical and surgical

* *Corresponding author*.
E-mail address: [redacted] (S. Hajibandeh).
[1] Equally contributed to this paper and joined first authorship is proposed.
https://doi.org/10.1016/j.surge.2019.09.006
1479-666X/

illnesses including gastrointestinal bleeding, myocardial infarction, abdominal aortic aneurysm and pulmonary embolism.[3–7] There are possible explanations for the observed weekend effect.[8–13] It has been argued that patients admitted at a weekend may be clinically more unwell and differences in case mix or severity of illness may result in worse outcomes.[13] Moreover, differences in staffing levels and reduced availability of resources such as imaging or pathology services at weekends may cause delays in diagnostics and procedures.[8–12]

Although the weekend effect has been investigated in various medical and surgical settings, the effect of operating during weekend on postoperative mortality in patients undergoing emergency General Surgery procedures is not well-established. In view of this, a systematic review and meta-analysis was perfomed to investigate the impact of weekend effect on postoperative mortality in patients undergoing emergency General Surgery operations across the world.

Methods

This systematic review was performed according to an agreed predefined protocol and was conducted and presented according to Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) statement standards.[14]

Criteria for considering studies for this review

Types of studies

All observational studies investigating the impact of weekend effect on postoperative mortality in patients undergoing emergency General Surgery operations were included.

Types of participants

The study population comprised of participants of any age and gender undergoing emergency General Surgery procedures. The procedures of interest included emergency segmental or total colectomy, small bowel resection, cholecystectomy, operative management of perforated viscus, lysis of peritoneal adhesions, appendectomy, and laparotomy.

Types of exposures

Exposure of interest. Emergency General Surgery operation during weekend was considered as exposure of interest. The weekend was defined as Saturday, Sunday and public holidays.

Comparison of interest. Emergency General Surgery operation during weekdays was considered as comparison of interest. The weekdays was defined as Monday, Tuesday, Wednesday, Thursday and Friday.

Types of outcome measures

Postoperative mortality was considered as outcome of interest.

Search methods for identification of studies

Electronic searches. Two authors independently searched the following electronic databases: MEDLINE, EMBASE, CINAHL, and the Cochrane Central Register of Controlled Trials (CENTRAL). The last search was run on 15 May 2019. Thesaurus headings, search operators and limits in each of the above databases were adapted accordingly. The literature search strategy is outlined in Appendix I. In addition, World Health Organization International Clinical Trials Registry (http://apps.who.int/trialsearch/), ClinicalTrials.gov (http://clinicaltrials.gov/) and ISRCTN Register (http://www.isrctn.com/) were searched for details of ongoing and unpublished studies. No language restrictions were applied in our search strategies.

Searching other resources. The bibliographic lists of relevant articles and reviews were searched for further potentially eligible trials.

Data collection and analysis

Selection of studies

The title and abstract of articles identified from the literature searches were assessed independently by two authors. The full-texts of relevant reports were retrieved and those articles that met the eligibility criteria of our review were selected. Any discrepancies in study selection were resolved by discussion between the authors. An independent third author was consulted in the event of disagreement.

Data extraction and management

An electronic data extraction spreadsheet was created in line with Cochrane's data collection form for intervention reviews. The spreadsheet was pilot-tested in randomly selected articles and was adjusted accordingly. The data extraction spreadsheet included: Study-related data (first author, year of publication, country of origin of the corresponding author, journal in which the study was published, study design, study size, clinical condition of the study participants, type of exposure and comparison), baseline demographic and clinical information of the included populations, and outcome data. Two review authors independently collected and recorded data in the data extraction spreadsheet and disagreements were resolved by discussion. If no agreement could be reached, a third review author was consulted.

Assessment of risk of bias in included studies

Two authors independently assessed the methodological quality and risk of bias of the included articles using the Risk Of Bias In Non-randomized Studies – of Interventions (ROBINS-I) assessment tool. The ROBINS-I tool assesses methodological quality of studies in terms of the following domains: bias due to confounding, bias in selection of participants into the study, bias in classification of interventions, bias due to deviations from intended intervention, bias due to missing data, bias in measurement of outcomes, and bias in selection of the reported result. Disagreements were resolved by discussion between the reviewers. If no agreement could be reached, a third author acted as an adjudicator. A risk of bias graph was constructed to present the results.

Measures of treatment effect

The outcome of this study (postoperative mortality) was dichotomous variable; therefore, the odds ratio (OR) was calculated as the summary measure. The OR is the odds of an event in the weekend group compared to the weekday group. An OR of less than one would favour the weekend group and an OR of more than one would favour the weekday group.

Unit of analysis

The individual patient was used as the unit of analysis in our review.

Assessment of heterogeneity

Heterogeneity among the studies was assessed using the Cochran Q test ($\chi 2$).[15] Inconsistency was quantified by calculating I^2 and was interpreted using the following guide: 0%–50% may represent low heterogeneity, 50%–75% may represent moderate heterogeneity and 75%–100% may represent high heterogeneity.

Assessment of reporting biases

Funnel plot was constructed and its symmetry was evaluated to visually assess publication bias when postoperative mortality was reported by at least 10 studies.

Data synthesis

The Review Manager 5.3 software was used for data synthesis.[15] The extracted data were entered into Review Manager by an independent reviewer and checked by a second independent reviewer. Random or fixed effects modelling were used as appropriate for analysis; random effects models were used if considerable heterogeneity was found among the studies.[15] The fixed-effect model provides a result that may be viewed as a 'typical intervention effect' from the studies included in the analysis and was used in case of low heterogeneity. The random-effects model involves an assumption that the effects being estimated in the different studies are not identical and was used in case of considerable heterogeneity.[15] The results were reported in a forest plot with 95% confidence intervals (CIs). Information about dropouts, withdrawals, and other missing data were recorded and, if not reported, we contacted the study authors where possible. The analysis was based on intention-to-treat data from the individual clinical studies.

Sensitivity and subgroup analyses

In order to explore potential sources of heterogeneity and assess the robustness of our results, additional analyses were performed.[15] Sensitivity analysis is a repeat of the primary analysis or meta-analysis, substituting alternative decisions or ranges of values for decisions that were arbitrary or unclear. The primary analysis was repeated using the random effects and fixed effect model. In addition, the risk ratio (RR) and risk difference (RD) were calculated instead of OR. The effect of each study on the overall effect size and heterogeneity was assessed by repeating the analysis after removing one study at a time. Separate analyses were planned for studies with low risk of bias to assess the change in direction of the effect size. Moreover, where possible, subgroup analysis based on geographical region of the included population and type of General surgery procedures was planned.

Results

Results of the search

Searches of electronic databases identified 168 articles. Among the studies that were identified through search of electronic databases, 156 articles were not relevant to the topic of this study and were excluded directly. The remaining 12 studies were relevant to the topic of this study and after assessing their full-texts, 2 more articles were excluded; one article was excluded as it was a review article and one article was excluded as it did not provide adequate data even after contacting the corresponding author. Therefore, 10 studies[15–24] were selected for this review. These included 10 retrospective observational studies,[15–24] enrolling 394,646 patients from prospectively maintained national databases. Overall, 100,393 patients underwent emergency surgery during weekend and 294,253 patients underwent emergency surgery during weekdays. The literature search flow chart and baseline characteristics of the included studies are demonstrated in Fig. 1 and Table 1, respectively.

Risk of bias in included studies

The summary and results of methodological quality assessment of the 10 observational studies[16–25] are demonstrated graphically in Fig. 2.

Postoperative mortality

Worldwide

The results from 10 studies,[16–25] enrolling 394,646 patients, showed that the risk of postoperative mortality was higher in the weekend group compared to the weekday group (OR: 1.08, 95% CI 1.02, 1.14, $P = 0.008$, moderate quality evidence). A moderate level of heterogeneity among the studies existed ($I^2 = 53\%$, $P = 0.03$). The likelihood of publication bias was low based on the funnel plot (Fig. 3).

USA

The results from 4 studies,[21,23–25] enrolling 271,579 patients, showed that the risk of postoperative mortality was higher in the weekend group compared to the weekday group (OR: 1.12, 95% CI 1.01, 1.24, $P = 0.03$, moderate quality evidence). A moderate level of heterogeneity among the studies existed ($I^2 = 59\%$, $P = 0.06$) (Fig. 4).

UK

The results from 3 studies,[16,18,20] enrolling 116,555 patients, showed that there was no difference in the risk of postoperative mortality between the weekend and weekday groups (OR: 1.04, 95% CI 0.97, 1.11, $P = 0.30$, moderate quality evidence). A low level of heterogeneity among the studies existed ($I^2 = 19\%$, $P = 0.29$) (Fig. 4).

Europe
The results from 2 studies,[17,22] enrolling 5950 patients, showed that the risk of postoperative mortality was higher in the weekend group compared to the weekday group (OR: 1.37, 95% CI 1.11, 1.69, $P = 0.003$, moderate quality evidence). A low level of heterogeneity among the studies existed ($I^2 = 0\%$, $P = 0.003$) (Fig. 4).

South Africa
The results from one study,[19] enrolling 562 patients, showed that there was no difference in the risk of postoperative mortality between the weekend and weekday groups (OR: 0.79, 95% CI 0.44, 1.42, $P = 0.43$, moderate quality evidence). A low level of heterogeneity among the studies existed ($I^2 = 19\%$, $P = 0.29$) (Fig. 4).

Sensitivity analyses

Sensitivity analyses were performed to assess the robustness of the results. Removing one study at a time did not change the direction of the effect size and the overall heterogeneity. The direction of the effect size remained unchanged when RRs or RDs were calculated. The separate analyses for studies with low or moderate risk of bias did not affect the direction of the effect size. The use of random effects or fixed effect models did not affect the direction of the effect size.

Subgroup analyses

Trauma patients
Overall, 14,205 patients underwent emergency procedure due to trauma. There was no difference in the risk of postoperative mortality between the weekend and weekday groups (OR: 0.79, 95% CI 0.44, 1.42, $P = 0.43$, moderate quality evidence). A low level of heterogeneity among the studies existed ($I^2 = 19\%$, $P = 0.29$).

Discussion

A comprehensive systematic review and meta-analysis was performed to investigate the impact of weekend effect on postoperative mortality in patients undergoing emergency General Surgery operations. Ten observational studies[16–25] enrolling 394,646 patients from prospectively maintained national databases were identified. The results of analyses showed that globally emergency General surgery operation during weekend was associated with a higher risk of postoperative mortality compared to emergency operation during weekdays; however, the weekend effect was variable across the world. Although emergency General surgery operation during weekend was associated with a higher risk of postoperative mortality in the USA and Europe, there was no difference in postoperative mortality between weekend and weekday groups in the UK and South Africa. A low to moderate level of heterogeneity among the studies existed. The

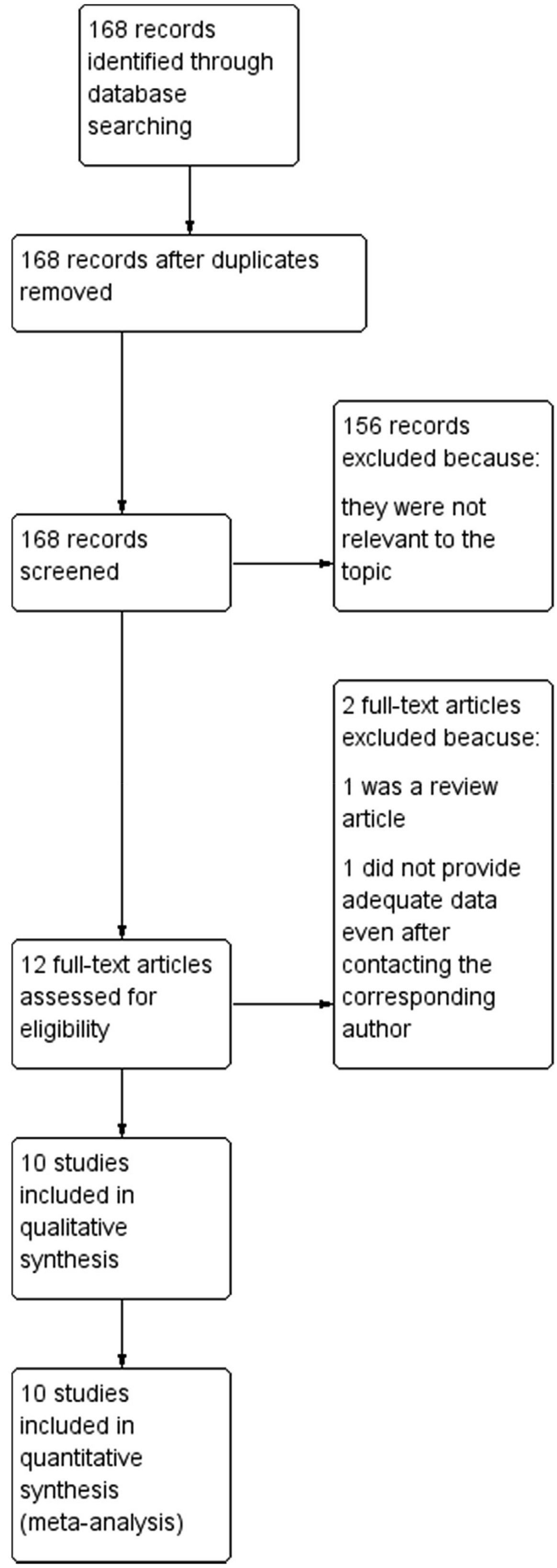


Fig. 1 – Study flow diagram.

Table 1 – Baseline Characteristics of the included studies.

First author, year	Country	Journal	Study design	Patient database source	Included populations	Sample size		
						Total	Weekend	Weekday
Nageswaran, 2019	UK	Ann R Coll Surg Engl	Retrospective observational study	National Emergency Laparotomy Audit (NELA) databases between 2014 and 2017	Patients undergoing emergency laparotomy	1717	587	1130
Huijts, 2018	Netherlands	Natl Compr Canc Netw	Retrospective observational study	Dutch ColoRectal Audit (DCRA) databases between 2012 and 2015	Patients undergoing emergency colorectal procedures	5224	830	4394
Gillies, 2017	UK	Br J Surg	Retrospective observational study	Information Services Division (ISD) Scotland between 2005 and 2007	Patients undergoing emergency General surgery procedures	50,844	19,345	31,499
Steenkamp, 2017	South Africa	Ann R Coll Surg Engl	Retrospective observational study	Hybrid electronic medical record system (HEMR) between 2012 and 2016	Patients undergoing emergency laparotomy for trauma	562	256	306
McCallum,2016	UK	Br J Surg	Retrospective observational study	Hospital Episode Statistics (HES) between 2000 and 2014	Patients undergoing emergency General surgery procedures	63,994	13,211	50,783
Zapf, 2015	USA	Surgery	Retrospective observational study	State Inpatient Database (SID) from Florida between 2007 and 2010	Patients undergoing emergency abdominal surgery	80,861	19,078	61,783
Knudsen,2015	Denmark	Acta Anaesthesiologica Scandinavica	Retrospective observational study	The Danish Clinical Register of Emergency Surgery (DCRES) between 2011 and 2013	Patients undergoing emergency surgery for perforated peptic ulcer	726	214	512
Ananthakrishnan, 2013	USA	Aliment Pharmacol Ther	Retrospective observational study	Nationwide Inpatient Sample (NIS) 2007	Patients undergoing emergency abdominal surgery	7112	1489	5623
Worni, 2012	USA	Arch Surg	Retrospective observational study	Nationwide Inpatient Sample (NIS) between 2002 and 2008.	Patients undergoing urgent surgery for acute diverticulitis	31,832	7066	24,766
Worni, 2012	USA	World J Surg	Retrospective observational study	Nationwide Inpatient Sample (NIS) between 1999 and 2008	Patients undergoing emergency appendicectomy	151,774	38,317	113,457

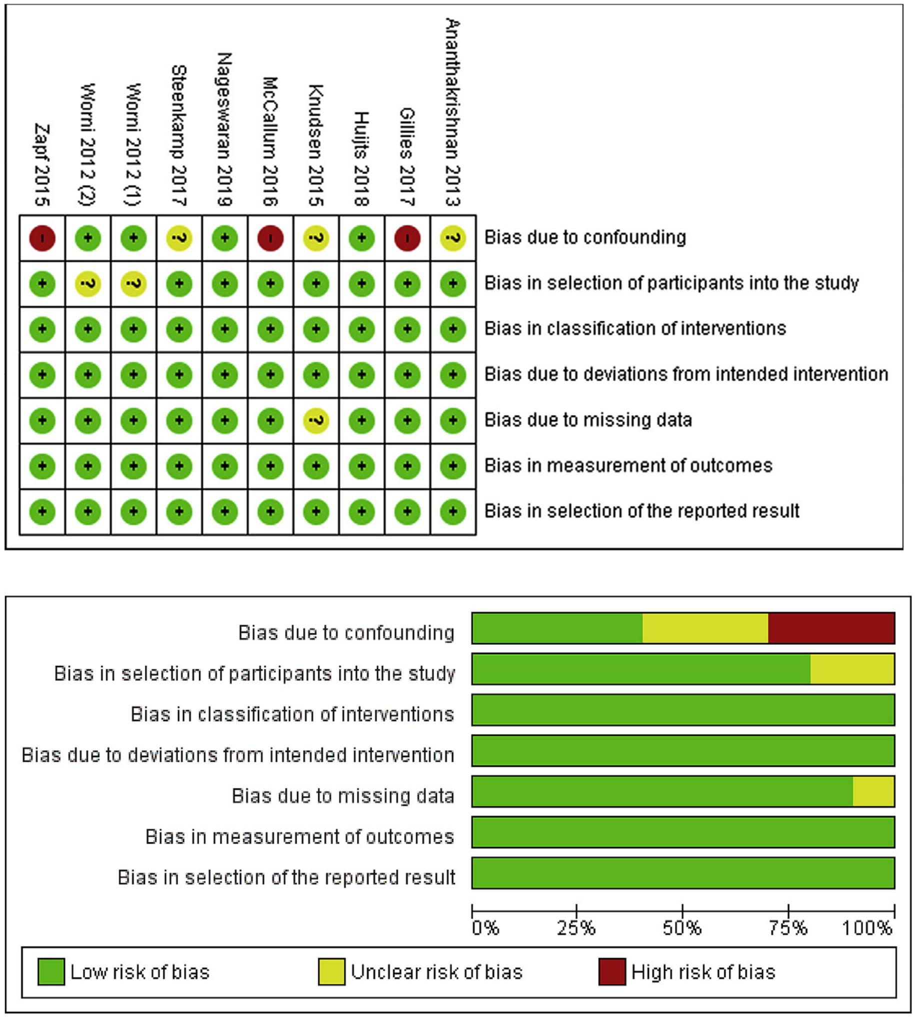


Fig. 2 – Risk of bias summary and graph showing authors' judgements about each risk of bias item for the 10 observational studies.

results remained consistent through sensitivity analyses. The quality of available evidence was moderate.

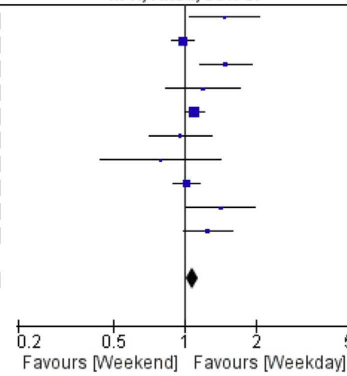
The increased postoperative mortality rate associated with operating during weekend has been attributed to various factors. It has been argued that patients presenting on weekends have more severe illness affecting the outcomes.[26] However, impact of weekend effect on mortality persisted even after adjusting for case-mix differences on the weekend in USA and Europe.[17,27] This may suggest that severity of illness may not be a contributing factor. Hospital resources are more limited on holidays and weekends; differences in staffing levels and reduced availability of resources such as imaging or pathology services at weekends may result in delays in diagnostics and procedures.[8–12] Considering that patients undergoing emergency General surgical procedures would often require high level of care, even small deficiencies in their quality of care may lead to adverse clinical outcomes. In the UK, weekend on-call surgical teams are often similar to the weekday emergency team, ensuring consistent coverage throughout the week and weekend. This may explain the findings that there was no difference in postoperative mortality between weekend and weekday groups in the UK. Moreover, recent improvements in healthcare within the UK including more rigorous management of sepsis, better access to intensive care beds and protocol-driven care for patients requiring emergency abdominal surgery might have controlled the weekend effect.[16]

Differences in staffing levels and availability of resources at weekends may explain the observed variability of weekend effect across the world; however, the current literature does not provide adequate evidence to compare the structure of on-call emergency General Surgery team on weekend in different countries and continents. This highlights a need for further studies focusing on differences in staffing levels and available resources at weekend in emergency General Surgery settings across the world.

