Quantification of Lipid Filtration and the Effects on Cerebral Injury During Cardiopulmonary Bypass

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Background. **Lipid microemboli (LME) are formed in pericardial suction blood which, when returned to the cardiopulmonary bypass (CPB) circuit, can pass through filter materials and are returned to the arterial cannula. LME have been observed to enter all major organs and have been associated with small capillary arteriolar dilatations in the brains of patients who have died after CPB. However, a causal relationship showing correlation between LME and organ dysfunction has not been demonstrated, or whether removal of LME results in improved organ function.**

Methods. **A prospective, single center, randomized controlled trial examined 30 patients (15 per group) undergoing coronary artery bypass grafting using CPB with or without a lipid-depleting filter. The effects of LME filtration on neurocognitive injury were assessed using neuron-specific enolase (NSE).**

Results. **The study group showed a significant reduction in LME after filtration of the pericardial suction blood ($p < 0.001$), whereas the control group exhibited a significant rise in LME ($p < 0.001$). There was a significant reduction in peak NSE release ($p = 0.013$) and significant attenuation throughout the postoperative period ($p = 0.002$). Correlation and regression analyses showed a significant relationship between the number of LME post-CPB and peak NSE release ($r = 0.42$, $p = 0.02$).**

Conclusions. **Several methods of LME filtration have been proposed, but none provided a suitable, efficacious method for use within the clinical setting. The RemoweLL CPB system removes significant numbers of LME from the cardiotomy suction. Furthermore, LME correlate to the release of a known marker of neurologic injury.**

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Major neurologic injury after cardiac operation using cardiopulmonary bypass (CPB) has an incidence of 1% to 5%, although select populations may have a stroke rate as high as 8% to 9% [1]. However, substantially more patients experience subtler forms of injury with studies observing postoperative cognitive and intellectual dysfunction in almost 50% of patients when examined by neuropsychological tests [2]. Furthermore, early postoperative neurologic dysfunction correlates with progression of cognitive decline and impaired quality of life during later years [3]. Much of this dysfunction has been attributed to the presence of lipid microemboli (LME) from the surgical environment, passed through the CPB circuit into the aortic arch and onto the cerebral vessels. The reflection of lipid emboli in the microcirculation of the brain has been observed as small capillary arteriolar dilatations at the bifurcations of cerebral vessels [4, 5]. Although work by Brooker and colleagues [5] showed a direct relationship between the use of cardiotomy suction and small capillary arteriolar dilatations, there has been no definitive proof that LME are responsible for neurologic or neurocognitive dysfunction after CPB [6]. One possible reason for this is that ischemic damage is attenuated by the surrounding capillary network, and dysfunction is thought to occur only when either several vessels in the same area are occluded or occlusion occurs within the white matter that is less densely vascularized [6].

Previous attempts to remove LME have met with limited success; a major problem associated with filtration is the deformability of fats, allowing them to pass through filters and into the systemic circulation of the patient. Much of the research examining lipid filtration is fundamentally flawed with several studies using soya oil as a reference fat which is substantially different from the liquid fat seen in human pericardial fat [7] or using excessive fat to gain higher measurement resolution which leads to the saturation and decrease in efficacy of the filter. Therefore, at present there are few suitable filtration methods for efficacious LME removal in the clinical setting once LME have entered the systemic circulation.

There have been several reports of increased concentrations of markers of neurologic dysfunction correlating to the duration of CPB [8]. One such marker is neuron-specific

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Abbreviations and Acronyms

CPB = cardiopulmonary bypass
LME = lipid microemboli
NSE = neuron-specific enolase
PSB = pericardial suction blood

enolase (NSE), an enzyme that catalyzes the conversion of 2-phospho-D-glycerate to phosphoenolpyruvate in the glycolytic pathway and is found in neurons and neuroendocrine cells, with α and γ subunits being specific to neurons [9]. Damage to the neuron cell membrane causes leakage of NSE into the blood and cerebrospinal fluid where it may be detected. NSE exhibits an increased response to CPB, and serum levels of NSE demonstrate a significant association with postoperative neurocognitive outcome [10]. Other markers, such as S100β, have shown nonspecificity and an inability to correlate with neurologic or neuropsychological outcome [11].

