Filter lifespan in critically ill adults receiving continuous renal replacement therapy: the effect of patient and treatment-related variables

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ABSTRACT

Objective: To examine the effects of patient and treatment-related variables on filter lifespan in critically ill adults receiving continuous renal replacement therapy (CRRT).

Design and setting: This was a single-centre, retrospective, observational study conducted in a tertiary referral centre in metropolitan Melbourne, Australia. All CRRT filters used over a 44-month period from 1 January 2008 to 31 August 2011 were assessed for their hours of function before being stopped non-electively (due to clotting) or electively. Analyses were performed primarily for all CRRT filters and secondarily for those ceased non-electively during the study period. To assess for any relationship with filter life, we performed multivariable regression analyses for blood flow rate, anticoagulation type, vascular access site, vascular catheter type, reason for stopping the filter circuit, platelet count and activated partial prothrombin time.

Results: A total of 1332 treatments in 355 patients were assessed for filter life. Of these, 474 were electively ceased, leaving 858 filter circuits for secondary analysis. In both analyses, higher blood flow rate predicted longer filter lifespan ($P = 0.03$ for all filters and $P = 0.04$ for non-electively ceased filters). Vascular catheter type was predictive of increased filter lifespan in the non-electively ceased filters ($P = 0.002$) but not on analysis of all filters. Type of anticoagulation and vascular access site were not predictive of filter lifespan in either analysis. Of the patient haematological variables, only platelet count was predictive of increased filter lifespan ($P = 0.003$ for all filters and $P < 0.001$ for non-electively ceased filters).

Conclusions: Our study found that an increased CRRT filter lifespan is associated with higher blood flow rates and lower platelet count. Vascular catheter design may also be a factor.

Crit Care Resusc 2014; 16: 225–231

Continuous renal replacement therapy (CRRT) is commonly used to assist solute control and relieve fluid overload in critically ill patients with acute kidney injury, especially those with haemodynamic instability.[1-3] CRRT is preferred to intermittent haemodialysis in critically ill patients because it allows a more gradual correction of acid–base balance, fluid overload, and azotaemic control that is comparable to that provided by the native kidney.[1-3] Due to the more gentle nature of CRRT, it can also be used in patients with chronic or end-stage renal disease who are critically ill and likely to be haemodynamically unstable with dialysis.

One of the greatest challenges of CRRT is ensuring continuity, and therefore adequacy, of treatment.[4] Frequent filter circuit loss can lead to significant differences between prescribed and delivered doses of CRRT, resulting in poor uraemic control and adverse patient outcomes.[3,5] Therefore, ensuring adequate filter circuit life and continuity of treatment are important goals of CRRT. Premature circuit clotting is one of the most common causes of inadequate solute, fluid balance and acid–base control.[4,6-8] Activation of the clotting cascade, high haematocrit levels, circuit turbulence and stasis in the circuit due to poor vascular access are common causes of premature circuit clotting.[4,6-10] Endogenous patient factors may play a role.[11] In addition, slow or ineffective troubleshooting of alarms at the bedside may lead to premature circuit clotting through excessive blood pump interruptions. Frequent clotting of circuits leads to excessive blood loss, higher treatment cost and increased nursing workload.[6,8,11]

Despite the problems associated with inadequate filter lifespan in patients undergoing CRRT, few studies have investigated the effect of patient and treatment-related variables on filter lifespan. We therefore conducted a multivariable study to examine the effect of these variables on filter lifespan.

Methods

Design and setting

This retrospective study was conducted in a tertiary, 24-bed, adult intensive care unit in metropolitan Melbourne, Australia, and included all patients undergoing CRRT during the 44-month period from 1 January 2008 to 31 August 2011.

Ethics considerations

The study was approved as a quality assurance project by our hospital's human research ethics committee. The need for informed consent from patients treated with CRRT was waived.

Data collection

Data were collected for all patients requiring CRRT. The primary investigator (W D) collected data retrospectively by reviewing the medical file and the ICU charts, where patient and CRRT details, including reason for stopping the filter circuit, are routinely recorded. A simple case report form was designed for data collection, and all data were entered into a Microsoft Excel 2007 spreadsheet. Two separate databases were then created:

1. All filter circuits used during the study period, regardless of reason for cessation, were included in the primary analysis.
2. Circuits ceased electively, due to a medical decision to cease treatment, death, a procedure, radiology scan or other event required out of the ICU, were then excluded from the primary database, leaving only filters ceased non-electively (due to clotting or clogging) in the secondary analysis.