In this review, a systematic approach was used to provide a summary of the best available comparative evidence and to assess the risk of bias of relevant studies. The results remained consistent through sensitivity analyses and the between-study heterogeneity was low to moderate. All of these, together with a very large sample size, would make the conclusions of this study from the best available evidence robust with low risk of type 2 or type 1 error. However, the

Study or Subgroup	Weekend Events	Weekend Total	Weekday Events	Weekday Total	Weight	Odds Ratio M-H, Fixed, 95% CI	A	B	C	D	E	F	G
Ananthakrishnan 2013	48	1489	125	5623	2.1%	1.47 [1.05, 2.05]	?	+	+	+	+	+	+
Gillies 2017	552	19345	916	31499	27.7%	0.98 [0.88, 1.09]	−	+	+	+	+	+	+
Huijts 2018	84	830	311	4394	3.6%	1.48 [1.15, 1.90]	+	+	+	+	+	+	+
Knudsen 2015	60	214	126	512	2.2%	1.19 [0.83, 1.71]	?	+	+	+	?	+	+
McCallum 2016	587	13211	2074	50783	33.5%	1.09 [0.99, 1.20]	−	+	+	+	+	+	+
Nageswaran 2019	72	587	144	1130	3.5%	0.96 [0.71, 1.30]	+	+	+	+	+	+	+
Steenkamp 2017	21	256	31	306	1.1%	0.79 [0.44, 1.42]	?	+	+	+	+	+	+
Worni 2012 (1)	324	7066	1118	24766	19.4%	1.02 [0.90, 1.15]	+	?	+	+	+	+	+
Worni 2012 (2)	51	38317	107	113457	2.2%	1.41 [1.01, 1.97]	+	?	+	+	+	+	+
Zapf 2015	95	19078	247	61783	4.7%	1.25 [0.98, 1.58]	−	+	+	+	+	+	+
Total (95% CI)		**100393**		**294253**	**100.0%**	**1.08 [1.02, 1.14]**							
Total events	1894		5199										

Heterogeneity: Chi² = 18.97, df = 9 (P = 0.03); I² = 53%
Test for overall effect: Z = 2.66 (P = 0.008)



Risk of bias legend
(A) Bias due to confounding
(B) Bias in selection of participants into the study
(C) Bias in classification of interventions
(D) Bias due to deviations from intended intervention
(E) Bias due to missing data
(F) Bias in measurement of outcomes
(G) Bias in selection of the reported result

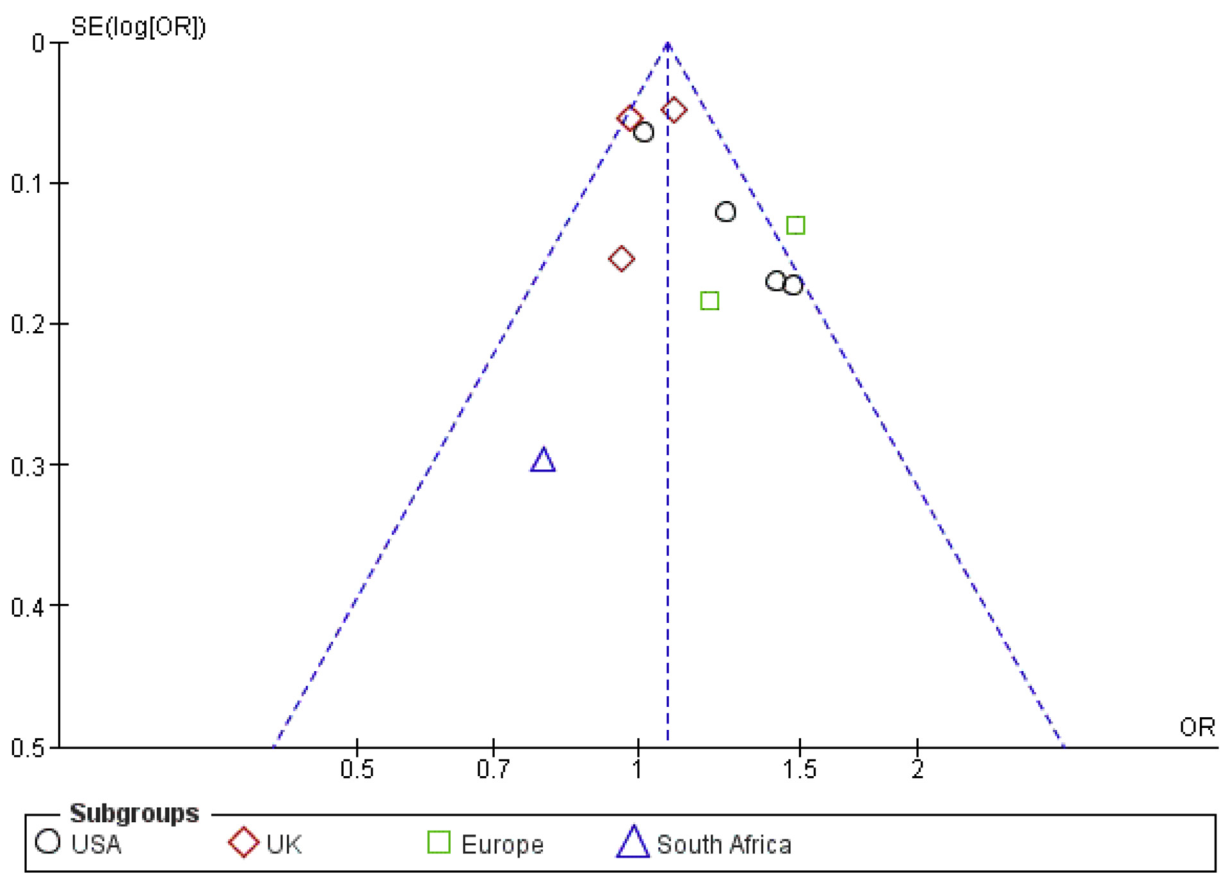
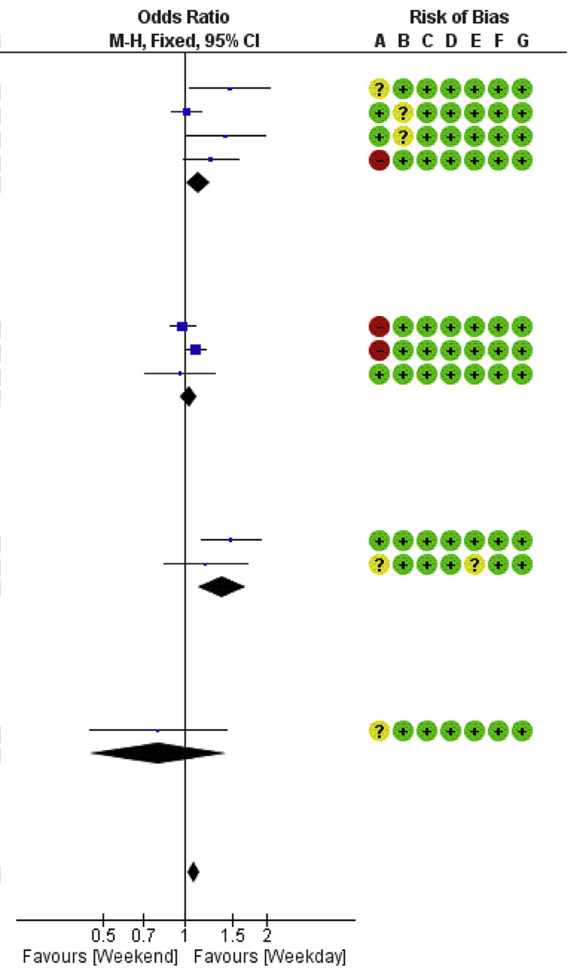


Fig. 3 – Forest plot and funnel plot of the comparison of postoperative mortality between the weekend and weekday groups.

Study or Subgroup	Weekend Events	Weekend Total	Weekday Events	Weekday Total	Weight	Odds Ratio M-H, Fixed, 95% CI
1.2.1 USA						
Ananthakrishnan 2013	48	1489	125	5623	2.1%	1.47 [1.05, 2.05]
Worni 2012 (1)	324	7066	1118	24766	19.4%	1.02 [0.90, 1.15]
Worni 2012 (2)	51	38317	107	113457	2.2%	1.41 [1.01, 1.97]
Zapf 2015	95	19078	247	61783	4.7%	1.25 [0.98, 1.58]
Subtotal (95% CI)		**65950**		**205629**	**28.4%**	**1.12 [1.01, 1.24]**
Total events	518		1597			
Heterogeneity: Chi² = 7.32, df = 3 (P = 0.06); I² = 59%						
Test for overall effect: Z = 2.17 (P = 0.03)						
1.2.2 UK						
Gillies 2017	552	19345	916	31499	27.7%	0.98 [0.88, 1.09]
McCallum 2016	587	13211	2074	50783	33.5%	1.09 [0.99, 1.20]
Nageswaran 2019	72	587	144	1130	3.5%	0.96 [0.71, 1.30]
Subtotal (95% CI)		**33143**		**83412**	**64.7%**	**1.04 [0.97, 1.11]**
Total events	1211		3134			
Heterogeneity: Chi² = 2.48, df = 2 (P = 0.29); I² = 19%						
Test for overall effect: Z = 1.04 (P = 0.30)						
1.2.3 Europe						
Huijts 2018	84	830	311	4394	3.6%	1.48 [1.15, 1.90]
Knudsen 2015	60	214	126	512	2.2%	1.19 [0.83, 1.71]
Subtotal (95% CI)		**1044**		**4906**	**5.8%**	**1.37 [1.11, 1.69]**
Total events	144		437			
Heterogeneity: Chi² = 0.91, df = 1 (P = 0.34); I² = 0%						
Test for overall effect: Z = 2.98 (P = 0.003)						
1.2.4 South Africa						
Steenkamp 2017	21	256	31	306	1.1%	0.79 [0.44, 1.42]
Subtotal (95% CI)		**256**		**306**	**1.1%**	**0.79 [0.44, 1.42]**
Total events	21		31			
Heterogeneity: Not applicable						
Test for overall effect: Z = 0.78 (P = 0.43)						
Total (95% CI)		**100393**		**294253**	**100.0%**	**1.08 [1.02, 1.14]**
Total events	1894		5199			
Heterogeneity: Chi² = 18.97, df = 9 (P = 0.03); I² = 53%						
Test for overall effect: Z = 2.66 (P = 0.008)						
Test for subgroup differences: Chi² = 7.95, df = 3 (P = 0.05), I² = 62.3%						



Risk of bias legend
(A) Bias due to confounding
(B) Bias in selection of participants into the study
(C) Bias in classification of interventions
(D) Bias due to deviations from intended intervention
(E) Bias due to missing data
(F) Bias in measurement of outcomes
(G) Bias in selection of the reported result

Fig. 4 – Subgroup analysis of the comparison of postoperative mortality between the weekend and weekday groups based on geographical region of the included population.

reported outcomes of this review should be viewed and interpreted in the context of inherent limitations. Firstly, the available evidence is derived from data from large administrative databases that may subject the results to unmeasured confounding bias. Moreover, the available data did not allow adjusting for case-mix differences and subgroup analyses based on type of procedures. Among the included studies, only one study reported the grade of operating surgeon. This did not allow subgroup analysis based on the grade of the operating surgeon. Moreover, the data from the included studies were limited to UK, USA, Europe and South Africa. This would limit our conclusions on the impact of weekend effect in other parts of the world. Nevertheless, considering the nature of this subject, performing a randomised controlled trial is not possible. On the other hand, performing prospective studies with very large sample size may be associated with significant challenges in terms of costs and practicalities and may not necessarily provide a higher level of evidence.[28] Therefore, regardless of the aforementioned limitations, meta-analysis of large administrative databases would still serve the best available evidence in this subject and may be used for robust conclusions.

Conclusions

The weekend effect in emergency General Surgery is variable across the world. Although it seems to be significant in the USA and Europe, it does not increase the risk of postoperative mortality in the UK. Considering that randomised trials are not practical and performing prospective studies are associated with challenges, meta-analysis of large administrative databases serves the best available evidence. Future studies should focus on differences in staffing levels and available resources at weekends in emergency General Surgery settings across the world.

Author contributions

Conception and design: SH, SH.
Data collection: SH, SH.
Analysis and interpretation: SH, SH, TS.
Writing the article: SH, SH.
Critical revision of the article: SH, SH, TS.
Final approval of the article: SH, SH, TS.
Statistical analysis: SH, SH.

Ethical approval

Not required.

Funding

This research received no specific grant from any funding agency in the public, commercial, or not-for-profit sectors.

Declaration of Competing Interest

There are no funding sources for this work and no conflicts of interest and financial disclosures for the authors.

Appendix I

Search No	Search strategy[†]
#1	weekend: TI,AB,KW
#2	weekend near2 effect: TI,AB,KW
#3	weekend-effect: TI,AB,KW
#4	#1 OR #2 OR #3
#5	emergency near 2 surgery: TI,AB,KW
#6	MeSH descriptor: [laparotomy] explode all trees
#7	general near 2 surgery: TI,AB,KW
#8	#5 OR #6 OR #7
#9	#4 AND #8

[†] This search strategy was adopted for following databases: MEDLINE, EMBASE, CINAHL and the Cochrane Central Register of Controlled Trials (CENTRAL)

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Full text 11

Article 11. Effect of surgeon's seniority and subspeciality interest on mortality after emergency laparotomy: A systematic review and meta-analysis

Citation: Al-Sarireh H, Al-Sarireh A, Mann K, Hajibandeh S, **Hajibandeh S**. Effect of surgeon's seniority and subspeciality interest on mortality after emergency laparotomy: A systematic review and meta-analysis. Colorectal Dis. 2024 Aug;26(8):1495-1504. doi: 10.1111/codi.17079.

Contribution: Conception, design, data collection, data analysis, write up, and critical revision

Received: 6 April 2024 | Revised: 28 May 2024 | Accepted: 31 May 2024

DOI: 10.1111/codi.17079

META-ANALYSIS

Effect of surgeon's seniority and subspeciality interest on mortality after emergency laparotomy: A systematic review and meta-analysis

Hashim Al-Sarireh[1] | Ahmad Al-Sarireh[2] | Karan Mann[3] | Shahin Hajibandeh[4] | Shahab Hajibandeh[3]

[1]University of Leeds, Leeds, UK

[2]University of Cambridge, Cambridge, UK

[3]Department of General Surgery, Morriston Hospital, Swansea, UK

[4]Department of General Surgery, Royal Stoke University Hospital, Stoke-on-Trent, UK

Correspondence
Shahab Hajibandeh, Department of Hepatobiliary and Pancreatic Surgery, Morriston Hospital, Swansea, UK.
Email: [redacted]

Abstract

Aim: To evaluate effect of surgeon's seniority (trainee surgeon vs. consultant surgeon) and surgeon's subspeciality interest on postoperative mortality in patients undergoing emergency laparotomy (EL).

Method: A systematic review was conducted and reported according to the Cochrane Handbook for Systematic Reviews and the PRISMA statement standards, respectively. We evaluated all studies comparing the risk of postoperative mortality in patients undergoing EL between (a) trainee surgeon and consultant surgeon, and (b) surgeon without and with subspeciality interest related to pathology. Random effects modelling was applied for the analyses. The certainty of evidence was assessed using the GRADE system.

Results: Analysis of 256 844 patients from 13 studies showed no difference in the risk of postoperative mortality between trainee-led and consultant-led EL (OR: 0.76, $p=0.12$). However, EL performed by a surgeon without subspeciality interest related to the pathology was associated with a higher risk of postoperative mortality compared with a surgeon with subspeciality interest (OR: 1.38, $p<0.00001$). In lower gastrointestinal (GI) pathologies, EL done by upper GI surgeons resulted in higher risk of mortality compared with lower GI surgeons (OR: 1.43, $p<0.00001$). In upper GI pathologies, EL done by lower GI surgeons resulted in higher risk of mortality compared with upper GI surgeons (OR: 1.29, $p=0.05$).

Conclusion: While confounding by indication cannot be excluded, level 2 evidence with moderate certainty suggests that trainee-led EL may not increase the risk of postoperative mortality but EL by a surgeon with subspeciality interest related to the pathology may reduce the risk of mortality.

KEYWORDS
emergency laparotomy, mortality, speciality, traineeship

Hashim Al-Sarireh and Ahmad Al-Sarireh are joint first authors.

PROSPERO registration number: CRD42024530160

INTRODUCTION

Emergency laparotomy carries a high risk of mortality and there are ongoing efforts to identify important predictors of mortality after emergency laparotomy [1]. Identifying the predictors of mortality allows accurate risk assessment and the reversible risk factors to be addressed where possible. The main predictors of mortality after emergency laparotomy include American Society of Anaesthesiologists (ASA) status [2], sarcopenia [1, 3], clinical frailty [3], age over 80 [4], peritoneal contamination [5], and need for bowel resection [5]. While the main focus of available literature has been on predictors related to severity of the underlying abdominal pathology and the physical status of the patient, the predictive significance of variables related to the operating surgeon is worth evaluating.

Two important variables related to operating surgeon may be surgeon's seniority and surgeon's subspeciality interest. Due to the modern shift toward competency-based training which aims to enhance both training and patient safety [6, 7], the number of emergency laparotomies performed independently by competent trainees is increasing; this raises an argument that performing a high risk and complex operation by a less experienced surgeon may negatively affect the outcomes [8]. On the other hand, there is also a modern shift toward subspecialization in elective general surgery, raising an argument that the safe emergency service may be impaired by reducing the exposure of surgeons to a broad range of surgical disciplines [9].

Colorectal pathologies constitute up to 50% of indications for emergency laparotomy [10], and many centres are moving toward having dual speciality emergency service meaning that lower gastrointestinal (GI) pathologies are likely to be operated by lower GI surgeons and upper GI pathologies are likely to be operated by upper GI surgeons [11]. This means that contribution to the emergency surgery rota has become an ever-increasing part of specialist colorectal surgeons and consequently, the Association of Coloproctology of Great Britain and Ireland (ACPGBI) has produced detailed evidence-based guidelines on the management and treatment of emergency colorectal conditions [12]. While such a shift toward subspecialization may seem reasonable based on the number of emergency colorectal pathologies, it may have a negative impact on maintaining specialist colorectal skills such as pelvic dissection and on completing sufficient colorectal cancer resections [13]. On the other hand, ACPGBI members generally believe that emergency colorectal resections should have the input of a surgeon who performs elective colorectal resections [14].

Despite the aforementioned controversies, the predictive value of surgeon's seniority and surgeon's subspeciality interest on outcomes after emergency laparotomy is poorly understood. Consequently, in the present study, we aimed to conduct a systematic review and meta-analysis to evaluate the effect of surgeon's seniority (trainee surgeon vs. consultant surgeon) and surgeon's subspeciality interest on postoperative mortality in patients undergoing emergency laparotomy.

METHODS

This study was protocoled (PROSPERO registration no.: CRD42024530160) and was conducted in compliance with the Cochrane Handbook for Systematic Reviews (version 6.4) [15], and the review was reported in compliance with Preferred Reporting Items for Systematic reviews and Meta-Analyses (PRISMA) 2020 statement standards [16].

Eligibility criteria

Study design

All randomized controlled trials and comparative observational studies (cohort studies, case–control studies, and case-series) were considered for inclusion.

Population

All patients aged 18 years or over, who underwent non-traumatic emergency laparotomy, were considered eligible for inclusion. The list of indications of interest for emergency laparotomy included intestinal ischaemia, visceral perforation, small or large bowel obstruction, intra-abdominal bleeding, and intra-abdominal sepsis of any source (collection, anastomotic leak, colitis, intestinal fistula).

Exposure of interest and comparison

For surgeon's seniority research question, a trainee surgeon was considered as exposure of interest and a consultant surgeon as comparison. For surgeon's subspeciality interest research question, a surgeon without subspeciality interest related to the pathology was considered as exposure of interest and a surgeon with subspeciality interest related to the pathology was considered as comparison. A lower GI surgeon was defined as a qualified specialist in general surgery who focused their elective practice on colorectal resection and an upper GI surgeon was defined as a qualified specialist in general surgery who focused their elective practice on oesophagogastric or hepatobiliary operations.

Outcomes

Thirty-day postoperative mortality, defined as death due to any cause occurring within 30 days after emergency laparotomy, was the outcome measure.

Search methods

A comprehensive search strategy was created by two independent authors with experience in evidence synthesis using proper search limits, keywords, thesaurus headings, and operators (Appendix 1). The search strategy had no language restrictions and was last run on 15 March 2024. The reference lists of relevant systematic reviews, and original studies were also evaluated to find more eligible studies.

Study selection and data extraction

The title and abstract of the identified articles were screened and the full texts of relevant articles were retrieved by two independent authors who included the studies that met the eligibility criteria. An electronic data collection proforma was evaluated based on randomly selected studies and included information on name of the first author, year of publication, name of journal, type of study design, description of included population, sample size of each study, age, gender, ASA status, and postoperative mortality data. The two independent authors discussed and resolved disagreements during study data extraction and a third independent author was consulted if required.

Risk of bias assessment

Two independent authors evaluated the methodological quality of the included studies using the Quality in Prognosis Studies (QUIPS) tool which evaluates the risk of bias in studies of prognostic factors in terms of study participation, study attrition, prognostic factor measurement, outcome measurement, study confounding, and statistical analysis and reporting [17].

Data analysis

Review Manager 5.4 software was used for meta-analysis. The OR was calculated as summary measure for postoperative mortality. Random effects modelling was used for analyses and forest plots with 95% CIs were constructed to present the results. Individual patients were considered as unit of analysis and where applicable intention to treat information data from the included studies were used for data analysis. The statistical heterogeneity was measured as I^2 using Cochran Q test (χ^2) and it was classified as low heterogeneity when I^2 was 0%–25%, moderate heterogeneity when I^2 was 25%–75%, and high heterogeneity when I^2 was 75%–100%. Risk of publication bias was evaluated by constructing funnel plots for outcomes reported by at least 10 studies.