The aim of the present study was to establish if a new lipid filtration system (RemoweLL, Eurosets s.r.l, Mirandola, Italy), which takes a unique approach and prevents the entry of LME into the systemic circulation using a siphon mechanism (rather than filtering once systemic infiltration has occurred), could remove LME from the pericardial suction blood (PSB) and to determine whether this could attenuate the release of NSE.

Material and Methods

After institutional review board and research ethics committee approval (10/H0606/30), a prospective, single-center, single-blind, randomized, controlled study was performed in 30 patients undergoing coronary artery bypass grafting with CPB assigned to either a control or intervention (RemoweLL) extracorporeal circuit at University Hospital Southampton (Southampton, United Kingdom). The study was conducted between March 2013 and December 2015. Exclusion criteria included emergency or previous cardiac operation, morbid obesity, renal or pulmonary dysfunction, and evidence of existing cognitive impairment, as judged at the presurgical assessment and after consultation with the patient's general practitioner. All patients provided written, informed consent for inclusion in this study.

Operative Details

Both intervention and control groups received the same anesthetic regime. Anesthesia was induced with midazolam, fentanyl, and pancuronium and maintained using intermittent positive pressure ventilation with oxygen-enriched air and isofluorane. During CPB, a propofol infusion was used to maintain anesthesia. The CPB circuit consisted of a microporous hollow fiber membrane oxygenator (containing a heat exchanger) with integrated cardiotomy reservoir. This contained either a conventional cardiotomy filter (Control; Admiral, Eurosets s.r.l.) or a lipid/leucocyte filter (Intervention; RemoweLL, Eurosets s.r.l). The circuit was primed with 2 L of lactated Ringer's solution (Baxter, Thetford, United Kingdom) and mannitol 20% w/v (2.5 mL/kg; Baxter) that contained 5000 units of heparin (Wockhart, Wrexham, United Kingdom). Before the establishment of CPB, 3 mg/kg body weight of heparin were administered and supplemented as required to maintain an activated clotting time of greater than 480 seconds. Continuous nonpulsatile blood flow was delivered to the patient using a multiflow roller pump (HL20; Maquet Getinge Group, Gothenburg, Sweden) at an indexed flow rate of 2.4 L/m^2/min. Alpha stat blood gas management was used to control acid-base balance. Mean arterial pressure was maintained between 50 and 60 mm Hg with pharmacologic manipulation if necessary. All patients were systemically cooled to nasopharyngeal temperatures between 32°C and 34°C. After aortic clamping, electromechanical diastolic arrest was induced with the delivery of cold (4°C) blood cardioplegic solution (IVEX Pharmaceuticals, Larne, Northern Ireland). Biochemical compatibility was maintained using sodium bicarbonate as a buffering agent. Distal anastomoses were completed during a single period of aortic clamping. Proximal anastomoses were performed on a beating heart using an aortic partial occluding clamp. CPB was terminated after the patient was rewarmed to a nasopharyngeal temperature of 36°C. The PSB was sent to the integrated cardiotomy reservoir where it was kept separated from the systemic circulation until immediately before the end of the CPB period, when it was reintroduced through the venous reservoir back into the systemic circulation.

Lipid Analysis

Lipid emboli detection was performed using light microscopy. A collection chamber was inserted proximal to the cardiotomy reservoir. At the start of CPB, blood was collected from the chamber as the initial baseline LME count. After reintroduction of the PSB into the systemic circulation, a sample was taken from the arterial sampling line to give a postfiltration sample. Part of the sample (100 μL) was diluted one tenth with saline (1000 μL) and agitated for 2 to 3 minutes to homogenise. Ten microliters was placed onto a Thoma cell counting chamber, and lipids were counted under light microscopy with 40/0.65 optics. The lipids could be seen as spherical nonnucleated cells (Fig 1). The number of the lipids per microliter was obtained by counting the average number of lipids in four small squares (Y) and inserted into the formula $X = Y \times 16 \times 100$ where 16 equals the number of small squares (total volume 0.1 μL) and 100 equals the dilution factor.