CRRT machines and protocol

During the study period, patients were treated using either the Prismaflex (Gambro) or the Infomed HF440 (Infomed SA) CRRT machine. The filter circuit used for the Prismaflex was the AN69 ST100 hollow fibre membrane (Gambro). Prismaflex filter circuits were primed with either 5 mg of enoxaparin or 2500 IU of unfractionated heparin diluted in 1 L of 0.9% saline, followed by a further 1 L of saline without heparin. The mode for renal replacement with this machine was continuous venovenous haemodiafiltration, as per our ICU policy. The dose of CRRT when using the Prismaflex was either 2 L of dialysis and 2 L of ultrafiltration per hour, or 30 mL/kg/h of effluent with equal substitution fluid and loss as required.

The Infomed HF440 haemofiltration machine was used for a trial period of about 6 weeks with a limited number of patients. The machine uses a hollow fibre polyethersulfone membrane (DF-140, Infomed SA), and no anticoagulation was added to the priming fluid. The mode used with this machine was continuous venovenous haemofiltration. The dose calculation was similar for both the machines.

Lactate haemofiltration replacement fluid (Lactasol, Gambro) was used for all patients unless metabolic acidosis was present or the patient was at high risk of an ischaemic event that required close monitoring of lactate levels. In these cases, a bicarbonate-buffered fluid (Hemosol, Gambro) was used.

Access devices

Throughout the study period, a total of 82 patients received treatment through cuffed long-term dual lumen catheters. All other patients received treatment using temporary vascular access devices. There was a change in the type of temporary vascular access catheter used for CRRT during the study period. From January 2008 until January 2011, CRRT was delivered using the Arrowgard Blue catheter (Arrow International). In January 2011, the Arrowgard Blue catheter was replaced with the Niagara catheter (Bard Canada), which was then used until August 2011. The two short-term catheters were not used concurrently.

The Arrowgard Blue catheter was a 16 or 20 cm long 12 Fr, or 25 cm long 14 Fr 2 or 3 lumen polyurethane antimicrobial surface treated vascular access device. The Niagara was a 15, 20 or 24 cm long 13.5 Fr double lumen polyurethane catheter.

Anticoagulation

The two primary anticoagulants used during the study were unfractionated heparin and enoxaparin (a low-molecular-weight heparin). Enoxaparin was the default mode of anticoagulation for patients receiving CRRT and was administered prefilter at a rate of 1.5 mg/kg, delivered over a 24-hour period. Where enoxaparin was not appropriate, patients were administered prefilter heparin at 1000 IU/h and protamine systemically at 10 mg/h. No heparin loading dose was given. Prefilter heparin only was used in 52 filter circuits, at a dose between 250 IU/h and 1000 IU/h. Patients requiring therapeutic anticoagulation were placed on a heparin infusion via peripheral or central access, and the heparin rate was titrated to a measured activated partial prothrombin time (APTT) of between 50 and 75 s. If coagulopathy was present or there was a high risk of bleeding, no anticoagulation was used, as prescribed by the attending ICU physician.

Patient and treatment-related variables

Patient demographic data and disease severity score (Acute Physiology and Chronic Health Evaluation [APACHE] II and APACHE III) were obtained at ICU admission. Patient-related variables recorded for each filter circuit were APTT, international normalised ratio (INR), haemoglobin level and platelet count.

Treatment-related variables recorded for each filter circuit were blood flow rate, anticoagulation type and rate, vascular access site, vascular catheter type, reason for stopping the filter circuit, and filter lifespan. The inclusion of vascular catheter type as a covariate in the modelling is important for investigating the comparative performance of each of the catheter types used and filter life, in addition to controlling for the change in device from Arrowgard Blue to Niagara catheters during the observation period.