Subgroup analyses

Subgroup analysis was performed for lower GI and upper GI pathologies indicating emergency laparotomy.

Sensitivity analyses

In order to evaluate the consistency and robustness of the results, a sensitivity analysis was performed for the outcomes reported by a minimum number of four studies: (a) Leave-one-out analysis to investigate effect of each study on the pooled outcomes and (b) separate analysis of studies with low overall risk of bias.

Certainty of evidence

Certainty of evidence was judged based on the recommended standards and domains by the GRADE system [18].

RESULTS

Search of electronic databases resulted in 297 articles among which 283 articles were excluded because they were not relevant to our research questions. Among the remaining 14 articles, one was excluded as it did not provide stratified data related to emergency laparotomy. Consequently, 13 studies [19–31] enrolling a total of 256 844 patients were eligible for inclusion; nine studies [19–27] (56 979 patients) compared surgeons with and without subspeciality interest related to pathology and five studies [22, 28–31] (200 223 patients) compared trainee surgeons and consultant surgeons. Table 1 summarizes the detail related to the included studies and Figure 1 outlines the study flow diagram.

Risk of bias assessment

Figure 2 highlights the outcomes of methodological quality assessment based on the QUIPS tool. All the included studies were judged to be of low risk of bias in terms of study participation, study attrition, prognostic factor measurement, outcome measurement, and statistical analysis and reporting. Due to the retrospective nature of the included studies and limited available data about important confounders, the risk of bias in terms of study confounding was judged to be unclear in 12 studies and high in one study.

Surgeon's subspeciality interest and postoperative mortality

Analysis of 56 979 patients from nine studies showed that emergency laparotomy performed by a surgeon without subspeciality interest related to the pathology was associated with a higher risk of postoperative mortality compared with a surgeon with subspeciality interest (OR: 1.38, 95% CI: 1.24–1.54, $p < 0.00001$). The between-study heterogeneity was low ($I^2 = 11\%$, $p = 0.34$) (Figure 3A). The GRADE certainty of evidence was moderate.

TABLE 1 Baseline characteristics of the included studies.

	First author/year	Country	Journal	Design	Included population	Sample size: Total	Sample size: Surgeon without subspeciality of interest	Sample size: Surgeon with subspeciality of interest	Anatomical location of pathology indicating emergency laparotomy: Lower GI	Anatomical location of pathology indicating emergency laparotomy: Upper GI
Surgeon's subspeciality	Bunce 2023	UK	World J Surg	Retrospective observational	Patients undergoing emergency laparotomy for inflammatory bowel disease	3330	852	2478	Distal small bowel Colon	Not applicable
	Arnarson 2023	Sweden	World J Emerg Surg	Retrospective observational	Patients undergoing emergency laparotomy for colon cancer	656	337	319	Colon	Not applicable
	Green 2023	UK	Eur J Trauma Emerg Surg	Retrospective observational	Patients undergoing emergency laparotomy for adhesive small bowel obstruction	2439	1439	1000	Small bowel	Not applicable
	Hallam 2020	UK	Ann R Coll Surg Engl	Retrospective observational	Patients undergoing non-traumatic emergency laparotomy	358	79	279	Colon	Stomach Duodenum
	Young 2020	UK	Colorectal Dis	Retrospective observational	Patients undergoing emergency open colorectal resections	7016	2747	4269	Colon	Not applicable
	Boyd-Carson 2019	UK	BJS	Retrospective observational	Patients undergoing non-traumatic emergency laparotomy	33 819	15 159	18 660	Colon	Stomach Duodenum
	Brown 2019	UK	Int J Surg	Retrospective observational	Patients undergoing non-traumatic emergency laparotomy	9102	2725	6377	Colon Small bowel	Stomach Duodenum Small bowel
	Khan 2015	UK	Acta Chir Belg	Retrospective observational	Patients undergoing emergency laparotomy for gastric pathology	63	40	23	Not applicable	Stomach Duodenum
	Gibbons 2015	Australia	ANZ J Surg	Retrospective observational	Patients undergoing emergency left colonic resections	196	109	87	Colon	Not applicable

	First author/year	Country	Journal	Design	Included population	Total	Trainee surgeon	Consultant surgeon
Surgeon's seniority	Rahman 2023	UK	Ann Surg	Retrospective observational	Patients undergoing non-traumatic emergency laparotomy	111 583	8121	103 462
	Pohl 2021	South Africa	J Surg Educ	Retrospective observational	Patients undergoing non-traumatic emergency laparotomy	543	137	406
	Gilbert 2021	UK	Eur J Trauma Emerg Surg	Retrospective observational	Patients undergoing non-traumatic emergency laparotomy	130	45	85
	Boyd-Carson 2020	UK	BJS	Retrospective observational	Patients undergoing non-traumatic emergency laparotomy	87 367	6825	80 542
	Hallam 2020	UK	Ann R Coll Surg Engl	Retrospective observational	Patients undergoing non-traumatic emergency laparotomy	600	57	543

Abbreviation: GI, gastrointestinal.

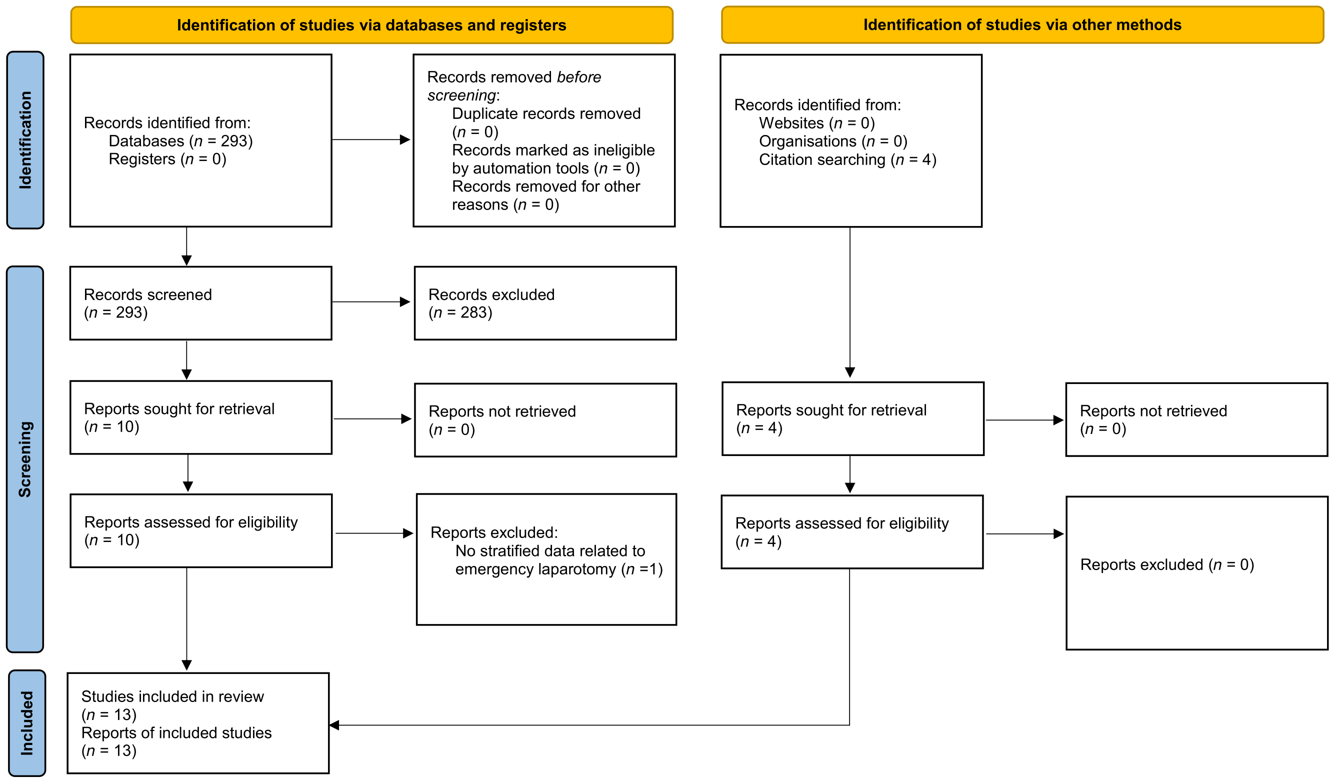
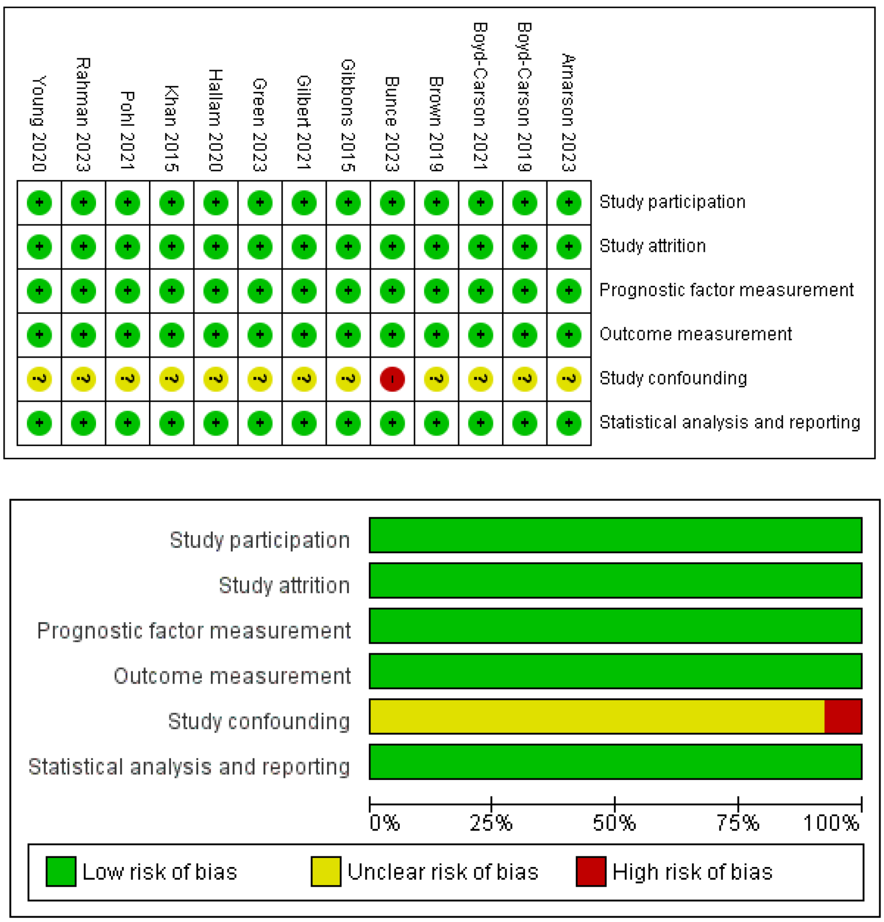


FIGURE 1 Study Preferred Reporting Items for Systematic reviews and Meta-Analyses (PRISMA) flow diagram.

FIGURE 2 The outcomes of methodological quality assessment of the included studies using the Quality in Prognosis Studies (QUIPS) tool.



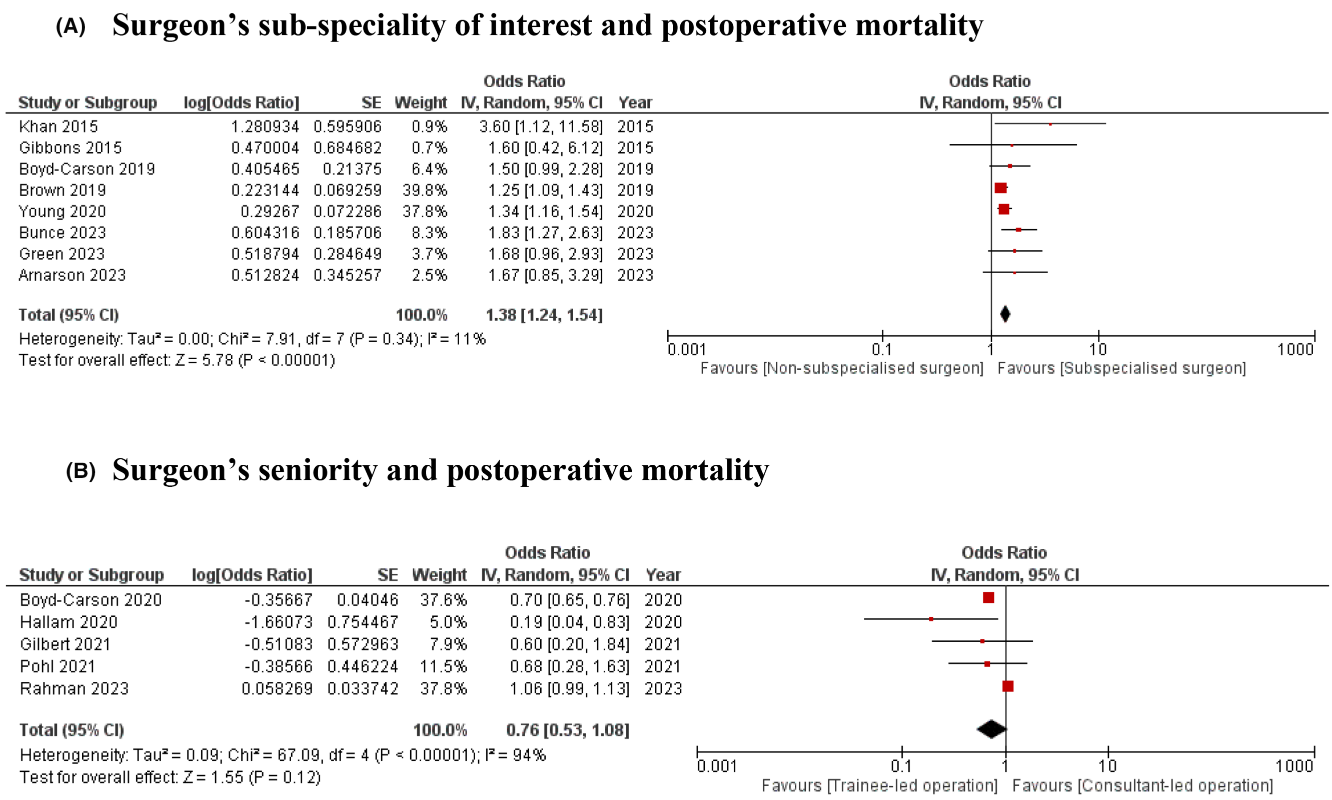


FIGURE 3 Forest plots of postoperative mortality for the following research questions. (A) Surgeon's subspeciality of interest and postoperative mortality. (B) Surgeon's seniority and postoperative mortality.

Lower GI pathologies

When indication for emergency laparotomy was related to lower GI pathologies, laparotomies done by upper GI surgeons resulted in higher risk of mortality compared with lower GI surgeons (OR: 1.43, 95% CI: 1.26–1.62, $p<0.00001$). The between-study heterogeneity was moderate ($I^2=46\%$, $p=0.07$) (Figure 4). The GRADE certainty of evidence was moderate.

Upper GI pathologies

When indication for emergency laparotomy was related to upper GI pathologies, laparotomies done by lower GI surgeons resulted in higher risk of mortality compared with upper GI surgeons (OR: 1.29, 95% CI: 1.00–1.67, $p=0.05$). The between-study heterogeneity was moderate ($I^2=57\%$, $p=0.07$) (Figure 4). The GRADE certainty of evidence was moderate.

Surgeon's seniority and postoperative mortality

Analysis of 200 223 patients from five studies showed no difference in the risk of postoperative mortality between trainee surgeons and consultant surgeons (OR: 0.76, 95% CI: 0.53–1.08, $p=0.12$). The between-study heterogeneity was high ($I^2=94\%$, $p<0.00001$) (Figure 4). The GRADE certainty of evidence was moderate.

Sensitivity analyses

For surgeon's subspeciality interest comparison, leave-one-out analysis and separate analysis of studies with low overall risk of bias showed consistency of the findings. However, for surgeon's seniority comparison, removal of the study by Rahman et al. [28], moved the direction of the effect in favour of trainee surgeon and reduced the heterogeneity from 94% to 2%.

DISCUSSION

We conducted a systematic review and meta-analysis to evaluate the effect of surgeon's seniority and surgeon's subspeciality interest on postoperative mortality in patients undergoing emergency laparotomy. Analysis of 256 844 patients from 13 studies suggested that emergency laparotomy performed by a surgeon without subspeciality interest related to the pathology was associated with a higher risk of postoperative mortality compared with a surgeon with subspeciality interest; however, there was no difference in the risk of postoperative mortality between trainee surgeon

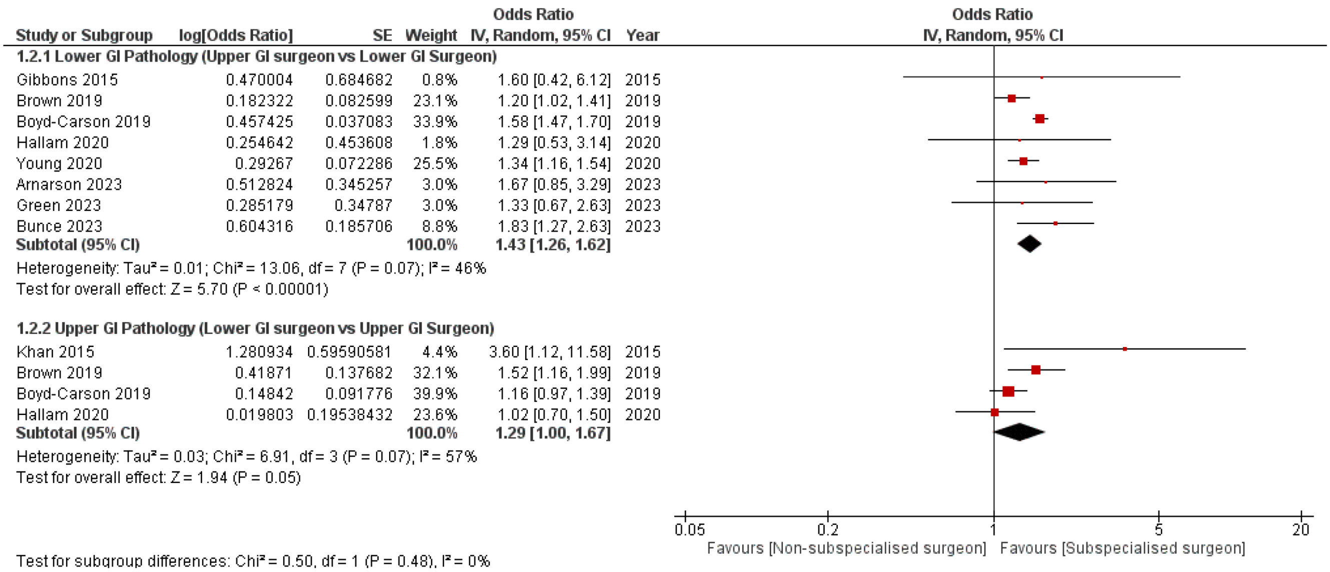


FIGURE 4 Forest plot for subgroup analysis of postoperative mortality based on upper and lower gastrointestinal (GI) pathologies for surgeon's speciality of interest research question.

and consultant surgeon. The GRADE certainty of the available evidence was moderate.

This study is the first systematic review in the literature to evaluate the predictive value of surgeon's seniority and surgeon's subspeciality interest on mortality after emergency laparotomy; therefore, there is no review to directly compare our findings with. Nevertheless, our results may be compared with findings of studies in other settings. Chowdhury et al. [32] conducted a systematic review of 163 studies examining 42 different surgical procedures across 13 surgical specialities and concluded that high surgeon volume and specialization are associated with improved patient outcomes [32]. Other systematic reviews in cancer surgery [33] and paediatric surgery [34] were not conclusive due to inconsistency and limitations of available data. D'Souza et al. [35] conducted a systematic review to evaluate effect of trainee involvement in a wide range of procedures across different specialties and concluded that trainee involvement does not increase the risk of mortality [35]. In contrast, Kasotakis et al. [8] analysed 41 010 patients who underwent a wide range of emergency general surgery procedures and concluded that trainee participation is associated with adverse outcomes in emergency general surgery; however, there were many uncontrolled confounders in the study by Kasotakis et al. [8] which should be taken into account before accepting their findings.

It is interesting to observe that most of the included studies were from the UK. This may be due to the fact that emergency general surgery is not yet a well-defined subspeciality in the UK. Although all UK general surgical trainees must demonstrate competency in emergency general surgery procedures before completion of their training [24], most declare their subspecialities early and concentrate mainly on developing the competencies related to their declared subspeciality interest, which would fall broadly speaking into upper or lower GI categories. As a compensatory mechanism, most hospitals in the UK are moving toward having dual speciality emergency service meaning that lower GI pathologies are likely to be operated by lower GI surgeons and upper GI pathologies are likely to be operated by upper GI surgeons. Consequently, it is very crucial to establish the impact of surgeon's subspeciality interest on mortality in the UK; this may explain why most of the eligible studies in this review are from the UK. The above explanation may also be used to justify the lower mortality rate found in the current study when emergency laparotomy was performed by a surgeon with subspeciality interest related to the pathology indicating emergency laparotomy. Whether a dedicated emergency general surgery subspeciality could result in comparable or even better outcomes remains unanswered.