Cerebral Injury

Blood samples were taken for analysis of NSE before CPB, 5 minutes before the end of CPB, and 6 and 24 hours after CPB as described previously by Bonacchi and colleagues [12]. Commercially available enzyme-linked immunosorbent assays were performed at King's College Hospital, London. Briefly, 25 μL of sample was added to each well of prepared antibody solution (horseradish peroxidase anti-NSE and biotin anti-NSE; 100 μL) and

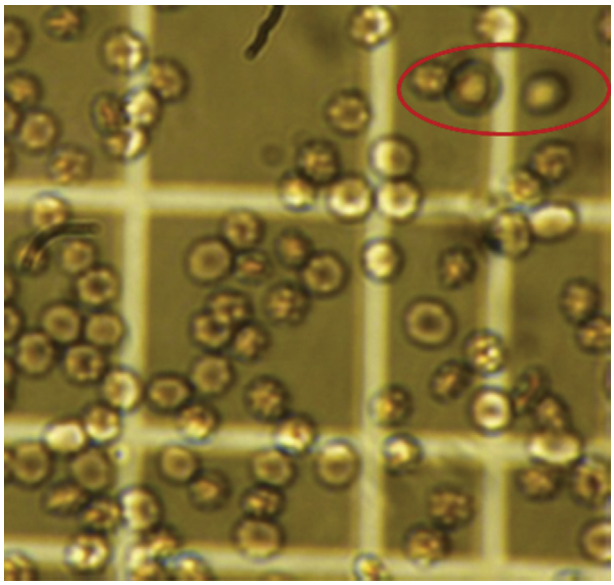

Fig 1. Lipid microemboli under microscopy. Lipid microemboli observed as nonnucleated spherical cells (red circle) taken under light microscopy with 40/0.65 optics.

incubated at room temperature for 1 hour. After washing the sample was added to a 3,3′,5,5′-tetramethylbenzidine/horseradish peroxidase substrate and incubated for a further 30 minutes before absorbance was read at 620nm.

Statistical Analysis

In vivo data (unpublished) showed that the numbers of LME in the RemoweLL system after filtration compared with a standard circuit was 1095 (579) particles/mL versus 2970 (1405.29) particles/mL, giving a mean percentage removal of 63% (8.4%) and effect size of 1.745. Previous studies have shown that the lower the serum concentrations of NSE, the better the outcome of patients after CPB. For this reason a tentative a priori power calculation was undertaken based on the work of Bonacchi and colleagues [12] whereby the mean postoperative peak serum NSE concentration was 17.7 (6.5) μg/L. An assumption was made that for a significant, clinically relevant, difference in peak circulating NSE, a minimum reduction of 33% should be seen in the study group compared with control group, assuming equal SDs in both groups. From these assumptions an effect size of 0.923 was calculated. The number of patients in each study group (25 per group) was determined by an a priori power calculation using G*Power Version 3.1.0 (Universität, Kiel, Germany) to achieve a power (1-β) of 0.95 with α of 0.001 for the primary objective (LME removal) and a power (1-β) of 80% and α of 0.05 for the secondary objective (peak NSE concentration). However, no data were available to indicate the direct relationship that LME filtration will have on biochemical markers of organ injury; for this reason, and after consultation with a statistician, an interim assessment using the Haybittle-Peto boundary was prospectively planned after 20 patients. This showed an effect size of 3.5 for the primary objective and 1.2 for the secondary objective. Therefore, a revised power calculation showed a cohort of 30 patients (15 per group) was required for the same assumptions as above.

Primary and secondary end points were analyzed using the SPSS statistical package (SPSS, Chicago, Illinois), and a post hoc power analysis was used to compute achieved power for the secondary objective. This was independently verified. Assessment of normal distribution was performed using the Shapiro-Wilk test, and confirmed using a QQ Plot. Normally distributed data were tested using *t* test for two independent samples, and nonnormally distributed values were log-transformed and, if shown to be normally distributed, tested as above. If still nonnormally distributed, data were tested using Mann-Whitney test for two independent samples. Two-factor analysis of variance tests were undertaken to examine repeated measures. All tests were considered to be two tailed. Correlation and regression analyses using Pearson's coefficient were used to examine any relationships between LME numbers and NSE concentrations. A *p* value less than 0.05 was considered significant. Normally distributed data are presented as mean (SD), and nonnormally distributed data are presented as median (interquartile range). Both data are graphically displayed as box and whisker plots.

