Acute Effect of a Single Session of Lipoprotein Apheresis on Central Haemodynamics in Patients with Familial Hypercholesterolaemia

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Dear Editor

We read with interest the paper by Pottle et al demonstrating a 62.5% reduction in major adverse cardiovascular events following introduction of lipoprotein apheresis (LA)[1]. Previous work has shown that LA results in improvements in coronary and peripheral vasomotor function, which may, in part account for the associated improvements in clinical outcomes, alongside the reduction in atherogenic ApoB-containing particles[2, 3]. However, pulse wave velocity (PWV) and Augmentation index (AIx) appear unchanged post-LA[4, 5], but its influence on other cardiovascular physiological biomarkers is less well known. We therefore hypothesised that a single lipoprotein apheresis treatment would improve measures of central haemodynamics derived non-invasively from the pulse-pressure waveform.

Twelve non-smokers with heterozygous familial hypercholesterolaemia underwent LA treatment locally. Patients withheld vasoactive medications on the study day, fasted and avoided caffeine ≥4h prior.

Vascular measurements were taken immediately before vascular cannulation and repeated within an hour of treatment completion. Waveforms for carotid to femoral PWV and pulse wave analysis (PWA) were captured using the Vicorder (Skidmore Medical, Bristol UK)[3]. Augmentation pressure (AP), AIx, Total Peripheral Resistance (TPR), cardiac output (CO), stroke volume (SV) and Subendocardial Viability Ratio (SEVR) were derived using a transfer function.

Blood samples were collected pre- and post-apheresis to assess the lipid profile.

Analyses were performed using SPSS software (Version 25.0, SPSS inc., Chicago, Illinois). Variables were checked for normality using the Shapiro-Wilk test. Differences pre-/post-LA were tested using paired t-test or Wilcoxon-signed rank test.

The local Research Ethics Committee approved the study. All participants provided informed consent.

Brachial systolic blood pressure and pulse pressure increased post-LA; no differences were seen in HR, cSBP, cPP, PWV, AP or AIx (table). TPR decreased by -0.17 ± 0.22 peripheral resistance units (p=0.026), CO increased by 1.09 ± 1.07 L/min (p=0.007) and SEVR decreased by -15.63 ± 19.40 % (p=0.023) (figure). Two participants had taken atenolol on the morning of the study; after excluding these participants changes in SEVR and CO remained significant, but TPR was unchanged.

We observed a significant increase in CO and fall in SEVR in a cohort of hyperlipidaemic patients undergoing LA. SEVR represents the ratio between myocardial oxygen supply and demand, the immediate decrease in SEVR was unexpected given previous findings of short-term improvements in myocardial perfusion post-LA[6]. Another study reported an immediate improvement in coronary flow reserve post-LA due to coronary vasodilation but not increased myocardial oxygen uptake[7], in keeping with our observations including decrease in TPR and improvement in peripheral vasomotor function in these patients[3]. Patients undergoing haemodialysis, have reduced myocardial perfusion despite maintained coronary blood flow, indicating the potential for LA to induce transient ischaemia by increasing CO and cardiac work[8]. Detailed coronary blood flow studies would be required to characterise this more precisely. We observed an 8% relative reduction in SEVR post-LA. Although less than the difference in SEVR between healthy and diabetic patients (15%), a similar fall in SEVR is observed following whole body cold exposure (6%), a well-recognised cardiovascular stressor[9, 10].

None of the measures of arterial stiffness (PWV, AP, AIx) were changed by LA, in keeping with previous studies[4,5]. PWV predominantly measure vessel wall mechanical properties, AP and AIx reflect changes in wave reflection, influenced by cardiac cycle length and pulsewave speed/intensity. Although a decrease in TPR may have been expected to influence AIx (reduced wave reflection), this was likely counteracted by the increased pulsewave intensity secondary to higher CO.

Study limitations include: Measurements were only made at a single time point, immediately post LA. We could not adjust fully for medications effects in this small study. Two patients took haemodynamically active medications before LA, but their exclusion did not alter associations with CO and SEVR, although the change in TPR post-LA was no longer significant.

To conclude TPR is reduced acutely by LA, consistent with previous studies. However, the increased CO and concomitant net fall in SEVR suggests an adverse early impact on myocardial work and perfusion - an important consideration for LA in high coronary risk patients. Prospective evaluation in a larger cohort is required to explore the potential clinical significance of these effects.