Regarding the impact of surgeon's seniority on postoperative mortality, because most of the included studies were from the UK, we should again refer to the UK general surgery training system. In the UK, general surgical trainees' competencies are assessed based on operative case volume, various summative and formative assessments, and informal judgement by supervising consultants [23]. Based on these assessments, the supervising consultant may decide to authorize a trainee to perform an operation independently. Therefore, the UK trainees who are allowed to perform emergency laparotomies independently are likely to be competent for such procedure. On the other hand, the emergency laparotomies which are performed independently by trainees are likely to be less complex than those performed by consultants. All of the above may explain comparable mortality rates found between the trainee surgeons and consultant surgeons in the current study. Moreover, lower mortality rates associated with trainee-led laparotomies seen in our sensitivity analyses could simply be due to confounding effect of more competent trainees doing less complex laparotomies. Nevertheless, at least it could be safely argued that trainee involvement does not increase the risk of mortality after emergency laparotomy.

The duration of training and training requirements in general surgery varies among different countries. Whewel et al. [36] showed that the number of years in postgraduate training ranges from 4 years in Colombia to 10 years in the UK. On the other hand, the training systems were heterogeneous in terms of management, teaching, academic and operative competencies, mandatory courses, working hour regulations, selection process into training and formal examination [36]. Such variations should be taken into account when comparing trainees in different countries. Four out of five studies included in the surgeon's seniority of interest comparison were from the UK which would reduce the confounding effect of the aforementioned variation. One study [29] was from South Africa in which duration of postgraduate training is 6 years and the training system is different from the UK in terms of the domains mentioned above. Nevertheless, sensitivity analysis showed consistency of the results when the study from South Africa was removed from the analyses, hence the confounding effect of difference in training system on outcomes was judged to be minimal in the current study.

The definition of lower and upper GI surgeons varies among different countries. In the UK, a consultant surgeon is defined as a surgeon whose name appears on the specialist register and may work as colorectal, oesophagogastric, hepatobiliary, transplant, endocrine, or breast surgeon depending on the speciality interest in which they achieved a Certificate of Completion of Training [37]. Seven out of nine studies included in the surgeon's subspeciality interest comparison were from the UK and followed the same definition. The other two studies were from Australia and Sweden which defined lower GI surgeons as a surgeon with post fellowship training or subspeciality in colorectal surgery. Consequently, the definition of exposure in the surgeon's subspeciality interest comparison was homogenous among the included studies.

The border between upper and lower GI surgery remains the subject of debate. The ligament of Treitz is recognized as the conventional boundary between the upper and the lower GI tract; however, classification of pathologies as upper or lower GI based on the ligament of Treitz may raise practical issues in an emergency general surgery setting. While pathologies confined to distal small bowel (such as small bowel Crohn's disease) and colon can be clearly classified as lower GI pathologies and those confined to stomach and duodenum as upper GI pathologies, treatment of pathologies in very proximal jejunum may require mobilization of duodenojejunal flexure which requires the skills of an upper GI surgeon. Among the included studies in this review, the lower GI pathologies were mainly confined to distal small bowel and colon and the upper GI pathologies were confined to stomach and duodenum. Consequently, the current study cannot provide robust evidence on the effect of surgeon's subspeciality interest on outcomes of pathologies located very close to the ligament of Treitz; however, it may be logical to argue that such pathologies may be better operated by, or in collaboration with, an upper GI surgeon.

The current study had the following limitations. None of the included studies were randomized, hence the results may be subject to inevitable selection bias. Due to the retrospective nature of the included studies and the subject of interest which is related to surgeon's seniority and subspeciality interest, confounding by indication cannot be excluded. Nevertheless, we downgraded the certainty of the evidence accordingly. Most of the included studies were from the UK and this may have affected generalizability and applicability of the findings. Neither surgeon's seniority comparison nor surgeon's subspeciality interest comparison were reported by more than 10 studies, hence formal assessment of publication bias using a funnel plot was not feasible.

CONCLUSIONS

While confounding by indication cannot be excluded, level 2 evidence with moderate certainty suggests that trainee-led emergency laparotomy may not increase the risk of postoperative mortality but emergency laparotomy by a surgeon with subspeciality interest related to the pathology may reduce the risk of mortality.

AUTHOR CONTRIBUTIONS

Hashim Al-Sarireh: Validation; data curation; writing – original draft; writing – review and editing. **Ahmad Al-Sarireh:** Validation; data curation; writing – original draft; writing – review and editing. **Karan Mann:** Validation; writing – original draft; writing – review and editing. **Shahin Hajibandeh:** Formal analysis; visualization; writing – original draft; writing – review and editing; methodology. **Shahab Hajibandeh:** Conceptualization; methodology; formal analysis; validation; data curation; supervision; visualization; project administration; writing – original draft; writing – review and editing; resources; investigation.

FUNDING INFORMATION

There are no funding sources for this study.

CONFLICT OF INTEREST STATEMENT

All authors declare there are no conflicts of interest.

DATA AVAILABILITY STATEMENT

The data and materials related to this study will be available upon reasonable request from the corresponding author.

ETHICS STATEMENT

Considering the nature of this study, ethical approval was not required.

INFORMED CONSENT

Considering the nature of this study, informed consent was not required.

ORCID

Hashim Al-Sarireh https://orcid.org/0009-0002-7794-4096
Ahmad Al-Sarireh https://orcid.org/0009-0000-9882-5075
Shahin Hajibandeh https://orcid.org/0000-0001-6159-1068
Shahab Hajibandeh https://orcid.org/0000-0002-3294-4335

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How to cite this article: Al-Sarireh H, Al-Sarireh A, Mann K, Hajibandeh S, Hajibandeh S. Effect of surgeon's seniority and subspeciality interest on mortality after emergency laparotomy: A systematic review and meta-analysis. Colorectal Dis. 2024;26:1495–1504. https://doi.org/10.1111/codi.17079

APPENDIX 1

Search	Search description	Action
Search #1	MeSH term: (traineeship)	Explode all trees
Search #2	Trainee	T,A,K
Search #3	Resident	T,A,K
Search #4	Registrar	T,A,K
Search #5	Sub-speciali*	T,A,K
Search #6	Subspeciali*	T,A,K
Search #7	Speciali*	T,A,K
Search #8	#1 OR #2 OR #3 OR #4 OR #5 OR #6 OR #7	Combined with OR
Search #9	MeSH term: (laparotomy)	Explode all trees
Search #10	Emergency laparotomy	T,A,K
Search #11	#9 OR #10	Combined with OR
Search #12	#8 AND #11	Combined with AND

Abbreviations: A, abstracts; K, keywords; T, titles.

The developed strategy was applied and adopted on the following electronic sources MEDLINE, CINAHL, CENTRAL, Scopus, World Health Organization International Clinical Trials Registry, International Standard Randomized Controlled Trial Number Registry, ClinicalTrials.gov, the European Association for Grey Literature Exploitation, System for Information on Grey Literature.

Full text 12

Article 12. Development and Validation of HAS (Hajibandeh Index, ASA Status, Sarcopenia) - A Novel Model for Predicting Mortality After Emergency Laparotomy

Citation: Hajibandeh S, Hajibandeh S, Hughes I, Mitra K, Puthiyakunnel Saji A, Clayton A, Alessandri G, Duncan T, Cornish J, Morris C, O'Reilly D, Kumar N. Development and Validation of HAS (Hajibandeh Index, ASA Status, Sarcopenia) - A Novel Model for Predicting Mortality After Emergency Laparotomy. Ann Surg. 2024 Mar 1;279(3):501-509. doi: 10.1097/SLA.0000000000005897.

Contribution: Conception, design, data collection, data analysis, write up, and critical revision

Development and Validation of HAS (Hajibandeh Index, ASA Status, Sarcopenia) - A Novel Model for Predicting Mortality After Emergency Laparotomy

Shahab Hajibandeh, MRCS,✉ Shahin Hajibandeh, MRCS,† Ioan Hughes, MD,* Kalyan Mitra, MD,* Alwin Puthiyakunnel Saji,‡ Amy Clayton, FRCR,§ Giorgio Alessandri, FRCS,* Trish Duncan, FRCS,* Julie Cornish, FRCS,* Chris Morris, FRCS,* David O'Reilly, FRCS,* and Nagappan Kumar, FRCS**

Objectives: To develop and validate a predictive model to predict the risk of postoperative mortality after emergency laparotomy taking into account the following variables: age, age ≥ 80, ASA status, clinical frailty score, sarcopenia, Hajibandeh Index (HI), bowel resection, and intraperitoneal contamination.

Summary Background Data: The discriminative powers of the currently available predictive tools range between adequate and strong; none has demonstrated excellent discrimination yet.

Methods: The TRIPOD and STROCSS statement standards were followed to protocol and conduct a retrospective cohort study of adult patients who underwent emergency laparotomy due to non-traumatic acute abdominal pathology between 2017 and 2022. Multivariable binary logistic regression analysis was used to develop and validate the model via two protocols (Protocol A and B). The model performance was evaluated in terms of discrimination (ROC curve analysis), calibration (calibration diagram and Hosmer-Lemeshow test), and classification (classification table).

Results: One thousand forty-three patients were included (statistical power = 94%). Multivariable analysis kept HI (Protocol-A: $P = 0.0004$; Protocol-B: $P = 0.0017$), ASA status (Protocol-A: $P = 0.0068$; Protocol-B: $P = 0.0007$), and sarcopenia (Protocol-A: $P < 0.0001$; Protocol-B: $P < 0.0001$) as final predictors of 30-day postoperative mortality in both protocols; hence the model was called HAS (HI, ASA status, sarcopenia). The HAS demonstrated excellent discrimination (AUC: 0.96, $P < 0.0001$), excellent calibration ($P < 0.0001$), and excellent classification (95%) via both protocols.

Conclusions: The HAS is the first model demonstrating excellent discrimination, calibration, and classification in predicting the risk of 30-day mortality following emergency laparotomy. The HAS model seems promising and is worth attention for external validation using the calculator provided. HAS mortality risk calculator https://app.airrange.io/#/element/xr3b_E6yLor9R2c8KXViSAeOSK.

From the *Department of General Surgery, University Hospital of Wales, Cardiff, UK; †Department of General Surgery, Royal Stoke University Hospital, Stoke-on-Trent, UK; ‡School of Medicine, Cardiff University, Cardiff, UK; and §Department of Radiology, University Hospital of Wales, Cardiff, UK.

[redacted]

Author contributions: Conception and design: S.H. Data collection: I.H., K.M., A.P.S., and S.H. Analysis and interpretation: All authors. Writing the article: S.H. and S.H. Critical revision of the article: All authors. Final approval of the article: All authors.

The authors declare no conflict of interest.

Supplemental Digital Content is available for this article. Direct URL citations are provided in the HTML and PDF versions of this article on the journal's website, www.annalsofsurgery.com.

ISSN: 0003-4932/24/27903-0501

DOI: 10.1097/SLA.0000000000005897

Keywords: laparotomy, mortality, hajibandeh index, ASA status, sarcopenia

(*Ann Surg* 2024;279:501–509)

Predicting the risk of postoperative mortality after emergency laparotomy (EL), which is known to be associated with a high risk of morbidity and mortality, has been an area of interest recently. There have been various risk assessment tools for predicting the risk of mortality following EL, including Mannheim peritonitis index (MPI),[1] American College of Surgeons National Surgical Quality Improvement Program (ACS NSQIP) Surgical Risk Calculator,[2] Portsmouth-physiological and operative severity score for the enumeration of mortality and morbidity (P-POSSUM),[3] and National Emergency Laparotomy Audit (NELA) score.[4] The area under the curve (AUC) of the currently available tools suggests that their discriminative power range is between adequate (AUC: 0.70–0.79) and strong (AUC: 0.80–0.89); none has demonstrated excellent discrimination (AUC: 0.90–1.00) yet.[5–9] On the other hand, the currently available tools have been criticized for underestimation or overestimation of mortality risk, being less accurate for older and frail patients, and not taking into account the modern predictors of mortality.[5–11]

We learned from previous studies that the modern predictors of mortality in patients undergoing EL include age over 80,[12,13] sarcopenia,[14] frailty,[15,16] American Society of Anesthesiologists (ASA) status,[12,13] need for bowel resection,[12] and presence of intraperitoneal contamination.[13] In addition to the above predictors, the Hajibandeh Index (HI), derived from combined levels of C-reactive protein (CRP), lactate, neutrophils, lymphocytes, and albumin, is a strong predictor of mortality in patients undergoing EL.[9,17] A risk prediction model derived from the above predictors may potentially be the best tool with excellent discriminative power for predicting the risk of postoperative mortality in patients undergoing EL. Consequently, we aimed to develop and validate a predictive model using the above modern predictors to predict the risk of mortality following EL.

METHODS

Reporting Standards, and Ethical Approval

The Transparent Reporting of a multivariable prediction model for Individual Prognosis or Diagnosis (TRIPOD) statement standards[18] and the Strengthening the Reporting of Cohort

Studies in Surgery (STROCSS) guideline for observational studies[19] were followed to protocol, conduct, and present this study. The study was compliant with the Helsinki medical research ethical principles, and it was approved by the Health Research Authority (HRA) and Health and Care Research Wales (HCRW) through the Integrated Research Application System (IRAS) (IRAS ID: 320962). Moreover, the study was approved by the local Research and Development (RD) department (RD reference: 8446/AUG/2022).

Study Design and Patient Selection

The study design was a retrospective cohort study with prospective data collection approach. It was conducted in a tertiary General Surgery center at a teaching hospital in South Wales. All adult patients (aged over 18) with non-traumatic acute abdominal pathology who underwent EL between January 2017 and January 2022 in our center were identified from the prospectively maintained hospital electronic medical record system and were considered for inclusion. Patients who underwent EL due to small bowel obstruction, large bowel obstruction, visceral perforation, intestinal ischemia, intra-abdominal collection, intra-abdominal bleeding, and intra-abdominal sepsis of any source (anastomotic leak, colitis, intestinal fistula) were included and those who underwent EL due to abdominal trauma were excluded.

Primary and Secondary Outcomes

The primary outcome was 30-day postoperative mortality which was defined as death due to any cause occurring within 30 days after EL. The secondary outcomes included in-hospital mortality and 90-day postoperative mortality, which were defined as death due to any cause occurring during hospital stay and within 90 days after EL, respectively.

Potential Predictors and Definitions

The following variables were included in multivariable analysis for the development of the model: age, age $\geq$ 80, ASA status, clinical frailty scale (CFS), sarcopenia, HI, need for bowel resection, and presence of intraperitoneal contamination.

The ASA status was defined and classed as ASA I (a normal healthy patient), ASA II (a patient with mild systemic disease), ASA III (a patient with severe systemic disease), ASA IV (a patient with severe systemic disease that is a constant threat to life), ASA V (a moribund patient who is not expected to survive without the operation), and ASA VI (a declared brain-dead patient whose organs are being removed for donor purposes).[20]

The frailty was measured by CFS, which was defined and classed as CFS 1 (very fit), CFS 2 (well, no active disease symptoms), CFS 3 (managing well, medical problems are well controlled, not regularly active), CFS 4 (vulnerable, not dependent, symptoms limit activities), CFS 5 (mildly frail, more evident slowing, need help in high order instrumental activities of daily living), CFS 6 (moderately frail, need help with all outside activities and with keeping house), CFS 7 (severely frail, completely dependent for personal care), CFS 8 (very severely frail, completely dependent, approaching the end of life), and CFS 9 (terminally ill, approaching the end of life, life expectancy $<$ 6 mo).[21]

Sarcopenia was measured by calculating the cross-sectional area of both right and left psoas muscles at the level of the bottom of L3 vertebral body on the 0.625mm thick axial abdominal CT scan using the picture archiving and communication system (PACS) used in our center (FUJIFILM Medical Corp. Ltd., Tokyo, Japan. Software: Synapse V5.7.240.16413). This value was adjusted based on each patient's height to calculate the psoas muscle index (PMI) (mm^2/m^2). The age and sex-specific cut-off values reported by Kim et al. [22] were used to define sarcopenia.[22]

The HI was calculated using the formula shown in Supplementary File 1, Supplemental Digital Content 1, http://links.lww.com/SLA/E609. It includes preoperative levels of CRP, neutrophils, and lactate as nominators and preoperative levels of albumin and lymphocytes as denominators.[9,17]

Data Collection

An electronic data collection sheet was created for data collection. The prospectively maintained electronic hospital records were used as the source for data collection. The following data items for each patient were collected: age, gender, CFS, sarcopenia, ASA status, indication for laparotomy, the procedure performed, need for bowel resection, presence and nature of peritoneal contamination, components of the HI, and mortality outcomes. The authors who collected data related to potential predictors were separate from the authors who collected mortality data.

Data Synthesis and Statistical Analyses

The MedCalc 13.0 software was used for statistical analyses. The demographics, clinical characteristics, and outcome data were presented using simple descriptive statistics. Data were summarized with mean $\pm$ standard deviation (SD) or median and interquartile range (IQR) for continuous variables, and frequencies/percentages for categorical variables. Continuous variables were compared using a t-test or Mann-Whitney test as appropriate and dichotomous variables were compared using the chi-squared test. The steps of statistical analyses are described below:

Sample Size Calculation

Although sample size calculation may not be applicable for retrospective studies, we determined the required sample size. The accuracy of the currently available tools ranges between 80 and 85%.[5–9] Based on the assumption that the proposed model would have an accuracy of 90%, the study required a sample size of 316 patients to achieve statistical power of 80%. Considering that the study had two cohorts (development and validation), a total of 632 patients were required for statistical power of 80%. The sample size of the current study is 1043 resulting in the statistical power of 94%.

Model Development

Postoperative 30-day mortality was considered as the dependent variable and the following were considered as independent variables: age, age $\geq$ 80, ASA status, CFS, sarcopenia, HI, need for bowel resection, and presence of intraperitoneal contamination. Firstly, all independent variables were entered into the binary logistic regression model in one single step. Any variable that was not a predictor of postoperative mortality was removed, and any variable that was found to be an independent predictor of postoperative mortality was selected for inclusion in the backward elimination multivariable model. Subsequently, a multivariable binary logistic regression model was constructed using the backward elimination approach; entering the already identified independent predictors of postoperative mortality into the model if their associated P values were < 0.05 and removing them from the model if their associated P values were > 0.1. The final developed model included only the variables that remained statistically significant predictors after backward elimination multivariable analysis. The collinearity between the variables included in the model were evaluated by collinearity diagnostic statistics; we calculated the variance inflation factor (VIF) and tolerance for each variable as measures of collinearity. The VIF greater than 5 and tolerance lower than 0.2 were considered evidence for collinearity. Moreover, we determined the relative importance of each variable included in the model for ease of interpretation in terms of contributing effect of each variable to the model. We calculated indices that measure the importance of each variable in the model and estimated the variability in the predicted response based on a range of variations for each variable. The effect of the variable was considered important relative to the model if variation in the variable resulted in high variability in the response.

Model Validation

In order to assess the consistency and robustness of the findings, the model was developed and validated twice via protocol A and protocol B:

Validation protocol A: The entire sample size was randomly allocated to the development cohort and validation cohort in a 1:1 ratio using a random number generator. The model was developed in the development cohort, and it was used to predict the risk of postoperative mortality in the validation cohort.

Validation protocol B: The population in the development and validation cohorts used in the validation protocol A were swapped (crossover) and the above steps were repeated.

Model Performance

The performance of the model was evaluated in terms of discrimination, calibration, and classification. The discrimination of the model was evaluated using the method described by DeLong et al.;[23] the receiver operating characteristic (ROC) curve analysis was performed to determine the standard error of the AUC and to calculate an exact binomial confidence interval for the AUC. The calibration of the model was evaluated using the Hosmer-Lemeshow (H-L) test (goodness of fit test) and by visual assessment of plotted diagram of the expected and observed mortality rates. Moreover, the observed deaths to expected deaths ratio (O/E ratio) was calculated in order to assess whether the model overestimates or underestimates the risk of postoperative mortality. The classification of the model was evaluated by the creation of a classification table which helped to determine the proportion of cases who were correctly classified as dead or alive. It was constructed by cross-classifying the observed values and the predicted values for postoperative mortality using a cut-off value of 0.5. All statistical tests were two-tailed, and statistical significance was assumed at $P < 0.05$.

Deviations from the Registered Protocol

The study remained compliant with the prospectively registered protocol, and there was no deviations from it.

RESULTS

Baseline Characteristics of the Included Population

A total of 1069 patients underwent EL due to non-traumatic abdominal pathology between January 2017 and January 2021; 26 patients were excluded due to unavailable preoperative biomarkers (24 patients) or preoperative CT scan (2 patients). Consequently, 1043 patients were included for analysis. Ninety-day follow-up data were available for all patients. After randomization, 522 patients were allocated to development cohort A and 521 patients to validation cohort A (Fig. 1). The included population in both cohorts were comparable in terms of baseline characteristics, as shown in Table 1.

Postoperative Mortality

The risks of 30-day mortality, in-hospital mortality, and 90-day mortality were 7%, 9%, and 9% in the development cohort A and 9%, 11%, and 12% in the validation cohort A, respectively. There was no difference between the development and validation cohorts in terms of 30-day mortality ($P = 0.1669$), in-hospital mortality ($P = 0.4045$), and 90-day mortality ($P = 0.3064$).