Results

Thirty patients successfully completed the study. Demographic data are shown in Table 1. No significant differences were found between the two patient groups.

Table 1. Patient Demographic Characteristics

Characteristic	Control	Intervention	*p* Value
Men	12.00	11.00	
Diabetes	2.00	3.00	
Statin	8.00	8.00	
Age, years	69.93 (7.54)	69.33 (7.29)	0.83
Height, m	1.76 (0.10)	1.71 (0.08)	0.10
Weight, kg	87.51 (13.37)	82.84 (14.90)	0.37
Body mass index, kg/m^2	28.15 (3.56)	28.31 (4.15)	0.91
Body surface area, m^2	2.07 (0.20)	1.98 (0.21)	0.24
Calculated flow, L/min	4.96 (0.47)	4.74 (0.50)	0.24
Bypass time, minutes	101.40 (22.01)	88.47 (23.51)	0.13
X-clamp time, minutes	62.67 (17.67)	51.20 (17.11)	0.08
Procedure, CABG × N	3.33 (0.49)	3.13 (0.83)	0.43
Fluid balance, mL	1678.60 (842.38)	1562.27 (867.16)	0.71
Time of cardiotomy release, minutes	74.93 (19.27)	67 (17)	0.23
Volume in cardiotomy reservoir, mL	776.67 (632.14)	780.00 (567.20)	0.99

Data are presented as n or mean (SD).

Time of cardiotomy release was the amount of time the pericardial suction blood was left separated from the systemic circulation.

CABG = coronary artery bypass grafts; X-clamp = aortic cross-clamp.

However, there was a trend toward shorter cross-clamp time in the intervention (RemoweLL) group ($p = 0.08$). Both groups were evenly matched for sex, age, comorbidities, preoperative statin regime, and number of grafts. No differences were found in transfusion rates or hemoglobin levels between the two groups at any time point ($p > 0.05$), and no patients exhibited any gross neurologic deficits.

Both groups processed similar volumes of PSB (control: 776.67 [632.14] mL versus intervention: 780.00 [567.20] mL, $p = 0.99$), and the sedimentation time (the time PSB left in the cardiotomy reservoir) was similar in both groups (control: 74.93 [19.27] min versus intervention: 67 [17] min, $p = 0.23$). Baseline LME counts were similar in both groups (400 [200] n/μL versus 400 [400] n/μL, $p = 0.47$; Table 2), but a significant reduction was found in LME count with the RemoweLL lipid filter (100 [75], $p < 0.001$) compared with a significant rise in the control group (1,200 [200], $p < 0.001$; Fig 2). Postoperative differences between the control and intervention groups were significant (1,200 [200] versus 100 [75], respectively; $p < 0.001$].

Two-factor analysis of variance revealed a significant interaction between groups and NSE release ($p = 0.002$). No differences were found between the groups at baseline, and NSE release peaked in both groups at the end of CPB with significantly lower concentrations in the intervention group (control: 23 [6.5] μg/L versus intervention: 16 [7] μg/L, $p = 0.012$; Fig 3). Subsequent reductions were seen toward baseline in both groups, although those patients in the control group continued to show elevated NSE levels compared with patients in the intervention group ($p = 0.01$ 6 hours after CPB, $p = 0.004$ 24 hours after CPB). Compared with baseline values both groups remained statistically elevated at 24 hours after CPB (control: 10 [3.5] μg/L versus 14 [4] μg/L, $p = 0.003$; intervention: 10 [1] μg/L versus 11 [1.5] μg/L, $p = 0.03$]. Post hoc power analysis showed an effect size (d) of 1.1 for the secondary objective, demonstrating an achieved power (1-β) of 0.83.

Analysis of correlation showed no relationship between CPB time, volume of PSB, or sedimentation time and the numbers of LME (Table 3). However, comparison between NSE and post-CPB LME data showed that at the post-CPB, 6-hour post-CPB and 24-hour post-CPB time points, there was a significant positive correlation between NSE release and the number of LME observed ($r = 0.42$, 0.41, and 0.4 respectively). Further regression analysis showed a significant positive relationship between the two variables at each of the time points ($p = 0.02$, 0.02, and 0.03, respectively).