Statistical analyses

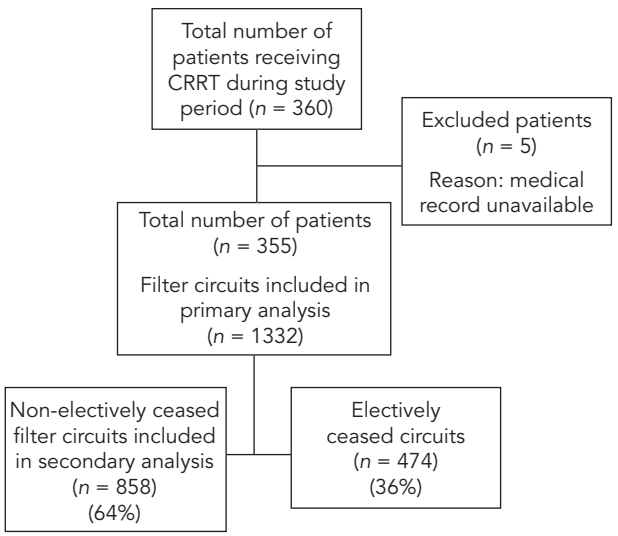
Categorical variables were summarised using frequency and percentage. Continuous variables were first assessed for skew and kurtosis and, in the presence of skew, tested for appropriateness of log or square-root transformation.

Table 1. Demographics of total patient population

No. of female patients	144
No. of male patients	211
APACHE II score, median (IQR)	25 (20–30)
APACHE III score, median (IQR)	90 (73–110)
Age in years, median (IQR)	62 (51–74)

APACHE = Acute Physiology and Chronic Health Evaluation.
IQR = interquartile range.

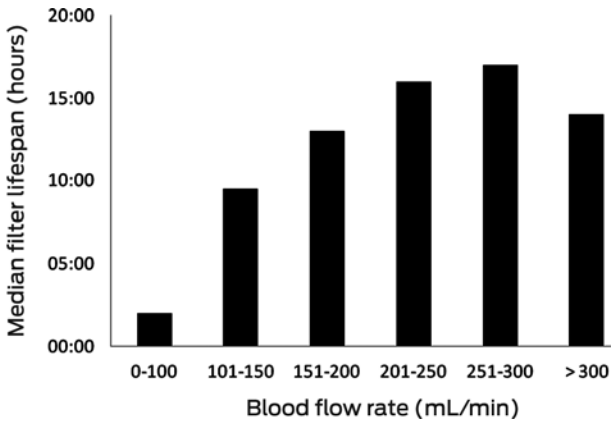
Figure 1. CONSORT diagram outlining the distribution of filters for the primary and secondary data analyses



CRRT = continuous renal replacement therapy.
CONSORT = Consolidated Standards of Reporting Trials.

Normally distributed variables were summarised using mean and standard error (SE), and significantly skewed variables were summarised using median, interquartile range (IQR) and range. Predictors of filter life were investigated using unadjusted and adjusted quantile median regression. Median regression was preferred to simple linear regression of the mean in this case due to significant skew in the filter life, which was resistant to common transformations. The ability for individual patients to contribute more than one CRRT treatment to the analysis was controlled for by using a censored least absolute deviations extension of the median regression to permit clustering of the analysis for each patient. Model specification error was assessed using a link test, while overall model goodness of fit was assessed using a He and Zhu omnibus lack-of-fit test for quantile regression. All reported *P* values were two-tailed, and for each analysis $P < 0.05$ was considered significant. All analyses were performed using Stata version 12.0 (StataCorp).

Figure 2. Relationship between blood flow rate and filter lifespan



Results

Data were collected on 1332 filter circuits and 355 patients. Demographic data for patients included in the study are outlined in Table 1. Figure 1 outlines the distribution of filter circuits for primary and secondary analyses. Median filter circuit life was 17 hours for all filter circuits, and 14 hours 20 minutes for non-electively ceased circuits. The relationship between blood flow rate and filter life is shown in Figure 2.

Results of the multivariable analyses of patient and treatment-related factors and their relationship to filter circuit life are shown in Table 2 for all filters and Table 3 for non-electively ceased filters. Table 4 outlines the distribution of filter circuits according to vascular access site.

Discussion

Blood flow rate

Our study found that blood flow rate affected filter life. An adequate blood flow rate is essential to overcome filter fibre resistance and prevent premature circuit clotting. Previous studies have shown an inverse relationship between blood flow reductions and filter lifespan.[4,6,7,9,10] In our analyses, filter lifespan for circuits run at blood flow rates lower than 200 mL/min was significantly lower than that for filters with blood flow rates higher than 200 mL/min. However, increasing blood flow rates to greater than 300 mL/min resulted in lower median filter circuit lifespan (Figure 2). Higher blood flow rates may increase access pressure and trigger frequent blood pump interruptions, causing premature circuit clotting. Our results suggest that an optimal blood flow rate is between 250 and 300 mL/min, but at least 200 mL/min. During the study period, over 65% of filter circuits were run at a blood flow rate greater than 200 mL/min. It is important to note that the ability to generate blood flow rates is highly dependent on access function.