Model Development

Protocol A

The initial binary logistic regression analysis model classed HI ($P = 0.0015$), ASA status ($P = 0.0054$), and sarcopenia ($P < 0.0001$) as statistically significant predictors of postoperative mortality and classed age ($P = 0.3978$), age $\geq$ 80 ($P = 0.1468$), CFS ($P = 0.2896$), need for bowel resection ($P = 0.1561$), and intraperitoneal contamination ($P = 0.459$) as insignificant variables. Subsequent backward elimination multivariable analysis classed HI ($P = 0.0004$), ASA status ($P = 0.0068$), and sarcopenia ($P < 0.0001$) as statistically significant predictors of postoperative mortality. Therefore, the developed model included HI, ASA status, and sarcopenia as predictors, which were used for prediction of 30-day mortality in the validation cohort (Table 2). The collinearity statistics suggested no significant collinearity between the included variables in the model (Table 3). In terms of the relative importance of each variable in the model, HI had relative importance of 22%, ASA had relative importance of 15%, and sarcopenia had relative importance of 69% (Table 3).

Protocol B

The initial binary logistic regression analysis model classed HI ($P = 0.0173$), ASA status ($P = 0.006$), and sarcopenia ($P < 0.0001$) as statistically significant predictors of postoperative mortality and classed age ($P = 0.5541$), age $\geq$ 80 ($P = 0.5699$), CFS ($P = 0.5475$), need for bowel resection ($P = 0.8961$), and intraperitoneal contamination ($P = 0.0510$) as insignificant variables. Subsequent backward elimination multivariable analysis classed HI ($P = 0.0017$), ASA status ($P = 0.0007$), and sarcopenia ($P < 0.0001$) as statistically significant predictors of postoperative mortality. Therefore, the developed model included HI, ASA status, and sarcopenia as predictors, which were used for prediction of 30-day mortality in the validation cohort. The collinearity statistics suggested no significant collinearity between the included variables in the model (Table 3). In terms of the relative importance of each variable in the model, HI had relative importance of 25%, ASA had relative importance of 18%, and sarcopenia had relative importance of 68% (Table 3).

Model Performance for the Primary Outcome (30-day Mortality)

Protocol A

Discrimination. The AUC for the developed model was 0.96 (95% CI 0.94–0.98, $P < 0.0001$) in the development cohort and 0.96 (95% CI 0.94–0.98, $P < 0.0001$) in the validation cohort (Fig. 2A, Table 4).

Calibration. The calibration diagram suggested that the model was well-calibrated ($P < 0.0001$) (Fig. 3A). Moreover, the H-L test confirmed good calibration of the model in the validation cohort ($P = 0.4860$). The observed number of deaths were

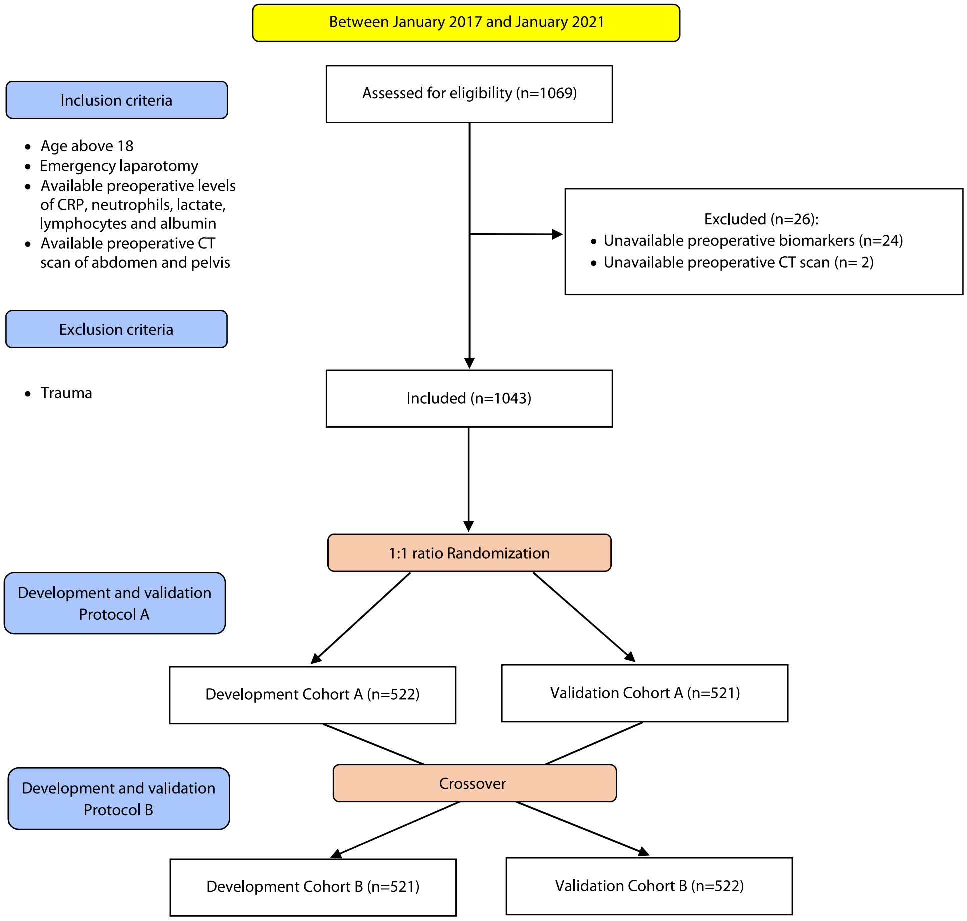

FIGURE 1. The study flow diagram.

48 in the validation cohort and the expected number of deaths based on the developed model was 36. The calculated O/E ratio was 1.3 suggesting no significant overestimation or underestimation (Table 4).

Classification. Analysis of the classification table showed that the model correctly classified 95% of cases in the development cohort and 95% of cases in the validation cohort (Table 4).

Protocol B

Discrimination. The AUC for the developed model was 0.96 (95% CI 0.94–0.98, $P<0.0001$) in the development cohort and 0.96 (95% CI 0.94–0.98, $P<0.0001$) in the validation cohort (Fig. 2B, Table 4).

Calibration. The calibration diagram suggested that the model was well-calibrated ($P<0.0001$) (Fig. 3B). Moreover, the H-L test confirmed good calibration of the model in the validation cohort ($P=0.3777$). The observed number of deaths were 35 in the validation cohort and the expected number of deaths based on the developed model was 47. The calculated O/E ratio was 0.8 suggesting no significant overestimation or underestimation (Table 4).

Classification. Analysis of the classification table showed that the model correctly classified 94% of cases in the development cohort and 95% of cases in the validation cohort (Table 4).

Secondary Outcomes

In-hospital Mortality

The AUC for the developed model was 0.88 (95% CI 0.85-0.91, $P<0.0001$). The calibration diagram ($P=0.0021$) and H-L test ($P=0.0602$) suggested that the model was well-calibrated. The calculated O/E ratio was 1.02 suggesting no significant overestimation or underestimation. The model correctly classified 92% of cases.

90-day Mortality

The AUC for the developed model was 0.88 (95% CI 0.85-0.91, $P<0.0001$). The calibration diagram ($P=0.0006$) and H-L test ($P=0.0501$) suggested that the model was well-calibrated. The calculated O/E ratio was 1.04 suggesting no significant overestimation or underestimation. The model correctly classified 93% of cases.

DISCUSSION

Considering the fact that none of the currently available preoperative risk predictive tools have demonstrated excellent discrimination in predicting the risk of postoperative mortality following EL and that they do not include modern predictors of postoperative mortality, we aimed to develop and validate a predictive model taking into account the following variables: age, age ≥ 80, ASA status, CFS, sarcopenia, HI, need for bowel resection,

TABLE 1. Baseline Characteristics of the Included Patients in the Development and Validation Cohorts

	Development Cohort (N = 522)	Validation Cohort (N = 521)	P*
Age, mean (95% CI)	62 (60–64)	62 (60-64)	0.8719
Age ≥ 80	98 (19%)	105 (20%)	0.6280
Male, n (%)	259 (50%)	255 (49%)	0.8766
Female, n (%)	263 (50%)	266 (51%)	0.8766
ASA, n (%)			
I	41 (8%)	38 (7%)	0.8218
II	187 (36%)	190 (37%)	0.8790
III	215 (41%)	215 (41%)	0.9705
IV	72 (14%)	76 (15%)	0.7804
V	7 (1%)	2 (0.4%)	0.1814
Clinical Frailty Scale, median (IQR)	2 (1-3)	2 (1-3)	0.4665
Indication for laparotomy, n (%)			
Small bowel obstruction	215 (41%)	196 (37%)	0.2646
Large bowel obstruction	70 (13%)	80 (15%)	0.4197
Perforated peptic ulcer	28 (5%)	30 (6%)	0.8866
Small bowel perforation	20 (4%)	19 (4%)	0.9951
Colonic perforation	90 (17%)	86 (17%)	0.8149
Intestinal ischaemia	21 (4%)	34 (7%)	0.0949
Intra-abdominal collection	15 (3%)	17 (3%)	0.853
Colitis	28 (5%)	27 (5%)	0.9941
Anastomotic leak	15 (3%)	14 (3%)	0.9958
Other	20 (4%)	18 (4%)	0.8734
Need for bowel resection, n (%)	281 (54%)	278 (53%)	0.9276
Intraperitoneal contamination, n (%)	141 (27%)	148 (28%)	0.1886
Preoperative HI , median (IQR)	12 (2-61)	15 (2-89)	0.0745
Sarcopenia, n (%)	53 (10%)	56 (11%)	0.8313
30-day mortality, n (%)	35 (7%)	48 (9%)	0.1669
In-hospital mortality, n (%)	48 (9%)	57 (11%)	0.4045
90-day mortality, n (%)	49 (9%)	60 (12%)	0.3064

*Continuous variables were compared using t-test or Mann-Whitney test as appropriate and dichotomous variables were compared using chi-squared test.

ASA indicates American Society of Anesthesiologists; CI, confidence interval; HI, Hajibandeh Index; IQR, interquartile range.

and presence of intraperitoneal contamination. A model was developed and validated via two different protocols analysing a total of 1043 patients undergoing EL for non-traumatic acute abdominal pathology. Backward elimination multivariable binary logistic regression analysis kept HI, ASA status, and sarcopenia (HAS) as final predictors of 30-day postoperative mortality in both protocols. The HAS demonstrated excellent discrimination (AUC: 0.96, $P < 0.0001$), excellent calibration ($P < 0.0001$), and excellent classification (95%) in predicting the risk of 30-day mortality following EL. The results remained consistent through both protocols used for the development and validation of the model. The statistical power of the study was 94% with no loss to follow up.

The HAS is the first preoperative predictive model which demonstrated excellent discrimination, excellent calibration, and excellent classification in predicting the risk of 30-day mortality following EL. None of the currently available preoperative risk tools which are commonly used for predicting mortality (ACS NSQIP Surgical Risk Calculator, P-POSSUM score, and NELA score) have demonstrated excellent performance so far; their performances range between adequate and strong. Barazanchi et al.[24] evaluated the predictive value of ACS NSQIP Surgical Risk Calculator, NELA score, and P-POSSUM score and reported AUC of 0.80, 0.83, and 0.71, respectively. Among the three predictive tools, the NELA score was the only well-calibrated model.[24] The evidence provided by other studies on the accuracy of ACS NSQIP Surgical Risk Calculator in predicting the risk of postoperative mortality specifically in EL is limited as either they have not exclusively included patients undergoing EL or they have not evaluated the performance of the model in terms of discrimination, calibration, and classification.[25] Unlike ACS NSQIP Surgical Risk Calculator,

TABLE 2. Results of Single Step and Backward Binary Logistic Regression Analysis Used for Development of the Model

	30-day Mortality as Dependent Variable			
	Single Step Binary Logistic Regression		Backward Elimination Binary Logistic Regression	
Independent Variable	Coefficient	P	Coefficient	P
Protocol A				
Age	−0.020494	0.3978	Eliminated	
Age ≥ 80	−1.18029	0.1468	Eliminated	
ASA status	1.16104	0.0054	0.9667	0.0068
Need for bowel resection	−0.81192	0.1561	Eliminated	
Intraperitoneal contamination	−0.46283	0.459	Eliminated	
Clinical frailty scale	0.19164	0.2896	Eliminated	
HI	0.0015849	0.0015	0.001656	0.0004
Sarcopenia	4.88484	< 0.0001	4.40152	< 0.0001
Protocol B				
Age	0.014667	0.5541	Eliminated	
Age ≥ 80	−0.39217	0.5699	Eliminated	
ASA status	0.87068	0.006	0.99154	0.0007
Need for bowel resection	−0.060478	0.8961	Eliminated	
Intraperitoneal contamination	1.0502	0.051	Eliminated	
Clinical frailty scale	0.10525	0.5475	Eliminated	
HI	0.0017499	0.0173	0.002114	0.0017
Sarcopenia	4.10905	< 0.0001	4.08003	< 0.0001

ASA indicates American Society of Anesthesiologists; HI, Hajibandeh Index.

TABLE 3. Relative Importance and Collinearity of the Variables Included in the HAS Model

			Collinearity	
	Variable	Relative Importance	VIF*	Tolerance†
Protocol A	HI	22%	1.098	0.911
	ASA	15%	0.878	0.878
	Sarcopenia	69%	0.941	0.941
Protocol B	HI	25%	1.072	0.933
	ASA	18%	1.064	0.940
	Sarcopenia	68%	1.111	0.900

ASA indicates American Society of Anesthesiologists; HI, Hajibandeh Index; VIF, variance inflation factor.

*VIF greater than 5 suggests collinearity.

†Tolerance lower than 0.2 suggests collinearity.

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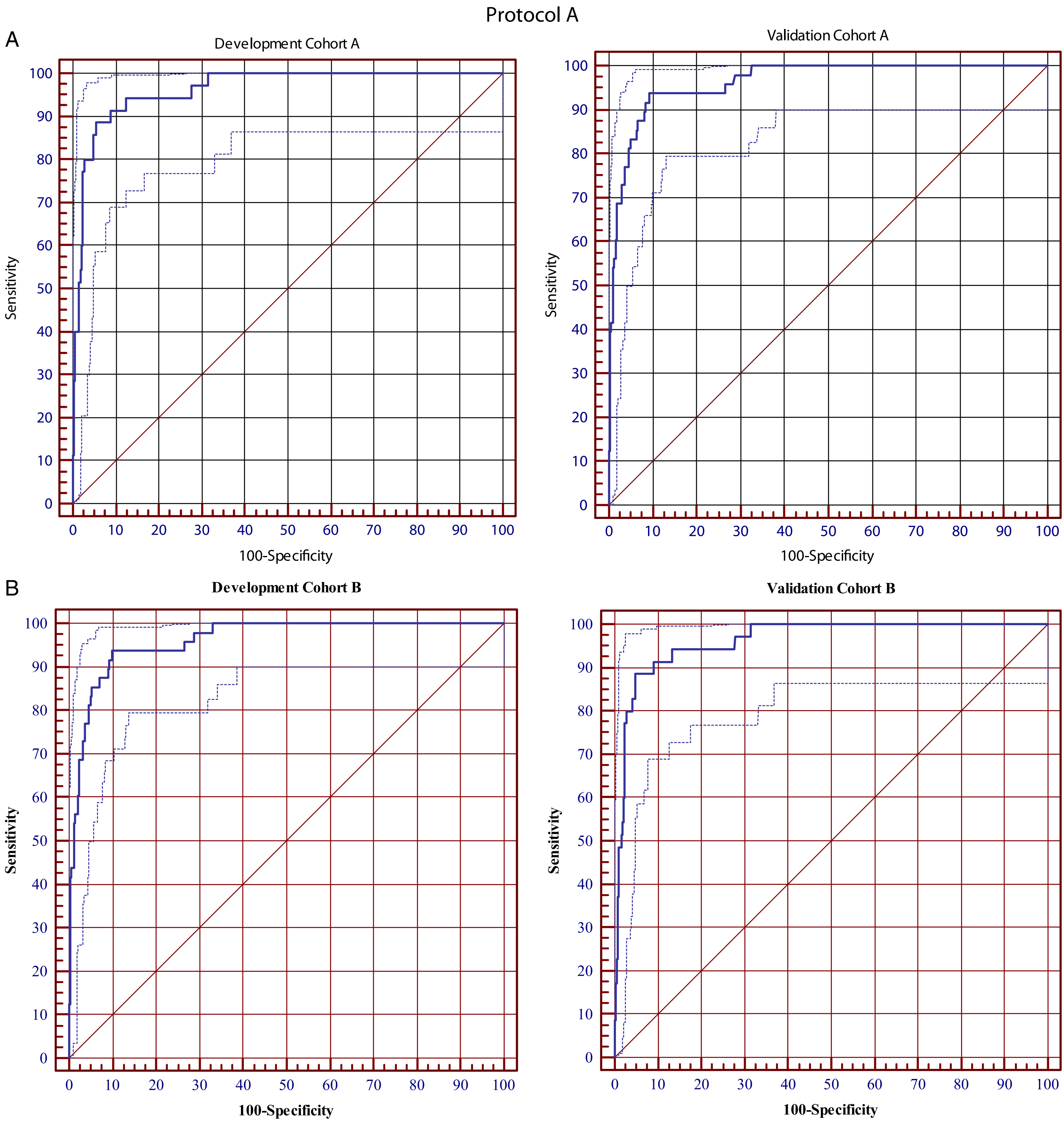

FIGURE 2. Receiver operating characteristic (ROC) curves of the predictive model in development and validation cohorts: (a) Protocol A; (b) Protocol B. The final model included Hajibandeh Index, ASA Status, sarcopenia as independent variables, and 30-day mortality as dependent variable.

the performance of the NELA score and P-POSSUM score have been extensively investigated. Thahir et al[5] reported AUC of 0.82 and 0.77 for NELA score and P-POSSUM score, respectively, and both models were found to be well-calibrated.[5] Lai et al.[7] and Barghash et al.[6] reported AUC of 0.86 and 0.79 for NELA score and AUC of 0.84 and 0.78 for P-POSSUM score, respectively.

The excellent performance of HAS model can be explained by several factors. The HAS model takes into account both severity of the underlying abdominal pathology and the physical status of the patient. The HI, as one of the included predictors in the HAS, is an objectively derived index from acute biomarkers which strongly reflects the severity of underlying abdominal pathology. As described previously, the HI includes

TABLE 4. The Performance of the Model in Terms of Discrimination, Calibration and Classification

	Discrimination		Calibration			Classification
	AUC (95% CI)	*P*	Hosmer-Lemeshow test *P**	Calibration Diagram *P*$	O/E Ratio	Cases Classified correctly
Protocol A						
Development cohort	0.96 (0.94–0.98)	< 0.0001	Not applicable	Not applicable	Not applicable	95%
Validation cohort	0.96 (0.94–0.98)	< 0.0001	0.486	< 0.0001	1.3	95%
Protocol B						
Development cohort	0.96 (0.94–0.98)	< 0.0001	Not applicable	Not applicable	Not applicable	94%
Validation cohort	0.96 (0.94–0.98)	< 0.0001	0.3777	< 0.0001	0.8	95%

CI indicates confidence interval; O/E ratio, observed deaths to expected deaths ratio.
**P*-value > 0.05 suggests good calibration.
$*P*-value < 0.05 suggests good calibration.

preoperative levels of CRP, neutrophils, and lactate as nominators and preoperative levels of albumin and lymphocytes as denominators.[9] Intraabdominal sepsis due to the presence of intestinal ischemia, tissue necrosis, or peritoneal contamination results in an increase in the levels of CRP, neutrophil, and lactate and results in a decrease in the levels of albumin and lymphocyte.[9] Therefore, the more severe the underlying sepsis due to abdominal pathology, the higher the HI.[9] The HI alone was found to be a strong predictor of postoperative mortality in our previous study.[9] The ASA status and sarcopenia, as other two predictors included in the HAS, can strongly reflect the physical status of the patient in terms of co-morbidities, frailty, and physiological reserve. There is no doubt that sarcopenia is a strong predictor of postoperative mortality in patients undergoing EL.[14,26] The fact that it remained in the strict multivariable elimination regression model after two sets of analyses suggests that sarcopenia may be a better reflector of a patient's physical status in comparison to age, being an octogenarian, and clinical frailty score; all of which were eliminated from the regression model. Finally, the strong predictive significance of ASA status in patients undergoing EL is very well established.[12,13]

Once externally validated by others, there are several aspects that may make the HAS an acceptable and practical tool to be used for predicting the risk of postoperative mortality in patients who need EL. It is simple and easy to use. The HI can be calculated easily within a few minutes from already available biomarkers based on the formula provided in Supplementary File 1. The ASA status of a patient can be determined by any clinicians within a few minutes of reviewing the patient. Finally, the radiological presence of sarcopenia can be easily determined from CT scan of the abdomen and pelvis using the technique described earlier; this does not necessarily require specialist radiological expertise and can take only a few minutes for each patient. Almost all patients with acute abdominal pathology undergo a CT scan prior to EL to establish the indication for operation, hence the same scan provides evidence for the presence or absence of radiological sarcopenia.