Table 2. Perioperative Data

Perioperative Characteristic	Control	Intervention	*p* Value
Pre-CPB LME count, n/μL	400 (200)	400 (400)	0.47
Post-release LME count, n/μL	1200 (200)	100 (75)	<0.001
Pre-CPB NSE, μg/L	10 (3.5)	10 (1)	0.32
End-CPB NSE, μg/L	23 (6.5)	16 (7)	0.012
6-Hour post-CPB NSE, μg/L	18 (6)	14 (4.5)	0.01
24-Hour post-CPB NSE, μg/L	14 (4)	11 (1.5)	0.004

Data are presented as median (interquartile range).

LME counts were taken from the start of cardiotomy suction (pre-CPB) and from the arterial sampling port after the reintroduction of pericardial suction blood from the cardiotomy reservoir. NSE was taken after induction of anesthesia and placement of central venous and arterial catheters. A significant difference was observed in the postrelease LME counts ($p < 0.001$) and at the end-CPB, 6-hour post-CPB, and 24-hour post-CPB NSE levels ($p < 0.05$).

CPB = cardiopulmonary bypass; LME = lipid microemboli; NSE = neuron-specific enolase.

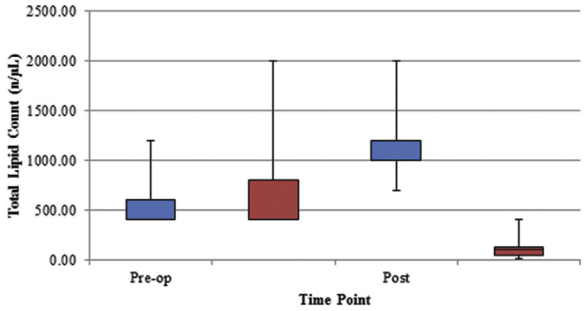

Fig 2. Before and after lipid microemboli (LME) counts. Data are presented as box and whiskers plots with boxes representing 25th to 75th centiles with median and whiskers as maximum and minimum values. Blue indicates the control group; red, the intervention group. Both groups showed significant changes in total LME counts compared with baseline and with each other ($p < 0.001$). The control group showed a mean increase of 115.7% in LME, and the filtration group saw an 82.8% decrease.

Comment

The role of LME in organ injury has been postulated, but so far no definitive causal evidence exists. For this reason, this study set out to establish the efficacy of a new LME

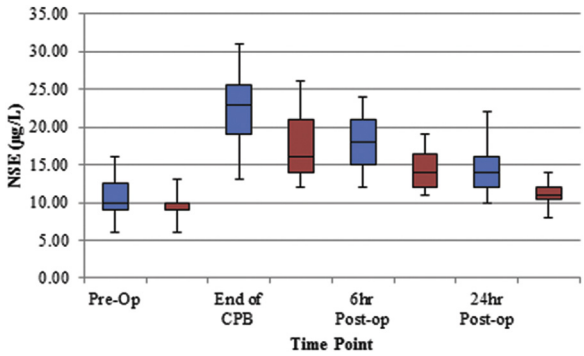

Fig 3. Neuron-specific enolase (NSE) release. Data are presented as box and whiskers plots with boxes representing 25th to 75th centiles with median and whiskers as maximum and minimum values. Blue indicates the control group; red; the intervention group. Both groups saw a significant increase with peak concentrations at the end of cardiopulmonary bypass ($p < 0.001$); however, there was a significantly attenuated peak in the filtration group compared with the control group ($p = 0.012$). Repeated-measures analysis of variance showed significantly less NSE release in the filtration group throughout the sampling period ($p = 0.002$).
(CPB = cardiopulmonary bypass; Post-op = postoperative; Pre-Op = preoperative.)

Table 3. Correlation Analysis

	Correlation			
Measure	Pre-CPB NSE	End-CPB NSE	6-Hour Post-CPB NSE	24-Hour Post-CPB NSE
Bypass time	0.25 (0.19)	0.28 (0.13)	0.02 (0.93)	0.29 (0.12)
Time of cardiotomy release	0.26 (0.17)	0.24 (0.19)	0.17 (0.36)	0.15 (0.44)
Cardiotomy volume	0.01 (0.96)	0.15 (0.42)	0.02 (0.93)	0.21 (0.26)
Pre-CPB LME count	0.13 (0.48)	0.16 (0.4)	0.05 (0.79)	0.13 (0.5)
Post-release LME count	0.27 (0.16)	0.42 (0.02)	0.41 (0.02)	0.4 (0.03)

Data are expressed as correlation coefficient, *r*, with *p* values in parentheses. All tests used Pearson's correlation. Critical *r* for 28 patients (d.f. = n-2) were 0.374 (0.05) and 0.588 (0.001).