Table 2. Median quantile regression with censored least absolute deviations analysis of filter circuit life and patient and treatment-related variables: all filter circuits

Predictor	Unadjusted coefficient (95% CI)	*P*	Adjusted coefficient (95% CI)	*P*
Haemoglobin, g/dL	−0.01 (−0.03, 0.01)	0.438		
Platelet, $\times 10^3$/μL	−0.64 (−1.12, −0.16)	0.009	−0.61 (−1.00, −0.21)	0.003
International normalised ratio	−0.61 (−1.58, 0.37)	0.222		
Activated partial prothrombin time, s	0.02 (0.01, 0.04)	0.031	0.01 (−0.02, 0.02)	0.707
APACHE II score	0.02 (−0.06, 0.09)	0.676		
APACHE III score	0.01 (−0.01, 0.03)	0.471		
Sex				
Male	0.50 (−0.50, 1.52)	0.337		
Female	1.00			
Blood flow rate, units of 100 mL/min	3.50 (1.95, 5.05)	< 0.001	1.49 (0.12, 2.85)	0.033
Vascular catheter type				
Niagara	2.00 (0.80, 3.20)	0.001	1.01 (−0.40, 2.41)	0.162
Arrowgard Blue	1.00		1.00	
Cuffed long-term dual-lumen catheter	1.00 (−0.96, 2.96)	0.316	0.03 (−2.26, 2.32)	0.981
Vascular access site				
Right internal jugular	1.17 (−0.31, 2.64)	0.122		
Left internal jugular	−0.67 (−2.13, 0.79)	0.371		
Right femoral	−0.33 (−1.43, 0.77)	0.552		
Left femoral	−0.50 (−1.60, 0.60)	0.374		
Right subclavian	0.42 (−3.53, 4.36)	0.836		
Left subclavian	−1.33 (−5.58, 2.91)	0.538		
Anticoagulation type				
Enoxaparin	1.00			
Regional heparin and protamine	0.00 (−1.76, 1.76)	1.000		
Anticoagulation type				
Regional heparin and protamine	1.00			
Low-dose heparin	−1.00 (−4.14, 2.14)	0.532		
Anticoagulation type				
Regional heparin and protamine	1.00			
Heparin infusion	1.25 (−0.67, 3.17)	0.201		
Anticoagulation type				
Enoxaparin	0.50 (−1.15, 2.15)	0.553		
Heparin — all types	0.33 (−1.15, 1.82)	0.660		
Other	−2.00 (−7.94, 3.94)	0.509		

APACHE = Acute Physiology and Chronic Health Evaluation.

Vascular access site

When comparing femoral and internal jugular access sites for CRRT, previous studies have failed to show a significant difference in filter circuit lifespan.[12,13] Both sites have disadvantages in terms of activation of filter clotting. Femoral catheters kink easily with patient repositioning, generating excess negative access pressures, especially in patients with high body mass index (BMI). Internal jugular catheters are prone to generating high access pressures when patients are coughing or agitated. The internal jugular site is often preferred over femoral due to decreased recirculation of filtered blood[14] and lower rates of catheter-related bloodstream infections in patients with high BMI.[12,13,15] During our study period, the femoral approach was favoured more often than the internal jugular approach for catheter insertion. Previous studies on femoral access catheters comparing the right and left sides found the right side was associated with longer filter lifespan compared with the left-sided approach.[16] Parienti et al[12] found the right-sided internal jugular site was associated with less catheter dysfunction

Table 3. Median quantile regression with censored least absolute deviations analysis of filter circuit life and patient and treatment-related variables: non-electively ceased filter circuits