The HAS model may not have the disadvantages of other predictive tools. The NELA risk score requires preoperative knowledge about intraperitoneal contamination and intraoperative blood loss, which are not necessarily available until the operation is done. The HI used in the HAS model is a strong predictor of intraperitoneal contamination, which is already available prior to operation.[17] On the other hand, the NELA score does not take into account the frailty of the patient,[24] and we have previously shown that its predictive performance in patients aged above 80 may not be as accurate as its performance in younger patients.[9] The inclusion of sarcopenia and ASA together in the HAS model can potentially resolve this issue.

Advances in artificial intelligence-based technology have allowed the development of predictive tools that take into account complex interactions between different variables within a model instead of linear interactions between the variables.[27–29]

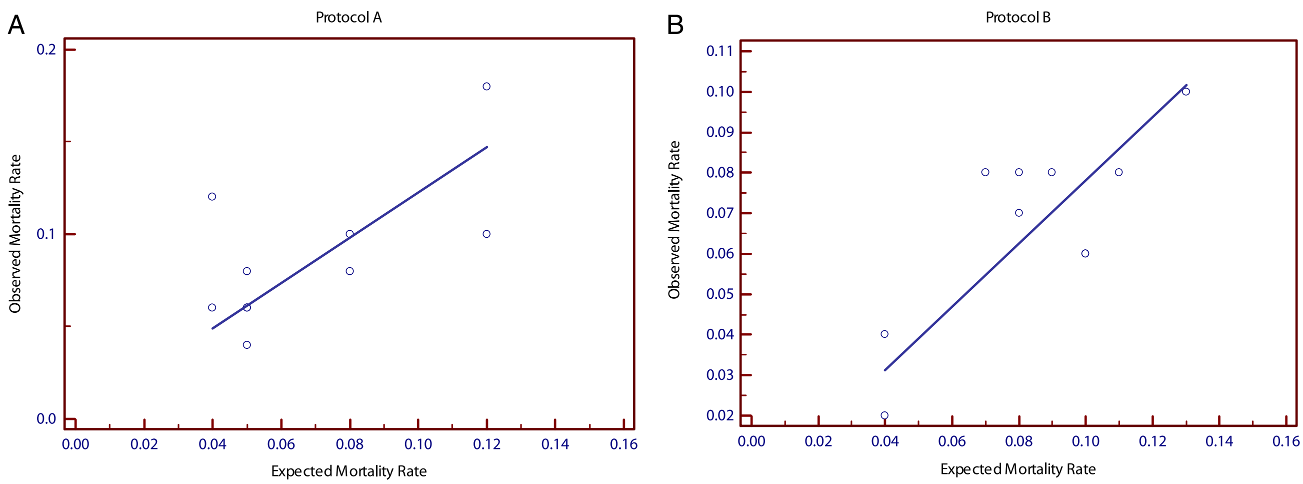

FIGURE 3. The calibration diagram based on the relationship between the observed and expected 30-day mortality risks: (a) Protocol A; (b) Protocol B.

The Predictive OpTimal Trees in Emergency Surgery Risk (POTTER) Calculator is a novel artificial intelligence-based predictive tool that has been developed and validated for predicting the risk of postoperative mortality in patients undergoing any type of emergency surgery with an AUC of 0.92.[27] Similar models have been developed based on generalized additive models with neural networks (GAM-NNs) architecture in other surgical settings.[29] The validation of POTTER in patients aged over 65 undergoing any emergency surgery showed AUC of 0.80.[28] The POTTER has demonstrated an AUC of between 0.77 and 0.84 in predicting 30-day mortality in patients undergoing EL.[30,31] The HAS model has the limitation of being linear in nature and does not have the advantages of artificial intelligence-based predictive tools. However, the predictive performance of the HAS model shown in this study was better than non-linear models in patients undergoing EL. Nevertheless, robust conclusions regarding the performance of the HAS model cannot be made until it is externally validated.

The results of the current study should be interpreted taking into account the following strengths and limitations. The strengths of the current study include (1) Use of objective and systematic approach compliant with the TRIPOD and STROCSS statement standards; (2) Statistical power of 94% with minimal risk of type 2 error; (3) Comparability of the development and validation cohorts in terms of baseline characteristics of the included patients; (4) Using two different protocols for development and validation of the model; (5) Consistency of the results through both protocols used for development and validation of the model. The limitations of the current study include: (1) Retrospective nature of the study and inevitable risk of selection bias; (2) Single-centre nature of the study; (3) Need for external validation by other studies. The single-center nature of the current study means that our results may not be generalizable, and the performance of the HAS model may be affected by various inter-institutional variables. It is well-recognized that the performance of developed predicted tools can be worse when externally validated by other researchers. Consequently, robust conclusions about the performance of HAS model and the extent to which our findings can be applied to other centers are heavily dependent on external validation by other researchers.

External Validation using HAS Mortality Risk Calculator

The HAS model seems promising and is worth attention for external validation. We would like to encourage other authors and researchers with an interest in emergency general surgery to externally validate the performance of HAS model using HAS mortality risk calculator https://app.airrange.io/#/element/xr3b_E6yLor9R2c8KXViSAeOSK, which is included in Supplementary File 2, Supplemental Digital Content 1, http://links.lww.com/SLA/E609. The results of external validation by future studies would help to determine whether or not the HAS model can be incorporated into routine practice.

CONCLUSIONS

The HAS (HI, ASA status, sarcopenia), developed and validated in this study, is the first model demonstrating excellent discrimination (AUC: 0.96), excellent calibration ($P < 0.0001$), and excellent classification (95%) in predicting the risk of 30-day mortality following EL. The HAS model seems promising and is worth attention for external validation. We would like to encourage other authors and researchers to externally validate the performance of the HAS using the calculator provided.

ACKNOWLEDGMENTS

We would like to thank Maureen Edgar (Research Governance Manager), Alun Meggy (Clinical Trials Manager), and Rachel Norman (Registration and Permissions Improvement Manager) in Cardiff & Vale University Health Board for their support in registration, protocoling, and approval of the study.

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DEFINITIONS OR ABBREVIATIONS

NELA: National Emergency Laparotomy Audit

ASA: American Society of Anaesthesiologists

CFS: Clinical Frailty Scale

ERAS: Enhanced Recovery after Surgery

CRP: C-reactive protein

STROCSS: Strengthening the Reporting of Cohort Studies in Surgery

TRIPOD: Transparent Reporting of a multivariable prediction model for Individual Prognosis or Diagnosis

PRISMA: Preferred Reporting Items for Systematic reviews and Meta-Analyses

SD: Standard Deviation

IQR: Interquartile Range

ROC: Receiver Operating Characteristic

AUC: Area Under the Curve

OR: Odds Ratio

CI: Confidence Intervals

HAS: Hajibandeh index, ASA status, Sarcopenia

UK: United Kingdom

CRITICAL REVIEW

Modern Predictors of Mortality in Patients Undergoing Emergency Laparotomy

Background

Emergency laparotomy refers to a surgical procedure that involves emergency access into the peritoneal cavity via a midline incision to treat a potentially life-threatening intra-abdominal pathology.[1] The most common indications for emergency laparotomy include perforation of intra-abdominal organs (stomach, small intestine, large intestine, gallbladder), intestinal obstruction, intestinal ischaemia, intra-abdominal bleeding (spontaneous, iatrogenic, postoperative, or traumatic) and complications of an operation or a procedure (collection, anastomotic leak, or bleeding).[1]

Approximately 40,000 emergency laparotomies are performed per year in the United Kingdom (UK); this accounts for up to 50% of workload and 90% of deaths in General surgery.[2,3] The risk of 30-day mortality after emergency laparotomy was approximately 12.7% in the UK in 2014; this improved to 9.2% in 2023 by compliance with the standards recommended by the National Emergency Laparotomy Audit (NELA).[4] Therefore, emergency laparotomy is a procedure with a high risk of mortality. This has encouraged researchers to explore the predictors of mortality in patients undergoing emergency laparotomy. The knowledge about important predictors of mortality after emergency laparotomy would help to predict the risk of mortality preoperatively, which provides a robust basis for perioperative decision-making and multidisciplinary planning before proceeding with a high-risk major operation.

The potential predictors of mortality may be related to the physical status of the patients, severity of the underlying abdominal pathology, healthcare setting and socioeconomic status of the patients. The potential predictors that could be related to the physical status of the patients include age 80 or over (≥ 80), the American Society of Anaesthesiologists (ASA) status, sarcopenia and the clinical frailty scale (CFS). The potential predictors that could be related to the severity of the underlying abdominal pathology include the intraperitoneal contamination index (Hajibandeh Index), presence of intraperitoneal contamination and the need for bowel resection. The variables that could be related to healthcare settings include the surgeon's seniority, the surgeon's subspeciality of interest, the weekend effect (operation during the weekend) and the application of enhanced recovery after surgery (ERAS) protocols in emergency surgery.

Age ≥ 80

The number of elderly patients undergoing emergency laparotomies is steadily rising due to the increased life expectancy and expansion of the ageing population.[5] It is predicted that the number of octogenarians will double within the next two decades;[6] therefore, the individuals aged 80 or over comprise a significant proportion of patients undergoing emergency laparotomy. However, the effect of being an octogenarian on mortality after emergency laparotomy is poorly understood.

ASA status

The ASA status is a strong reflector of an individual's comorbidities and physiological reserve and it is known to affect operative outcomes.[7] The critical thresholds of ASA status for increasing the risk of mortality after emergency laparotomy are unknown. Moreover, whether the prognostic significance of ASA status varies in the presence of other important predictors of mortality remains unanswered in patients undergoing emergency laparotomy.

Sarcopenia and CFS

The rapidly increasing number of elderly patients undergoing emergency laparotomies has encouraged researchers to determine how ageing-related physiological decline and vulnerability to complications in older adults can be measured objectively. Sarcopenia, which is defined as ageing-related loss of skeletal muscle mass, is a recognised objective measure of ageing-related physiological decline and vulnerability.[8] On the other hand, CFS is an objective scale that classifies individuals between CFS 1 and CFS 9 based on the extent of their frailty.[9] It is not known which one of the above potential predictors is a stronger predictor of mortality after emergency laparotomy and deserves to be included in preoperative predictive tools. Moreover, whether the prognostic significance of sarcopenia or CFS varies in the presence of other important predictors of mortality remains unanswered in patients undergoing emergency laparotomy.

Hajibandeh index, intraperitoneal contamination and the need for bowel resection

The presence of intraperitoneal contamination and the need for bowel resection reflect the severity of the underlying abdominal pathology and are recognised as causes of morbidity and mortality in patients with acute abdominal pathology.[10] However, the knowledge about the presence of intraperitoneal contamination and the need for bowel resection is only available intraoperatively. The Hajibandeh index is a novel index derived from biomarkers and can predict the presence and nature of intraperitoneal contamination preoperatively.[11] It includes preoperative levels of C-reactive protein (CRP), neutrophils and lactate as nominators (because their levels increase in abdominal sepsis) and it includes preoperative levels of albumin and lymphocytes as denominators (their levels decrease in abdominal sepsis).[11] Although the Hajibandeh index is a strong predictor of the presence of intraperitoneal contamination, whether it can predict the risk of mortality after emergency laparotomy needs further research.

Socioeconomic deprivation

Socioeconomic deprivation is defined as unmet needs due to lack of financial and nonfinancial resources and can influence an individual's health-seeking behaviour, lifestyle-related risk factors,[12,13] comorbidities[14,15] and access to healthcare.[16] It is multidimensional and determined based on various domains. The negative impact of deprivation on postoperative outcomes has been demonstrated in various surgical settings.[17,18] However, whether or not deprivation affects the risk of mortality after emergency laparotomy needs further research.

ERAS protocols

ERAS protocols are delivered via a multidisciplinary team approach and are developed to reduce perioperative surgical stress, maintain post-operative physiological function and enhance recovery in surgical patients.[19] The ERAS protocols can decrease the length of hospital stay and can improve outcomes in elective surgery.[20] However, the effect of ERAS protocols on mortality in patients undergoing emergency abdominal surgery, including emergency laparotomy, remains poorly understood.

Weekend effect

The "weekend effect" refers to variation in clinical outcomes in patients undergoing emergency laparotomy during weekends in comparison with weekdays and could be a potential healthcare setting-related predictor of mortality after emergency laparotomy. It may be caused either by differences in staffing levels and reduced availability of resources leading to delays in diagnostics and procedures, or by differences in case mix or severity of disease in patients presenting during the weekend.[21,22] However, the prognostic significance of the weekend effect specifically in patients undergoing emergency laparotomy has not been established.

Surgeon's seniority and subspeciality interest

Surgeon's seniority and surgeon's subspeciality interest are two potential predictors related to the operating surgeon. The modern surgical training has moved toward competency-based training, which focuses on both training and patient safety; consequently, there has been a rapid increase in the number of emergency laparotomies performed independently by competent trainees.[23,24] Some argue that performing a high-risk and complex operation by a less experienced surgeon may increase the risk of mortality.[25] On the other hand, the elective practice in General surgery has moved toward subspecialisation. Some may argue that this would impair the safe emergency service due to reducing the exposure of surgeons to a broad range of surgical disciplines, which in turn may increase the risk of mortality after emergency laparotomy.[26] Therefore, the effect of the surgeon's seniority and the surgeon's subspeciality interest on mortality after emergency laparotomy remains a subject of debate.

Aims

This thesis aims to develop a multivariable preoperative risk assessment tool from modern predictors of mortality to predict the risk of mortality in patients undergoing emergency laparotomy. In order to be able to predict the risk of mortality after emergency laparotomy, the following steps are required:

1. To evaluate and identify the individual variables predicting the risk of mortality after emergency laparotomy.
2. To develop and validate a multivariable predictive model taking into account the already identified potential predictors.

Hypotheses

The following hypotheses were synthesised:

Hypothesis 1. Age ≥ 80 is associated with increased risk of 30-day mortality after emergency laparotomy.

Hypothesis 2. Sex, ASA status, intraperitoneal contamination, bowel resection and abdominal malignancy are associated with increased risk of 30-day mortality in patients aged ≥ 80 undergoing emergency laparotomies.

Hypothesis 3. Sarcopenia and CFS are associated with increased risk of 30-day mortality after emergency laparotomy.

Hypothesis 4. Sarcopenia and ASA status synergistically increase the risk of 30-day mortality after emergency laparotomy.

Hypothesis 5. Hajibandeh index predicts the risk of 30-day mortality after emergency laparotomy.

Hypothesis 6. Hajibandeh index is more accurate than NELA score in predicting the risk of 30-day mortality after emergency laparotomy.

Hypothesis 7. Socioeconomic deprivation is associated with increased risk of 30-day mortality after emergency laparotomy.

Hypothesis 8. Application of ERAS protocols is associated with decreased risk of 30-day mortality after emergency laparotomy.

Hypothesis 9. Emergency laparotomy during the weekend is associated with a higher risk of 30-day mortality than emergency laparotomy during weekdays.

Hypothesis 10. Emergency laparotomy performed by a trainee surgeon is associated with increased risk of 30-day mortality.

Hypothesis 11. Emergency laparotomy performed by a surgeon with a subspeciality interest related to the pathology is associated with reduced risk of 30-day mortality.

Hypothesis 12. A predictive model, which is developed via a strict multivariable analysis of age ≥ 80, ASA status, CFS, sarcopenia, Hajibandeh index, the need for bowel resection and the presence of intraperitoneal contamination, is associated with excellent accuracy in predicting the risk of 30-day mortality after emergency laparotomy.

Methods

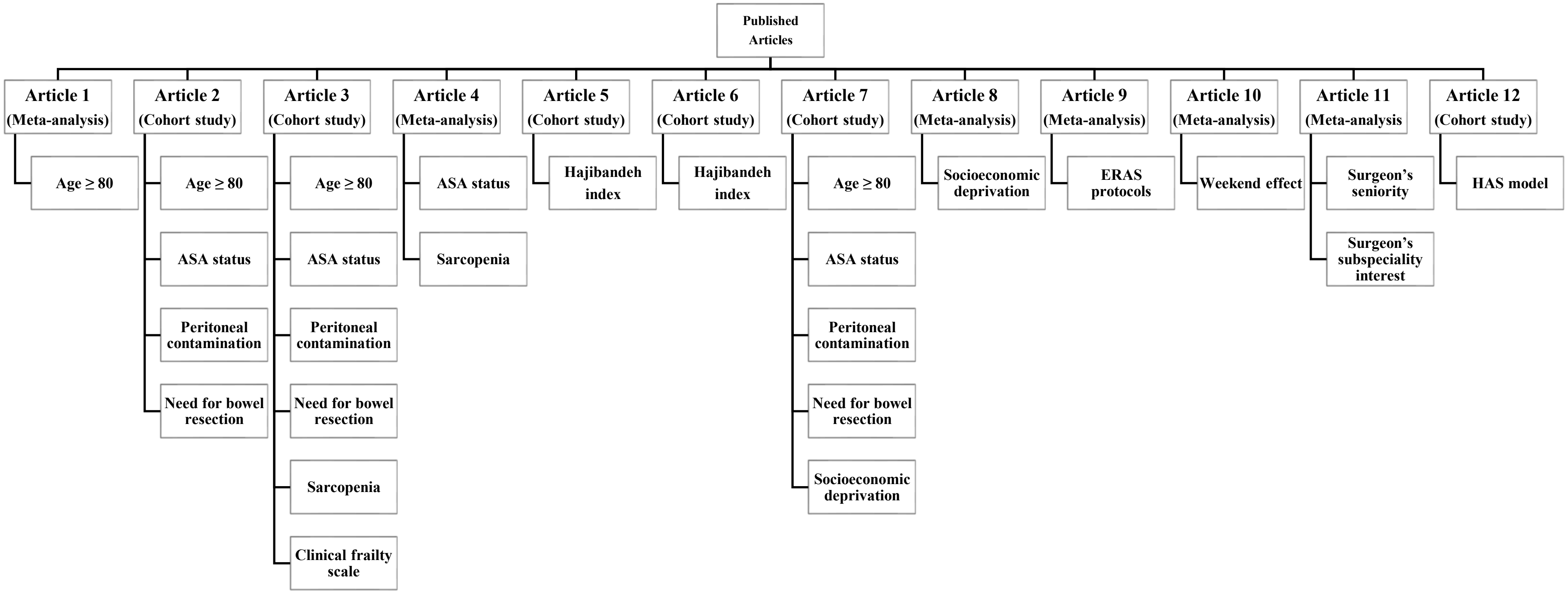
Twelve studies[27-38] were included in this thesis to evaluate the predictors of mortality after emergency laparotomy and to investigate the aforementioned hypotheses. The summary of the included articles and the predictors evaluated by each article are shown in **Figure 1**.

Study design

The type of study design for investigating each potential predictor of mortality after emergency laparotomy was selected based on the available evidence in the literature on each potential predictor. When a potential predictor of interest had not been adequately evaluated in other cohort studies by other authors, a new cohort study was designed and conducted to investigate the significance of the predictor of interest. When a potential predictor of interest had been evaluated in several cohort studies by other authors, a new meta-analysis of cohort studies was designed and conducted to escalate the level of evidence on the predictive value of the predictor of interest. Consequently, the included studies in this thesis were either a novel cohort study or a novel meta-analysis investigating the predictive performance of a potential predictor of mortality after emergency laparotomy.

Among the included 12 studies in this thesis, six[28,29,31-33,38] were cohort studies and six[27,30,34-37] were meta-analyses. The Hypothesis 1 was investigated in a meta-analysis;[27] the Hypothesis 2 was investigated in a retrospective cohort study;[28] the Hypothesis 3 was investigated in a retrospective cohort study;[29] the Hypothesis 4 was investigated in a meta-analysis;[30] the Hypothesis 5 was investigated in a prospective cohort study;[31] the Hypothesis 6 was investigated in a retrospective cohort study;[32] the Hypothesis 7 was investigated in a retrospective cohort study[33] and in a meta-analysis;[34] the Hypothesis 8 was investigated in a meta-analysis;[35] the Hypothesis 9 was investigated in a meta-analysis;[36] the Hypothesis 10 and Hypothesis 11 were investigated in a meta-analysis;[37] the Hypothesis 12 was investigated in a retrospective cohort study.[38]

Figure 1. Visual summary of the included articles and predictors evaluated



Methodological and reporting compliance

The design and reporting of five cohort studies[28,29,31-33] followed the Strengthening the Reporting of Cohort Studies in Surgery (STROCSS) statement standards.[39] The design and reporting of one cohort study[38] followed the recommended standards by the Transparent Reporting of a multivariable prediction model for Individual Prognosis or Diagnosis (TRIPOD)[40] as well as those by the STROCSS.[39] The design and reporting of the meta-analyses[27,30,34-37] followed the Cochrane Handbook for Systematic Reviews[41] and the Preferred Reporting Items for Systematic reviews and Meta-Analyses (PRISMA) statement standards.[42]

Patient eligibility criteria

All adult patients (age ≥ 18) who underwent emergency laparotomy due to non-traumatic acute abdominal pathologies were eligible for inclusion. The abdominal pathologies of interest included intestinal perforation, intestinal obstruction, intestinal ischaemia, intestinal fistula, intra-abdominal bleeding, intra-abdominal collection, colitis or anastomotic leak. Emergency laparotomy due to trauma was an exclusion criterion.

Outcome measure

30-day postoperative mortality, which was defined as death due to any cause occurring within 30 days after emergency laparotomy, was the outcome measure of interest.