CPB = cardiopulmonary bypass; LME = lipid microemboli; NSE = neuron-specific enolase.

filtration system that is situated in the cardiotomy reservoir of a CPB circuit, because this circuit component was shown to be the main source of LME in patients undergoing CPB [5]. The RemoweLL cardiotomy reservoir consists of two filtering mechanisms, as opposed to the traditional one used in standard cardiotomy reservoirs. The first uses a 40-μm membrane, similar to cardiotomy reservoirs, but specifically coated to provide multilayer filtration for leukocytes and lipids. The blood then passes into the sedimentation chamber where it is kept separate from the circulating volume to obtain a supernatant fluid. The supernatant fluid, rich in lipid particles, is blocked by the siphon (the second filtration method) at the base of the reservoir, which is then discarded after reinfusion of the lipid-filtered PSB (Fig 4). LME removal was assessed by counting the number of LME present in the PSB once the cardiotomy suction had been initiated and then again in the systemic circulation after reinfusion of PSB into the CPB circuit. The results show a significant efficacy for lipid removal compared with the control group. In the intervention group 82.8% of the LME were removed ($p < 0.001$) with a separation time of 67 minutes (time between cardiotomy suction initiation and reinfusion of PSB into the circulation). In the control group, a 115.7% increase as found in LME after reinfusion of PSB ($p < 0.001$). Although the separation time was longer at 75 minutes, this did not reach significance compared with the intervention group ($p = 0.23$). Although a propofol infusion

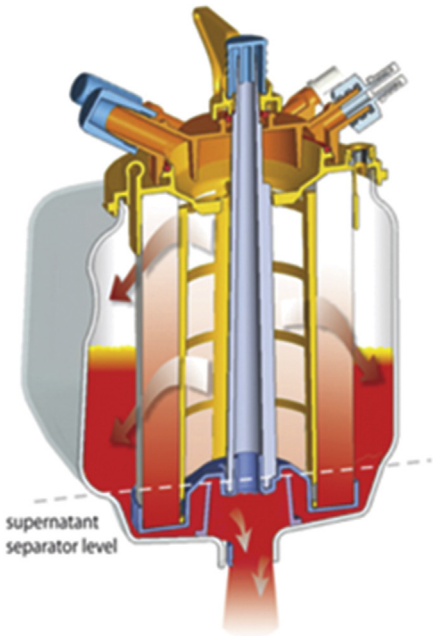

Fig 4. The RemoweLL lipid filtration system. The RemoweLL ECC system comprising two filtering mechanisms: a leucocyte filter and a lipid microemboli siphon. A 40-μm membrane provides multilayer filtration for leukocytes and lipids, whereas the siphon, at the base of the cardiotomy reservoir, prevents the reinfusion of the lipid-rich supernatant fluid that is then discarded.

was used for maintenance of anesthesia, it is unlikely this influenced LME numbers because both groups had the same dosage regime and there was no difference in triglyceride levels between the two groups (data not shown).

Despite advances in perfusion technology, current estimates of neurologic injury after CPB show that greater than 50% of patients have neuropsychological deficits during the first week after operation, 10% to 30% have long-term or permanent deficits, and 1% to 5% experience severe disability or die [13]. Current CPB circuitry does not prevent the passage of LME from the cardiotomy suction and into the patient's systemic circulation, and previous work has shown the distribution of LME throughout the major organs [14]. Of particular concern are the possible effects on neurologic function that LME pose; thousands of microemboli have been observed distributed throughout the brain [4].