Predictor	Unadjusted coefficient (95% CI)	*P*	Adjusted coefficient (95% CI)	*P*
Haemoglobin, g/dL	0.50 (– 0.77, 1.76)	0.439		
Platelet, $\times 10^3$/μL	– 0.70 (– 1.17, – 0.22)	0.004	– 0.77 (– 1.18, – 0.36)	< 0.001
International normalised ratio	0.45 (– 0.75, 1.66)	0.459		
Activated partial prothrombin time, s	– 0.01 (– 0.02, 0.02)	0.759		
APACHE II score	0.06 (– 0.01, 0.14)	0.101		
APACHE III score	0.02 (– 0.01, 0.03)	0.110		
Sex				
Male	– 0.50 (– 1.88, 0.88)	0.478		
Female	1.00			
Blood flow rate, units of 100 mL/min	3.33 (1.62, 5.05)	< 0.001	1.51 (0.09, 2.93)	0.037
Vascular catheter type				
Niagara	3.00 (1.49, 4.51)	< 0.001	2.48 (0.88, 4.08)	0.002
Arrowgard Blue	1.00		1.00	
Cuffed long-term dual-lumen catheter	0.58 (– 1.86, 3.02)	0.640	0.03 (– 2.50, 2.56)	0.981
Vascular access site				
Right internal jugular	1.75 (0.02, 3.48)	0.047	0.77 (– 0.73, 2.27)	0.216
Left internal jugular	0.42 (– 1.71, 2.54)	0.701		
Right femoral	– 0.50 (– 1.60, 0.60)	0.372		
Left femoral	– 1.75 (– 3.45, – 0.05)	0.044	– 1.04 (– 2.43, 0.34)	0.141
Right subclavian	2.00 (– 2.06, 6.05)	0.334		
Left subclavian	– 2.25 (– 6.12, 1.62)	0.254		
Anticoagulation type				
Enoxaparin	1.00			
Regional heparin and protamine	0.75 (– 1.03, 2.53)	0.408		
Anticoagulation type				
Regional heparin and protamine	1.00			
Low-dose heparin	0.00 (– 3.15, 3.15)	1.000		
Anticoagulation type				
Regional heparin and protamine	1.00			
Heparin infusion	1.92 (– 0.30, 4.13)	0.090		
Anticoagulation type				
Enoxaparin	– 1.67 (– 3.12, – 0.21)	0.025	– 0.52 (– 2.18, 1.13)	0.534
Heparin — all types	– 0.67 (– 1.98, 6.34)	0.320	0.97 (– 0.55, 2.48)	0.212
Other	0.50 (– 5.34, 6.34)	0.867	– 0.52 (– 6.79, 5.75)	0.871
Nil	1.00		1.00	

APACHE = Acute Physiology and Chronic Health Evaluation.

than the left side. In our multivariable analyses, there was no advantage to any insertion site in increasing filter lifespan.

Anticoagulation type

Our study found that there was no advantage to any of the types or methods of anticoagulation in prolonging filter lifespan and that using no anticoagulation was an effective strategy in patients with coagulopathy or at risk of haemorrhage. Patients receiving no anticoagulation had a lower median platelet count in both the all filters analysis (90×10^3/μL; IQR, 47–161×10^3/μL) and the non-electively ceased filters analysis (80×10^3/μL; IQR, 42–157×10^3/μL) than patients receiving anticoagulation (166×10^3/μL; IQR, 91–260×10^3/μL; and 196×10^3/μL IQR, 118–306×10^3/μL, respectively). Anticoagulation is necessary to prevent premature clotting of the filter circuit. The risk of bleeding must be balanced against the prolonging of filter circuit life. In cases where the risk of haemorrhage is high or coagulo-

Table 4. Distribution of filters by vascular access site

Site	Non-electively ceased filters* ($n = 858$)	All filters* ($n = 1332$)
Left femoral	235 (27%)	376 (28%)
Left internal jugular	110 (13%)	180 (14%)
Left subclavian	13 (1%)	18 (1%)
Long term catheter	49 (6%)	83 (6%)
Right femoral	248 (29%)	387 (29%)
Right internal jugular	188 (22%)	260 (20%)
Right subclavian	15 (2%)	25 (2%)
Unknown	0	3 (0.2%)

* No. of filters (% of total).

pathy exists, no anticoagulation may be an acceptable and safe alternative.[17] Enoxaparin use in CRRT is associated with effective prolongation of filter circuit life but may result in significant systemic anticoagulation.[18] Unfractionated heparin offers the advantage of being reversible with protamine, allowing anticoagulation of the filter circuit with minimal or no systemic anticoagulation of the patient. A study by Joannidis et al[19] evaluating the efficacy of low-molecular-weight heparin (enoxaparin) compared with unfractionated heparin found a significantly longer filter lifespan associated with the use of enoxaparin for anticoagulation. However, Reeves et al[20] found no difference in filter life between anticoagulation with low-molecular-weight heparin (dalteparin) compared with unfractionated heparin. Because of the large variation in dosing and delivery of anticoagulation between different ICUs, it is difficult to compare previous study results with our findings.