Potential predictors

The following individual variables were investigated as potential predictors:

- Age ≥ 80 (evaluated in three cohort studies[28,29,33] and one meta-analysis[27])
- ASA status (evaluated in three cohort studies[28,29,33] and two meta-analyses[27,30])
- Sarcopenia (evaluated in one cohort study[29] and one meta-analysis[30])
- CFS (evaluated in one cohort study[29])
- Hajibandeh index (evaluated in two cohort studies[31,32])

- Intraperitoneal contamination (evaluated in three cohort studies[28,29,33])
- Bowel resection (evaluated in three cohort studies[28,29,33])
- Socioeconomic deprivation (evaluated in one cohort study[33] and one meta-analysis[34])
- ERAS protocols (evaluated in one meta-analysis[35])
- Weekend effect (evaluated in one meta-analysis[36])
- Surgeon's seniority (evaluated in one meta-analysis[37])
- Surgeon's subspeciality interest (evaluated in one meta-analysis[37])

Multivariable predictive model

Based on the knowledge developed from the evaluation of the individual potential predictors of 30-day mortality after emergency laparotomy, a final multivariable predictive model was developed and validated in a retrospective cohort study.[38]

Data collection

Two independent authors were involved in data collection in all of the included studies. In case of disagreement between the findings of the first two authors, a third author provided an opinion to resolve the disagreement. The hospital medical records were used as a source for data collection in the cohort studies and the online electronic data resources were used as a source for data collection in the meta-analyses (information about withdrawals, dropouts and other missing data were recorded; if not reported, the study authors were contacted where possible). In each study, a data collection sheet was created, which included information about the baseline characteristics of the included patients in the cohort studies, baseline characteristics of the included studies in the meta-analyses, the potential predictors relevant to the subject of each study and 30-day mortality.

Statistical analyses

In the cohort studies,[28,29,31-33] simple descriptive statistics were used to summarise the baseline characteristics and outcome data. These included mean ± standard deviation (SD) or median and interquartile range (IQR) for continuous variables and percentages for dichotomous variables.[28,29,31-33] When the variables were compared, the continuous variables were compared using the t-test or Mann–

Whitney test as appropriate and the dichotomous variables were compared using the chi-squared test.[29,33,38] Binary logistic regression analyses were used to evaluate the association between the potential predictors (independent variables) and 30-day mortality (dependent variable) when appropriate.[28,29,31-33] When predictive performance of a model was evaluated, Receiver Operating Characteristic (ROC) curve analyses were used to evaluate the discrimination of the model by calculating the area under the curve (AUC);[29,31-33,38] the Hosmer-Lemeshow test (goodness of fit test)[38] or calibration diagram[32,38] were used to evaluate the calibration of the model; classification table[32,38] was used to evaluate the classification of the model. All statistical tests were two-tailed and statistical significance was assumed at $p < 0.05$.

In the meta-analyses,[27,30,34-37] comparative meta-analysis model was constructed to compare the risk of 30-day mortality between the groups with or without the exposure of interest, and the odds ratio (OR) was calculated as a summary measure.[27,30,34-37] When the pooled risk of 30-day mortality in patients with an exposure of interest was required,[27,30] proportion meta-analysis model was constructed to integrate the quantitative incidence of 30-day mortality from individual studies.[27,30] When indicated, meta-regression was performed to evaluate the effect of a specific variable on 30-day mortality.[30] The unit of analysis was the individual patient. Random or fixed effects modelling was used for the analyses as appropriate and forest plots with 95% confidence intervals (CIs) were used for presentation. Statistical heterogeneity was quantified as I^2 using Cochran's Q test (χ^2). Sensitivity analyses and subgroup analyses were conducted as appropriate to evaluate the robustness of the results.

Results

Age ≥ 80

This potential predictor was evaluated in three cohort studies[28,29,33] and one meta-analysis[27]:

- A meta-analysis of 66,701 octogenarians from 22 studies showed that the pooled risk of 30-day mortality after emergency laparotomy was 29% (95% CI 25-33%).[27] The risk of 30-day mortality was significantly higher in patients aged ≥ 80 compared with patients aged < 80 (OR: 4.07, 95% CI 2.40-6.89, p < 0.00001), patients aged 50 to 79 (OR: 2.03, 95% CI 1.68-2.45, p < 0.00001) and patients aged 70 to 79 (OR: 1.21, 95% CI 1.13-1.31, p < 0.00001).[27] These were novel findings that had not been reported in literature previously. The statistical between-study heterogeneity was high in this meta-analysis which can be explained by the variations in indications for emergency laparotomy among the included studies. The certainty of evidence was downgraded to moderate accordingly.
- A retrospective cohort study of 523 octogenarians undergoing emergency laparotomy showed that the risk of 30-day mortality was 21.8% (95% CI 18.3–25.6%).[28]
- A retrospective cohort study of 1,043 patients undergoing emergency laparotomy showed that age ≥ 80 was not an independent predictor of 30-day mortality (OR: 0.42, 95% CI 0.15–1.12, p = 0.0829) in a multivariable binary logistic regression analysis including the following variables: age ≥ 80, age, ASA status, bowel resection, peritoneal contamination, sarcopenia and CFS.[29] This was a novel finding as it was the first time in the literature that age ≥ 80 and sarcopenia were included in the same model.
- A retrospective cohort study of 1,723 patients undergoing emergency laparotomy showed that age ≥ 80 was an independent predictor of 30-day mortality (OR: 1.53, 95% CI 1.05–2.22, p = 0.027) in a multivariable binary logistic regression analysis including the following variables: age ≥ 80, ASA status, bowel resection, peritoneal contamination and socioeconomic deprivation.[33]

ASA status

This potential predictor was evaluated in three cohort studies[28,29,33] and two meta-analyses[27,30].

- A meta-analysis of 66,701 octogenarians from 22 studies showed that risk of 30-day mortality after emergency laparotomy increased with higher ASA status: 11% (95% CI 4%-20%) in octogenarians with ASA II status; 22% (95% CI 10%-36%) in octogenarians with ASA III status; 39% (95% CI 29%-48%) in octogenarians with ASA IV status and 94% (95% CI 77%-100%) in octogenarians with ASA V status.[27] This was a novel finding as this study was the first meta-analysis in the literature that reported ASA-stratified risks of mortality in octogenarians undergoing emergency laparotomy.
- A retrospective cohort study of 523 octogenarians undergoing emergency laparotomy showed that ASA status was an independent predictor of 30-day mortality (OR: 2.49, 95% CI 1.82–3.38, $p < 0.0001$) in a multivariable binary logistic regression analysis including the following variables: age ≥ 80, age, ASA status, peritoneal contamination, bowel resection and abdominal malignancy.[28]
- A retrospective cohort study of 1,043 patients undergoing emergency laparotomy showed that ASA status was an independent predictor of 30-day mortality (OR: 2.83, 95% CI 1.79–4.47, $p <0.0001$) in a multivariable binary logistic regression analysis including the following variables: age ≥ 80, age, ASA status, bowel resection, peritoneal contamination, sarcopenia and CFS.[29]
- A meta-analysis of 2,663 patients from seven studies showed that sarcopenia and ASA status independently and synergistically increased the risk of 30-day mortality after emergency laparotomy.[30] In sarcopenic patients, ASA status I–II (coefficient: − 0.09039, $p < 0.0001$) or ASA status III (coefficient: 0.01300, $p = 0.344$) did not increase the risk of 30-day mortality, but ASA status IV–V increased the risk of 30-day mortality (coefficient: 0.07612, $p < 0.0001$). In non-sarcopenic patients, ASA status I-II (coefficient: − 0.05841, $p < 0.0001$) did not increase the risk of 30-day

mortality. However, ASA status III (coefficient: 0.06830, $p < 0.0001$) and ASA status IV–V (coefficient: 0.17809, $p < 0.0001$) increased the risk of mortality.[30] Consequently, ASA status IV and ASA status III were the critical thresholds for increased risk of mortality in sarcopenic and non-sarcopenic patients undergoing emergency laparotomy, respectively.[30] These were novel findings as this study was the first in the literature that showed synergistic effect of sarcopenia and ASA status on mortality after emergency laparotomy. Moreover, this study was the first in the literature that defined critical ASA status thresholds for increased risk of mortality in sarcopenic patients. The statistical between-study heterogeneity was high in this meta-analysis which can be explained by the fact that the included studies defined and measured sarcopenia differently. The certainty of evidence was downgraded to moderate accordingly.

- A retrospective cohort study of 1,723 patients undergoing emergency laparotomy showed that ASA status was an independent predictor of 30-day mortality (OR: 3.28, 95% CI 2.60–4.13, $p < 0.001$) in a multivariable binary logistic regression analysis including the following variables: age ≥ 80, ASA status, bowel resection, peritoneal contamination and socioeconomic deprivation.[33]

Sarcopenia

This potential predictor was evaluated in one cohort study[29] and one meta-analysis[30]:

- A retrospective cohort study of 1,043 patients undergoing emergency laparotomy showed that sarcopenia was an independent predictor of 30-day mortality (OR: 76.16, 95% CI 37.06–156.52, $p <0.0001$) in a multivariable binary logistic regression analysis including the following variables: age ≥ 80, age, ASA status, bowel resection, peritoneal contamination, sarcopenia and CFS.[29] This was a novel finding as this study was the first in the literature that compared sarcopenia and CFS in patients undergoing emergency laparotomy.
- A meta-analysis of 2,663 patients from seven studies showed that the pooled risk of 30-day mortality in patients with and without sarcopenia

undergoing emergency laparotomy was 22.9% (95% CI 11.6–40.0%) and 6.2% (95% CI 2.9–13.0%), respectively. The risk was higher in patients with sarcopenia (OR: 4.45, 95% CI 1.32–14.98, p = 0.016).[30] The statistical between-study heterogeneity was high in this meta-analysis which can be explained by the fact that the included studies defined and measured sarcopenia differently. The certainty of evidence was downgraded to moderate accordingly.

CFS

This potential predictor was evaluated in one cohort study[29]:

- A retrospective cohort study of 1,043 patients undergoing emergency laparotomy showed that CFS was not an independent predictor of 30-day mortality (OR: 1.10, 95% CI 0.88–1.38, p=0.405) in a multivariable binary logistic regression analysis including the following variables: age ≥ 80, age, ASA status, bowel resection, peritoneal contamination, sarcopenia and CFS.[29] This was a novel finding as this study was the first in the literature that compared sarcopenia and CFS in patients undergoing emergency laparotomy.

Hajibandeh index

This potential predictor was evaluated in two cohort studies[31,32].

- A prospective cohort study of 269 patients showed that Hajibandeh index predicted the presence of purulent (AUC: 0.78, p < 0.0001) and feculent intraperitoneal contamination (AUC: 0.78, p < 0.0001) in patients with acute abdominal pathology and postoperative 30-day mortality (AUC: 0.70, 95% CI 0.64–0.75, p <0.0001) in patients undergoing emergency laparotomy.[31] The Hajibandeh index was an independent predictor of 30-day mortality after emergency laparotomy (OR: 3.24, 95% CI 1.48–7.11, p = 0.002).[31] This was a novel finding in the literature which had not been shown previously.
- A retrospective cohort study of 700 patients undergoing emergency laparotomy showed that the Hajibandeh index had very good

discrimination (AUC: 0.86, 95% CI 0.83–0.88, $p < 0.0001$) and calibration ($p = 0.0081$) in predicting the risk of 30-day mortality.[32] It classified 86% of cases correctly. The performance of the Hajibandeh index was comparable with the performance of the NELA score in predicting 30-day mortality (AUC: 0.86 vs 0.87, $p = 0.557$). However, the performance of the Hajibandeh index was significantly better than the NELA score in predicting postoperative 30-day mortality in patients aged ≥ 80 (AUC: 0.85 vs 0.72, $p = 0.0174$).[32] This was a novel finding in the literature which had not been shown previously.

Intraperitoneal contamination

This potential predictor was evaluated in three cohort studies[28,29,33]:

- A retrospective cohort study of 523 octogenarians undergoing emergency laparotomy showed that the presence of intraperitoneal contamination was an independent predictor of 30-day mortality (OR: 2.00, 95% CI 1.30–3.08, $p = 0.002$) in a multivariable binary logistic regression analysis including the following variables: age ≥ 80, age, ASA status, peritoneal contamination, bowel resection and abdominal malignancy.[28]
- A retrospective cohort study of 1,043 patients undergoing emergency laparotomy showed that the presence of intraperitoneal contamination was an independent predictor of 30-day mortality (OR: 2.37, 95% CI 1.15–4.91, $p = 0.0197$) in a multivariable binary logistic regression analysis including the following variables: age ≥ 80, age, ASA status, bowel resection, peritoneal contamination, sarcopenia and CFS.[29]
- A retrospective cohort study of 1,723 patients undergoing emergency laparotomy showed that the presence of intraperitoneal contamination was an independent predictor of 30-day mortality (OR: 2.12, 95% CI 1.50–3.00, $p < 0.001$) in a multivariable binary logistic regression analysis including the following variables: age ≥ 80, ASA status, bowel resection, peritoneal contamination and socioeconomic deprivation.[33]

Bowel resection

This potential predictor was evaluated in three cohort studies[28,29,33]:

- A retrospective cohort study of 523 octogenarians undergoing emergency laparotomy showed that the need for bowel resection was not an independent predictor of 30-day mortality (OR: 1.12, 95% CI 0.73–1.71, p = 0.600) in a multivariable binary logistic regression analysis including the following variables: age ≥ 80, age, ASA status, peritoneal contamination, bowel resection and abdominal malignancy.[28]
- A retrospective cohort study of 1,043 patients undergoing emergency laparotomy showed that the need for bowel resection was not an independent predictor of 30-day mortality (OR: 0.63, 95% CI 0.33–1.22, p = 0.1688) in a multivariable binary logistic regression analysis including the following variables: age ≥ 80, age, ASA status, bowel resection, peritoneal contamination, sarcopenia and CFS.[29]
- A retrospective cohort study of 1,723 patients undergoing emergency laparotomy showed that the need for bowel resection was an independent predictor of 30-day mortality (OR: 1.54, 95% CI 1.09–2.19, p = 0.018) in a multivariable binary logistic regression analysis including the following variables: age ≥ 80, ASA status, bowel resection, peritoneal contamination and socioeconomic deprivation.[33]

Socioeconomic deprivation

This potential predictor was evaluated in one cohort study[33] and one meta-analysis[34]:

- A retrospective cohort study of 1,723 patients undergoing emergency laparotomy showed the risk of 30-day mortality was higher in the most deprived quartile in comparison with the least deprived quartile (13.2% vs. 7.9%, p = 0.008). Socioeconomic deprivation was an independent predictor of 30-day mortality (OR: 1.03, 95% CI 1.01–1.06, p = 0.023) in a multivariable binary logistic regression analysis including the following variables: age ≥ 80, ASA status, bowel resection, peritoneal contamination and socioeconomic deprivation.[33] This was a novel finding in the literature as the study was the first in Wales that evaluated effect of socioeconomic deprivation on mortality after emergency laparotomy.

- A meta-analysis of 87,690 patients from four studies showed no difference in the unadjusted risk (OR: 1.57, 95% CI 0.92–2.68, p = 0.100) and adjusted risk (OR: 1.11, 95% CI 0.93–1.32, p = 0.230) of 30-day mortality between the most and least deprived groups.[34] This was a novel finding in the literature as this was the first meta-analysis in the literature evaluating prognostic significance of socioeconomic deprivation in emergency laparotomy setting. The statistical between-study heterogeneity was high which can be explained by the fact that the included studies used a different multiple deprivation index for assessment of socioeconomic status. The certainty of evidence was downgraded to moderate accordingly.

ERAS protocols

This potential predictor was evaluated in one meta-analysis[35]:

- A meta-analysis of 1,334 patients from six studies showed that although application of ERAS protocols reduced the risk of morbidity (OR: 0.60, 95% CI 0.45, 0.81, p = 0.0008), it did not affect the risk of 30-day mortality (risk difference: -0.001, 95% CI - 0.02, 0.02, p = 0.940) in patients undergoing emergency abdominal surgery including emergency laparotomy.[35] This was the first meta-analysis in literature that evaluated application of ERAS protocols in emergency abdominal surgery and the findings were novel. The statistical between-study heterogeneity was low in this meta-analysis.

Weekend effect

This potential predictor was evaluated in one meta-analysis[36]:

- A meta-analysis of 394,646 patients from 10 studies showed that the effect of operating during the weekend on the risk of 30-day mortality after emergency abdominal surgery, including emergency laparotomy, was variable across the world. It increased the risk of 30-day mortality in the Europe (OR: 1.37, 95% CI 1.11-1.69, p = 0.003) and USA (OR: 1.12, 95% CI 1.01-1.24, p = 0.030) but it did not affect the risk of mortality in the UK (OR: 1.04, 95% CI 0.97-1.11, p = 0.300) and South Africa (OR: 0.79, 95%

CI 0.44-1.42, p = 0.430).[36] This was the first meta-analysis in literature that evaluated prognostic significance of weekend effect in emergency abdominal surgery and the findings were novel. The between-study heterogeneity was moderate in this meta-analysis which can be explained by variations in the indications for emergency abdominal surgery among the included studies. The certainty of evidence was downgraded to moderate accordingly.

Surgeon's seniority

This potential predictor was evaluated in one meta-analysis[37]:

- A meta-analysis of 200,223 patients from five studies showed no difference in the risk of 30-day mortality when emergency laparotomy was performed by trainee surgeons or consultant surgeons (OR: 0.76, 95% CI: 0.53–1.08, p = 0.120).[37] This was the first meta-analysis in literature that evaluated prognostic significance of surgeon's seniority in emergency laparotomy and the findings were novel. The statistical between-study heterogeneity was high in this meta-analysis which can be explained by the variations in the pathologies indicating emergency laparotomy among the included studies. The certainty of evidence was downgraded to moderate accordingly.

Surgeon's subspeciality interest

This potential predictor was evaluated in one meta-analysis[37]:

- Analysis of 56,979 patients from nine studies showed that emergency laparotomies performed by surgeons without subspeciality interest related to the pathology were associated with a higher risk of postoperative mortality compared with surgeons with subspeciality interest (OR: 1.38, 95% CI: 1.24-1.54, $p < 0.00001$).[37] In upper gastrointestinal pathologies, emergency laparotomies performed by lower gastrointestinal surgeons resulted in a higher risk of mortality compared with upper gastrointestinal surgeons (OR: 1.29, 95% CI: 1.00-1.67, p = 0.05).[37] In lower gastrointestinal pathologies, emergency laparotomies performed by upper gastrointestinal surgeons resulted in a higher risk of mortality compared with lower gastrointestinal surgeons (OR: 1.43, 95% CI: 1.26-1.62, p < 0.00001).[37] This was the first meta-analysis in literature that evaluated prognostic significance of surgeon's subspeciality interest in emergency laparotomy and the findings were novel. The between-study heterogeneity was low to moderate in this meta-analysis.

Final multivariable predictive model

The final multivariable predictive model was developed and validated in one cohort study[38]:

- A retrospective cohort study of 1,043 patients undergoing emergency laparotomy developed and validated a predictive model via two different protocols (Protocol A and Protocol B) using a very strict multivariable analysis taking into account the following variables: age, age ≥ 80, ASA status, CFS, sarcopenia, Hajibandeh index, the need for bowel resection and the presence of intraperitoneal contamination.[38] In protocol A, the Hajibandeh index (p=0.0004), ASA status (p=0.0068) and sarcopenia (p < 0.0001) remained as final independent predictors of 30-day mortality after emergency laparotomy.[38] In protocol B, the Hajibandeh index (p=0.0017), ASA status (p=0.0007) and sarcopenia (p < 0.0001) remained as final independent predictors of 30-day mortality after emergency laparotomy.[38] The final model was called HAS (Hajibandeh index, ASA status, sarcopenia), which showed excellent discrimination (AUC: 0.96, 95% CI 0.94–0.98, p <0.0001), excellent calibration (p< 0.0001) and excellent classification (95% of cases were classified correctly).[38] This was a novel finding in the literature.

Discussion

This thesis evaluated the modern predictors of 30-day mortality in patients undergoing emergency laparotomy via 12 studies[17-38] comprising six cohort studies[28,29,31-33,38] and six meta-analyses.[27,30,34-37] The effects of important individual potential predictors on 30-day mortality after emergency laparotomy were evaluated separately. The potential predictors included age ≥ 80, ASA status, sarcopenia, CFS, the Hajibandeh index, the presence of intraperitoneal contamination, the need for bowel resection, socioeconomic deprivation, application of ERAS protocols, weekend effect, surgeon's seniority and surgeon's subspeciality interest. Subsequently, the identified important predictors were included in a strict multivariable analysis to develop and validate a final predictive model called HAS, which only identified the Hajibandeh index, ASA status and sarcopenia as the final significant predictors of 30-day mortality in patients undergoing emergency laparotomy.