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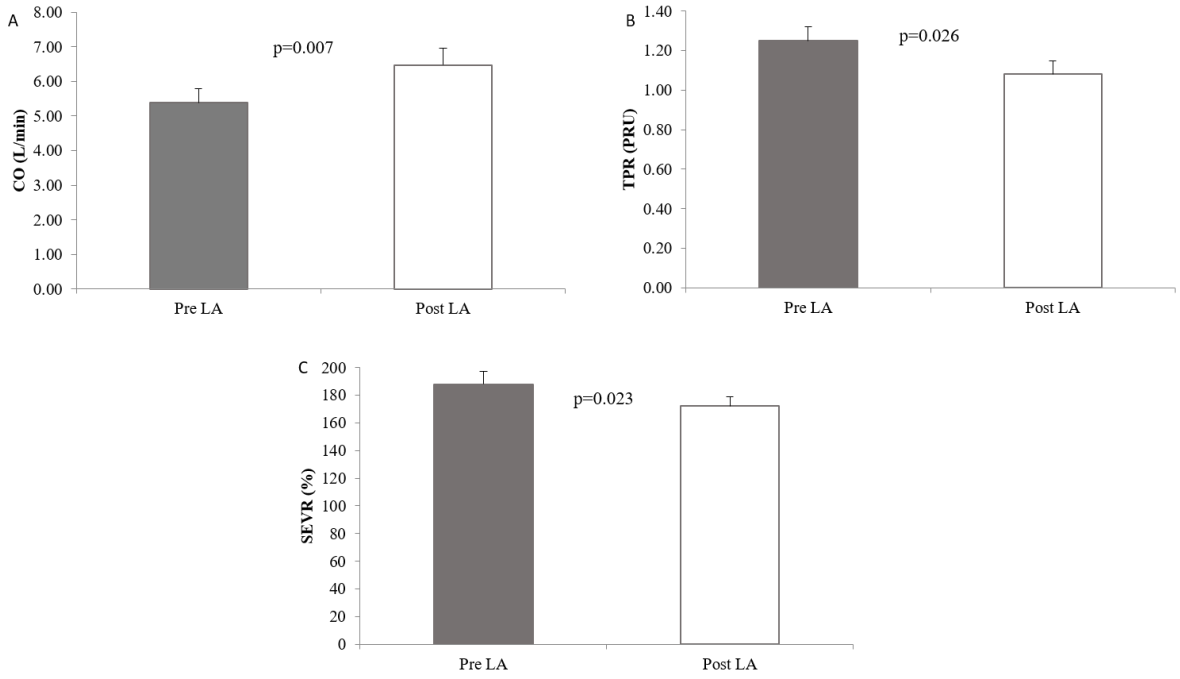

Figure: Measures of central haemodynamics pre and post a single session of lipoprotein apheresis (LA). **A** cardiac output (CO) **B** total peripheral resistance (TPR), and **C** subendocardial viability ratio (SEVR). Data presented as mean and standard error.

n=11	Pre LA	Post LA	p
Age (years)	59 ± 10		
Gender (M:F)	9:2		
BMI (kg/m^2)	30 ± 4		
Waist (cm)	101 ± 8		
Diabetes	5/11		
Presence of coronary disease	9/11		
Lipid lowering therapy			
Statins	9/11		
Ezetimibe	7/11		
Fibrates	1/11		
N-3 Fatty Acid	6/11		
Nitrates	2/11		
Total Cholesterol (mmol/L)	6.0 ± 1.6	2.7 ± 0.9	0.003
Low density lipoprotein (mmol/L)	4.0 ± 1.5	1.3 ± 0.7	0.003
Triglycerides (mmol/L)	1.7 ± 0.6	0.9 ± 0.4	0.003
High density lipoprotein (mmol/L)	1.1 ± 0.5	0.9 ± 0.5	0.003
Heart rate (bpm)	59 ± 11	61 ± 12	0.18
Stroke Volume (ml)	94 ± 30	107 ± 25	0.83
Peripheral systolic blood pressure (mmHg)	141 ± 18	150 ± 21	0.033
Peripheral diastolic blood pressure (mmHg)	83 ± 10	83 ± 10	0.73
Pulse pressure (mmHg)	59 ± 12	66 ± 14	0.035
Central blood pressure (mmHg)	139 ± 17	146 ± 18	0.07
Central pulse pressure (mmHg)	57 ± 12	63 ±12	0.09
Augmentation Pressure (mmHg)	14 ± 5	15 ± 6	0.45
Augmentation Index (%)	24 ± 6	23 ± 7	0.82
Pulse wave velocity (m/s)	9.19 ± 2.47	8.72 ± 2.95	0.3

Table: Patient characteristics, lipid parameters and peripheral and central haemodynamic measures pre and post a single lipoprotein apheresis treatment. BMI= body mass index.