Vascular catheter type

Blood flow through the vascular access catheter is dependent on catheter lumen diameter, length of catheter and blood viscosity. Previous studies by Kim et al[21] and Fealy et al[22] comparing the effect on filter circuit life of Niagara versus Medcomp catheters, and Niagara versus Dolphin catheters, found no significant relationship between filter circuit life and vascular catheter type. In our study, the Niagara catheter was associated with longer filter life than the Arrowgard Blue catheter in the analysis of non-electively ceased filters, but not in the analysis of all filters. There are key differences in the design of the two catheters. The Arrowgard Blue catheter has side holes for the flow of blood. If the holes become lodged against the wall of the blood vessel, high access pressures and frequent blood flow interruptions can result, causing premature circuit clotting and formation of thrombi around the inflow and outflow sites.[23] The Niagara catheter has a side-by-side shotgun design, which reduces the clotting problems associated with the presence of side holes. Internal lumen diameter is an important determinant of resistance, and a larger diameter may reduce turbulence of blood flow and the incidence of microclotting. The 16 cm and 20 cm Arrowgard Blue catheters have a smaller inner lumen diameter (2.05 mm) than the Niagara catheter (2.18 mm). However, the Arrowgard Blue 25 cm femoral catheter has a larger internal lumen diameter (2.58 mm) than the Niagara 24 cm femoral catheter (2.18 mm). It is likely that catheter design, in addition to internal lumen diameter, is a determinant of optimal access catheter function and the effect on filter life.

Patient-related haematological variables

Patient-related factors may have a significant effect on filter circuit life. Decisions regarding anticoagulation are usually informed by the coagulation profile of the patient. High haemoglobin levels may contribute to circuit clotting through increased blood viscosity. Previous studies have not found a correlation between filter circuit life and INR, APTT or haemoglobin concentration.[11,16] In a multivariable study, Kim et al[16] found lower platelet count was significantly correlated with longer filter circuit life. Zhang et al[11] demonstrated that a lower platelet count was associated with longer filter life, but this did not reach statistical significance. In our multivariable analysis examining INR, APTT, haemoglobin concentration and platelet count, only lower platelet count was found to be predictive of longer filter circuit lifespan, consistent with the findings of Kim et al.[16]

Strengths and limitations

This analysis is based on a large number of filter circuits used over more than 3 years in our ICU and represents important findings for access catheter design and site, anticoagulation type and blood flow rate not previously reported in the literature. The results can therefore be used to guide important decision making for choices in catheter insertion site, catheter design, type of anticoagulation and blood flow rate in the clinical setting. There are several limitations to our study. The analysis of all filters included those that were ceased electively and which may have contributed long lifespans had they not been electively ceased. The analysis of non-electively ceased filters did not include filters that were electively ceased but achieved long filter lifespans. The study was retrospective and conducted over a 44-month period, such that treatment-related changes over time may have affected the results, particularly in relation to the Niagara catheter, which was introduced for the final 8 months of the study. The effect of trialling the Infomed machine on a limited number of patients for a 6-week period is unknown, but it is possible that this may have resulted in reduced filter life initially

while nurses were unfamiliar with the new machine. This trial period was undertaken solely while the Arrowgard Blue catheter was in use. To our knowledge, no other major treatment-related changes were instituted over the period of the study. Significantly fewer Niagara catheters than Arrowgard Blue catheters were included in the study. A randomised controlled trial would be beneficial to further analyse the effect of vascular catheter design on filter circuit life. Finally, expertise of bedside nurses may play an important role in determining filter circuit lifespan.[4,24,25] This is a variable that was not accounted for in our study but would be useful to explore in future studies.

Conclusions

Blood flow rate and platelet count are important determinants of filter circuit survival time in CRRT and may be more important than anticoagulation approaches in some patients. Vascular access catheter design may also play a role in the determination of filter circuit life. Further investigation of these findings using controlled studies would be a logical next step in better understanding clotting and loss of CRRT filter circuits.

Acknowledgements

We thank Tim Spelman for his statistical analysis, and we acknowledge the generous support of Ian Baldwin and the Royal Melbourne Hospital Renal Special Interest Group.

Competing interests

None declared.

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