Summary of key findings

The results of the included studies in the thesis highlighted that among the variables related to the physical status of the patients, sarcopenia and the ASA status were strong and independent predictors of postoperative mortality after emergency laparotomy with no collinearity; however, age ≥ 80 was a weak predictor and the CFS was not an independent predictor of 30-day mortality. Among the variables related to the severity of the underlying abdominal pathology, the Hajibandeh index was a strong and independent predictor of mortality after emergency laparotomy; however, intraperitoneal contamination was a weak predictor and the need for bowel resection was not an independent predictor of 30-day mortality. Among the variables related to the healthcare setting and socioeconomic status of the patients, surgeon's subspeciality interest was a predictor of 30-day mortality after emergency laparotomy; however, application of ERAS protocols, weekend effect, surgeon's seniority, and socioeconomic deprivation were not independent predictors of 30-day mortality. The developed and validated HAS model, which included the Hajibandeh index, ASA status and sarcopenia as the main variables, was a strong predictor of mortality after emergency laparotomy with excellent predictive performance in terms of discrimination, calibration, and classification.

Interpretation of findings

The higher risk of mortality in patients aged ≥ 80 can be explained by the fact that patients aged ≥ 80 are more likely to be frail and are likely to have more comorbidities and higher ASA status. Therefore, increased vulnerability associated with ageing-related physiological deficits and decreased physiological reserve, together with the negative impact of the underlying abdominal pathology, would make emergency laparotomy a high-risk procedure in this cohort of patients. However, age ≥ 80 lost its predictive significance in any multivariable analyses that included sarcopenia as a variable. This is a novel finding that highlights that age on its own may not be a negative predictor of 30-day mortality. In fact, the frailty and comorbidities associated with age increase the risk of mortality. Therefore, octogenarians may not necessarily be at increased risk of mortality after emergency laparotomies compared to younger patients, provided that they are not frail and do not have major comorbidities.

Accepting that sarcopenia and CFS are two modern measures of frailty, inclusion of both in a single predictive tool may reduce the accuracy of the tool due to likely collinearity.[29] Therefore, between the two variables, only the stronger predictor should be included in preoperative predictive tools. Sarcopenia was a stronger predictor of postoperative mortality than CFS in patients undergoing emergency laparotomy, as it cancelled out the predictive value of CFS in multivariable analyses.[29] Therefore, sarcopenia deserves to be included in preoperative predictive tools.

The negative impact of sarcopenia on postoperative mortality can be explained by the fact that sarcopenia can be defined as an ageing-related decline in skeletal muscle mass and strength, which can lead to reduced mobility, loss of functionality and suboptimal breathing.[43] It can be considered as an objective measurement of ageing-related physiological decline and vulnerability; hence, its presence would increase the risk of morbidity and mortality after major emergency abdominal surgery. Sarcopenia and ASA status independently and synergistically increased the risk of mortality after emergency laparotomy with no significant collinearity;[30] therefore, both should be included in preoperative predictive tools. The prognostic significance of ASA status can be explained by the fact that the ASA status is directly related to the number and severity of comorbidities in patients undergoing emergency laparotomy; hence, the higher the ASA status, the higher the risk of complications, including mortality.

The strong performance of Hajibandeh index in predicting postoperative mortality can be explained by the fact that it is a strong predictor of peritoneal contamination and accurately reflects the severity of underlying abdominal pathology. When the underlying abdominal pathology is associated with tissue necrosis, intraperitoneal contamination, or intestinal ischaemia, the levels of nominators in the Hajibandeh index (lactate, neutrophil, and CRP) increase and the levels of denominators in the Hajibandeh index (lymphocyte and albumin) decrease which result in an increase in the Hajibandeh index; therefore, the more severe the underlying abdominal pathology, the higher Hajibandeh index.[11] When the Hajibandeh index was included in a multivariable analysis, it cancelled out the predictive effect of intraperitoneal contamination and the need for bowel resection. This highlights that the Hajibandeh index is a better measure of the severity of underlying abdominal pathology and sepsis compared with the presence of intraperitoneal contamination or the need for bowel resection. The possible explanation for this could be the fact that not all severe abdominal pathologies lead to intraperitoneal contamination or bowel resection. For example, intestinal ischaemia, which results in tissue necrosis, is associated with a very high risk of mortality. However, it does not lead to intraperitoneal contamination, but it would increase the Hajibandeh index. As another example, perforated duodenal ulcer may not lead to bowel resection, but it would increase the Hajibandeh index. Consequently, the Hajibandeh index may reflect the severity of underlying abdominal pathology better than intraperitoneal contamination or bowel resection; therefore, it should be included in preoperative predictive tools.

The nature of the emergency setting may explain the weak performance of socioeconomic deprivation in predicting mortality after emergency laparotomy.[33, 34] In fact, patients with acute abdominal pathologies seek medical help on an emergency basis due to the severity and rapid deterioration of their condition regardless of their socioeconomic status; therefore, their socioeconomic status may not affect their help-seeking behaviour.[33, 34] Consequently, it may be reasonable to argue that predictive performance of preoperative predictive tools may not improve by incorporation of socioeconomic deprivation as a predictor. The nature of emergency setting may also explain why application of ERAS protocols did not improve the mortality after emergency laparotomy. In fact, the main predictors of mortality after emergency laparotomy, including the Hajibandeh index, ASA status and sarcopenia, cannot be modified by components of ERAS protocols and they may compromise some components of ERAS, including early mobility, establishment of early nutrition, or early removal of drains or tubes.

The standardisation of emergency care may explain why weekend effect did not affect the risk of mortality after emergency laparotomy in the UK. The NELA recommended standards in perioperative management of patients undergoing emergency laparotomy during weekdays or weekend, which improved access to specialist emergency services; this, in turn, improved the operative mortality from 12.7% to 9.2%.[4]

The comparable mortality rates between the trainee surgeons and consultant surgeons can be explained by different factors. Most of the included studies in the meta-analysis were from the UK, in which the competencies of the trainees are assessed based on several summative and formative assessments, operative case volume, and informal judgement by supervising consultants.[44] On the other hand, when UK trainees are allowed to perform emergency laparotomies independently, they are likely to be competent for such a procedure based on the recommended standards in the UK surgical practice.[44] Moreover, the outcomes can be confounded by the fact that trainee surgeons are likely to perform less complex operations in comparison to consultants, hence fewer complications. Consequently, trainee-led operations may not increase the risk of 30-day mortality after emergency laparotomy.

Surgeon's subspeciality interest was a predictor of 30-day mortality after emergency laparotomy in one meta-analysis[37] included in this thesis. Most of the included studies in the meta-analysis were from the UK, in which emergency general surgery is not fully recognised as a subspeciality. General surgical trainees in the UK develop competencies required in emergency general surgery. However, they should declare their subspecialities early, which would fall into the upper or lower gastrointestinal categories.[37] Consequently, the emergency surgery cover has been shifted toward a dual speciality emergency service in which the lower gastrointestinal surgeons deal with lower gastrointestinal pathologies and the upper gastrointestinal surgeons deal with upper gastrointestinal pathologies.[37] This may explain why surgeons' subspeciality interest reduced the risk of 30-day mortality after emergency laparotomy in the UK.[37]

The excellent predictive performance of the HAS model may be justified by several factors. As discussed previously, the Hajibandeh index, which is one of the main components of the HAS model, strongly reflects the severity of underlying abdominal pathology and sepsis and is a strong predictor of 30-day mortality.[38] Therefore, the more severe the underlying sepsis due to abdominal pathology, the higher the Hajibandeh index.[38] Moreover, the other two components of the HAS model (ASA status and sarcopenia) strongly reflect patients' comorbidities, frailty and physiological reserve.[38]

Contextualization within existing literature

The findings of current study have external validity. The negative impact of age ≥ 80 on mortality in patients undergoing emergency laparotomy has been shown by other studies.[45-47] Aakre et al[45] conducted a retrospective cohort study of 106 patients aged ≥ 80 and reported 30-day mortality risk of 26%. In another retrospective cohort study of 163 patients aged ≥ 80, Simpson et al[46] reported postoperative mortality risk of 19.2%. Green et al[47] also reported postoperative mortality risk of 45% in 100 octogenarians who underwent emergency laparotomy.

The findings of current thesis on prognostic significance of sarcopenia and ASA status can also be supported by the findings of other studies. Akhtar et al[48] conducted a systematic review of 11 studies which concluded that ASA status was associated with increased risk of mortality after emergency laparotomy. Humphry et al[49] conducted a meta-analysis of 3,492 patients from 11 studies and concluded that sarcopenia was associated with increased risk of 30-day mortality. Keshavjee et al[50] reported increased risk of 30-day postoperative mortality in patients with sarcopenia undergoing surgery for colorectal cancer in a meta-analysis of 13,422 patients from 40 studies.

Although the studies included in this thesis did not identify CFS as a strong predictor of mortality after emergency laparotomy, previous cohort studies[51-53] suggested that CFS may be an effective tool for assessing preoperative vulnerability and frailty, which may predict mortality and morbidity after emergency surgery. Parmar et al[51] conducted a multicentre observational study including 937 patients from 49 centres which concluded that frailty measured by CFS was associated with increased risk of mortality after emergency laparotomy. In another study, Palaniappan et al.[52] analysed data from 2246 patients in a retrospective cohort study and concluded that frailty measured by CFS was associated with increased risk of mortality after emergency laparotomy. Youssef et al[53] also reached similar conclusions in a retrospective cohort study of 191 patients. The main reason for the difference in the findings of this thesis and the previous studies is that the current thesis included sarcopenia, which is a stronger predictor of mortality, in the multivariable analysis together with CFS; hence, the weaker predictor was eliminated by the model. However, the previous studies did not compare the predictive performance of CFS with other measures of frailty.

While the Hajibandeh index is a novel index, few studies validated its predictive performance. Srinivasan et al.[54] conducted a prospective observational study of 510 patients undergoing emergency laparotomy and concluded that Hajibandeh index has AUC of 0.92 in predicting postoperative mortality. Moreover, a cohort study and meta-analysis[11] (not included in this thesis) demonstrated that the Hajibandeh index is a strong predictor of peritoneal contamination and reflects the severity of underlying abdominal pathology.

Consistent with the findings of the current thesis, recent studies[55,56] have also supported the negative impact of intraperitoneal contamination on outcomes. Pathak et al[55] analysed 235 patients in a retrospective cohort study which concluded that Mannheim Peritonitis Index is a predictor of mortality after emergency laparotomy with AUC of 0.76. In another retrospective cohort study of 591 patients, Olausson et al[56] concluded that generalised peritonitis was associated with increased risk of postoperative mortality in patients undergoing emergency abdominal surgery.

Three cohort studies[57-59] conducted by other authors showed that socioeconomic deprivation is a weak but independent predictor of mortality after emergency laparotomy. Sakowitz et al[57] conducted a retrospective cohort study of 54,190 patients who underwent emergency laparotomy and concluded that socioeconomic deprivation is associated with increased risk of postoperative mortality after emergency laparotomy. Cain et al[58] analysed 9,332 patients who underwent emergency laparotomy and concluded that deprivation was associated with increased postoperative mortality. In another retrospective cohort study of 58,790 patients undergoing emergency laparotomy, Poulton et al[59] concluded that deprived patients have higher crude and risk-adjusted postoperative mortality. Nevertheless, the results of the pooled analysis adjusted for important confounders highlighted that the effect was not significant.[33]

Two updated meta-analyses[60,61] support the findings of this thesis showing that application of ERAS protocols does not improve mortality after emergency laparotomy. Amir et al[60] conducted a meta-analysis of 509 patients from six studies which concluded that application of ERAS protocols did not reduce the risk of mortality in patients undergoing emergency laparotomy. Al-Sarireh et al[61] also reached the same conclusions in a meta-analysis of 707 patients from nine studies.

Consistent with the results of this thesis, Patel et al[62] and Somasundram et al[63] did not find any association between operating during weekend and postoperative mortality in their retrospective cohort studies including 103 patients and 263 patients, respectively. More recently, Al-Sarireh et al[64] conducted a cohort study and complementary meta-analysis of 7,326 patients which concluded that the weekend effect does not influence the risk of mortality after emergency laparotomy.

While the effect of a surgeon's seniority and surgeon's subspeciality interest have not been evaluated previously in an emergency laparotomy setting, the findings in other settings are supportive of the findings of this thesis. D'Souza et al.[65] investigated the impact of trainee involvement on mortality in a wide range of procedures across different specialties and concluded that the risk of postoperative mortality was not affected by trainee involvement. Moreover, a systematic review of 163 studies evaluating 42 different surgical procedures across 13 surgical specialities conducted by Chowdhury et al.[66] concluded that high surgeon volume and specialisation are associated with improved patient outcomes.

While the HAS is a novel model, its predictive performance was evaluated by two cohort studies.[67,68] Soliman et al[67] conducted a retrospective cohort study of 117 patients which supported the external validity of the HAS model in predicting 30-day mortality after emergency laparotomy; the AUC of the HAS model for 30-day mortality was 0.90 (95% CI 0.83-0.95) and it was superior to the performance of NELA score. In another cohort study, Linganathan et al[68] compared predictive performance of HAS model and NELA score in 818 patients undergoing emergency laparotomy and concluded that the HAS model was superior to the NELA score in predicting mortality after emergency laparotomy.

Novel findings and implications for clinical practice

The included studies in this thesis were either a novel cohort study or a novel meta-analysis investigating the predictive performance of a potential predictor of mortality after emergency laparotomy. Therefore, there are several novel findings that are unique to this thesis and have not been shown previously. These are listed below:

- The frailty and comorbidities associated with age increase the risk of mortality after emergency laparotomy not the age on its own (moderate GRADE certainty).
- Sarcopenia is the best and most accurate measure of ageing-related physiological decline and vulnerability in predicting the risk of mortality after emergency laparotomy (moderate GRADE certainty).
- ASA status is a strong and independent predictor of mortality after emergency laparotomy (high GRADE certainty) with no collinearity with sarcopenia (moderate GRADE certainty).
- Hajibandeh index is a strong and independent predictor of mortality after emergency laparotomy (high GRADE certainty) and it reflects severity of underlying pathology better than peritoneal contamination and bowel resection (moderate GRADE certainty).
- Surgeon's subspeciality interest can predict the risk of mortality after emergency laparotomy.
- Socioeconomic deprivation (moderate GRADE certainty), weekend effect (high GRADE certainty), surgeon's seniority (moderate GRADE certainty), and application of ERAS protocols (high GRADE certainty) are not independent predictors of mortality after emergency laparotomy.

- The HAS model is the first model that incorporated Hajibandeh index and sarcopenia alongside the ASA status to predict the risk of mortality after emergency laparotomy. It is the first preoperative model that demonstrated AUC greater than 0.90 in predicting postoperative mortality in emergency laparotomy setting.

The above novel findings have the following implications for clinical practice:

- The Hajibandeh index, ASA status, and sarcopenia should comprise the base of the preoperative risk predictive tools which are used for predicting the risk of mortality in patients requiring emergency laparotomy.
- Presence or absence of sarcopenia should be routinely assessed and reported in preoperative CT scans performed as part of diagnostic pathway in patients with acute abdominal pathologies.
- A high Hajibandeh index in the presence of a radiological indication for emergency laparotomy should inform immediate damage control laparotomy to reduce the impact of peritoneal contamination or organ ischaemia.
- In the absence of a dedicated emergency General surgery subspeciality, dual speciality (upper and lower gastrointestinal surgery) emergency General surgery cover should become the routine practice to match subspeciality of the surgeon with the pathology indicating the emergency laparotomy.

Strengths and limitations

This thesis has strengths and limitations. In terms of strengths, the included studies in this thesis followed an objective and systematic approach in evidence synthesis and followed the recommended methodological and reporting standards appropriate for their design. All of the included studies in the thesis had relatively large sample sizes with a low risk of type 2 error. The baseline characteristics of the included population and outcome definitions were homogeneous among all of the included studies. Most of the important confounding factors had been recognised and were controlled by performing appropriate subgroup analyses and multivariate regression analyses. All of the included studies followed a predefined protocol to minimise the risk of reporting bias. On the other hand, data collection was performed by two independent authors in order to reduce the risk of selection bias. All of the included studies in this thesis investigated a novel research question and they were either the first meta-analysis in the literature on the subject or one of the largest cohort studies in the literature on the subject of interest. The included studies in the thesis were coherent and the results were complementary to each other. The included studies in the thesis underwent a comprehensive peer review by the experts in the field and were published in international peer-reviewed surgical journals with a good impact factor. All of the above would make the conclusions of the current thesis robust. In terms of the limitations, most of the included cohort studies had a retrospective design, which may subject their results to inevitable selection bias. The statistical between-study heterogeneity was moderate to high in most of the included meta-analyses. The observed between-study heterogeneity can be explained by the variations in indications for emergency laparotomy and variations in measuring sarcopenia or socioeconomic deprivation among the included studies in the meta-analyses. Nevertheless, the sensitivity analyses showed consistency of the results in all of the included meta-analyses and the certainty of evidence was downgraded when the heterogeneity was high. Therefore, the observed statistical between-study heterogeneity is not likely to affect the robustness of the findings of this thesis. Publication bias could not be assessed in most of the included meta-analyses as their sample size was less than 10 studies. The Hajibandeh index, which was a novel index developed and validated as part of the included studies in this thesis, has only been investigated by the same evidence synthesis group; hence, further studies by other evidence synthesis groups may provide more robust evidence on its predictive value. All of the included studies in this thesis were conducted in the UK; this may affect the generalisability of the findings in other countries.

Recommendations for future research

The HAS model which was developed and validated in this thesis is the first model in the literature with excellent discrimination, calibration and classification in predicting the risk of 30-day mortality in patients undergoing emergency laparotomy. This is the first model in the literature that included the Hajibandeh index, ASA status and sarcopenia together. It is simple to use and the required information are easily available. The components of the Hajibandeh index are routinely available as part of preoperative blood tests results, the ASA status can be easily determined by clinicians from the end of the bed, and presence of sarcopenia can be easily detected using the preoperative CT scan which is performed in almost all patients undergoing emergency laparotomy. Therefore, the HAS model deserves to be incorporated into routine practice. However, before incorporating the HAS model into real practice, further studies should be performed by other authors to externally validate the performance of the HAS model. The HAS model can be externally validated using the HAS mortality risk calculator.[69]

Conclusions

The strongest predictors of 30-day mortality after emergency laparotomy include the Hajibandeh index, ASA status and sarcopenia. The Hajibandeh index strongly reflects the severity of underlying abdominal pathology; the ASA status and sarcopenia strongly reflect the physical status of the patients. Other potential predictors include age ≥ 80, intraperitoneal contamination, socioeconomic deprivation and surgeon's subspeciality interest. However, these are weak predictors of 30-day mortality and their effects are cancelled out by the Hajibandeh index, ASA status and sarcopenia in multivariable models. The HAS (Hajibandeh index, ASA status, Sarcopenia) model is a promising model with excellent discrimination, calibration and classification in predicting the risk of 30-day mortality in patients undergoing emergency laparotomy. The HAS model is worth attention for external validation and other researchers with an interest in emergency general surgery are encouraged to externally validate the performance of the HAS model using the HAS mortality risk calculator;[69] this would help to determine whether or not the HAS model can be incorporated into routine practice.

Word count: 8772

APPENDIX I. STATUS OF THE PUBLISHED WORKS

Article	Status
Article 1. Meta-analysis of mortality risk in octogenarians undergoing emergency general surgery operations	Published: June 2021 DOI: 10.1016/j.surg.2020.11.027
Article 2. The risk and predictors of mortality in octogenarians undergoing emergency laparotomy: a multicentre retrospective cohort study	Published: September 2021 DOI: 10.1007/s00423-021-02168-y
Article 3. Sarcopenia versus clinical frailty scale in predicting the risk of postoperative mortality after emergency laparotomy: a retrospective cohort study	Published: February 2024 DOI: 10.1007/s00423-024-03252-9
Article 4. Synergistic effect of sarcopenia and ASA status in predicting mortality after emergency laparotomy: a systematic review and meta-analysis with meta-regression	Published: April 2025 DOI: 10.1007/s13304-025-02105-4
Article 5. Intraperitoneal contamination index (Hajibandeh index) predicts nature of peritoneal contamination and risk of postoperative mortality in patients with acute abdominal pathology: a prospective multicentre cohort study	Published: May 2021 DOI: 10.1007/s00384-020-03822-5
Article 6. Hajibandeh Index versus NELA score in predicting mortality following emergency laparotomy: A retrospective Cohort Study	Published: June 2022 DOI: 10.1016/j.ijsu.2022.106645
Article 7. Prognostic significance of socioeconomic deprivation in patients undergoing emergency laparotomy: A retrospective cohort study	Published: October 2024 DOI: 10.1002/wjs.12332
Article 8. Socioeconomic Deprivation and Risk of Operative Mortality After Emergency Laparotomy: A Systematic Review and Meta-Analysis	Published: April 2025 DOI: 10.1177/00031348251314151
Article 9. Meta-analysis of Enhanced Recovery After Surgery (ERAS) Protocols in Emergency Abdominal Surgery	Published: May 2020 DOI: 10.1007/s00268-019-05357-5
Article 10. Impact of weekend effect on postoperative mortality in patients undergoing emergency General surgery procedures: Meta-analysis of prospectively maintained national databases across the world	Published: August 2020 DOI: 10.1016/j.surge.2019.09.006
Article 11. Effect of surgeon's seniority and subspeciality interest on mortality after emergency laparotomy: A systematic review and meta-analysis	Published: August 2024 DOI: 10.1111/codi.17079
Article 12. Development and Validation of HAS (Hajibandeh Index, ASA Status, Sarcopenia) - A Novel Model for Predicting Mortality After Emergency Laparotomy	Published: March 2024 DOI: 10.1097/SLA.0000000000005897

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