NSE was chosen as a surrogate marker of neurologic function because serum levels of NSE exhibit a significant association with postoperative neurocognitive outcome [10], whereas other markers such as S100β have shown nonspecificity and an inability to correlate with neurologic or neuropsychological outcome [11]. Rasmussen and colleagues [15] found a significant correlation between the increase in NSE after CPB and the change in cognitive function at the time of discharge. They noted that patients with neurocognitive dysfunction had a significantly elevated mean NSE level (4.9 μg/L higher) than patients who did not at the point of discharge, and 3 μg/L higher in patients with neurocognitive dysfunction 3 months after the operation (although this did not reach significance). However, further work by these investigators speculated that this may be due to insufficient sample size to detect differences of this magnitude [16]. This study observed a peak reduction in NSE release in the filtration group at the end of CPB (control: 23 [6.5] μg/L versus intervention 16 [7] μg/L, $p = 0.013$) and further significant differences at both the 6 and 24 hours after CPB sample times (control: 18 [6] μg/L and 14 [4] μg/L versus intervention: 14 [4.5] μg/L and 11 [1.5] μg/L, $p = 0.01$ and 0.005, respectively). Moreover, we observed a direct correlation between the number of LME and NSE release. This study shows a difference in a known neurologic injury marker between groups of patients who have had LME filtered and patients undergoing standard CPB. Although it would be imprudent to extrapolate these results to long-term neurologic outcome, the results are suggestive that further work would be warranted and provide biochemical evidence for a role of LME in neurologic dysfunction. Note that the rise in NSE observed in this study was significantly higher than in the study by Bonacchi and colleagues [12]. They reported peaks of 17.7 [6.5] μg/L with and interquartile range of 9.8 to 25 in the CPB group, which is similar to the peak concentrations seen in the filtration group (16 [7] μg/L) but much lower than those in the control group (23 [6.5] μg/L]. However, there are two possible explanations for this observation. First, the group of patients in Bonacchi's work were younger than patients within this study (Bonacchi: range, 52 to 67 years; Admiral: range, 57 to 85 years; RemoweLL: range, 59 to 82 years). Previous data from Nygaard and colleagues [17] have shown a clear progression in increasing NSE concentrations with age from 24 to 84 years; therefore, a higher overall concentration in a more elderly group is to be expected. Second, and more importantly, the CPB group of Bonacchi and colleagues [12] did not have cardiotomy blood returned to them. The rationale behind this was that the study was investigating the use of S100β, which is also contained within the heart, aorta, and mediastinal tissues which are disrupted during cardiac operation, causing potential contamination from noncerebral sources [8]. This inadvertent observation from Bonacchi and colleagues [8] provides a further control for this study; the level of NSE increase seen in the filtration group is equivalent to discarding the PSB. However, there are major drawbacks in the discarding of PSB, not least is the increase in blood transfusion requirements and increase in postoperative bleeding [18].

Limitations

This study has several limitations. Although contemporary literature has been provided that identifies a relationship between LME, NSE, and cognitive function, whether LME filtration would attenuate adverse cerebral events cannot be answered, because the actions of LME will depend on which vessels are affected and whether they are located in areas of low or high vascularization. The aim of this study was to observe any biochemical data that would give an indication of benefit or, indeed, provide any evidence that there was a link between LME and neurologic dysfunction. The present study demonstrates that LME filtration is not only possible but also that prevention of LME from entering the patient's systemic circulation can attenuate the release of a known marker of neurologic injury.

The patient cohort under investigation was coronary artery bypass grafting–only patients. One reason for this was to isolate the effects of LME from gaseous emboli present once cardiac chambers are opened to atmosphere. This would prevent any interaction and would keep the group homogenous. However, one might argue that this was unnecessary, because gaseous emboli would be equal in both groups, and this study did not focus on clinical outcomes. Testing of the LME removal system in complex cases (such as redo, valves, aortic operation, etc.), that require longer bypass times and mandate the PSB to be recycled during CPB, were not examined. Further work into clinical outcomes should involve more complex cases and involve patient groups that were excluded in this study, especially because there is evidence that suggests patients with preexisting neurocognitive or renal impairment might benefit more from LME filtration.

Conclusion

This study has shown the efficacious filtration of LME in the clinical setting using the RemoweLL lipid filtration system and the subsequent attenuation of NSE release, a known marker of neurologic injury. Furthermore, our

data suggest that a direct correlation exists between the number of LME and the level of NSE release. Further work is now planned to determine whether this translates into longer term neurocognitive protection.

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