Strategies to minimise intraoperative blood loss during major surgery – a state-of-the-art review

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Submission category: Review article – Joint *Anaesthesia*/British Journal of Surgery Perioperative Care supplement

Word counts (excluding headings):

Abstract: 246

Manuscript: 3997

Abstract

Background: Reducing operative blood loss improves patient outcomes and reduces healthcare costs. The aim of this article is to review the current surgical, anaesthetic and haemostatic intraoperative blood conservation strategies.

Method: This is a narrative review based on a literature search of relevant databases up until 31 July 2019 for publications relevant to reducing blood loss in the surgical patient.

Results: Interventions can begin early in preoperative period through identification of patients at high risk of bleeding. Direct acting anticoagulants can be stopped 48 hours prior to most surgery in the presence of normal renal function. Aspirin can be continued for most procedures. Intraoperatively, cell salvage is recommended when anticipated blood loss is greater than 500 mls and this can be continued postoperatively in certain situations. Tranexamic acid is safe, cheap and efficacious and routine administration is recommended when anticipated blood loss is high. However, the optimal dose, timing and route of administration remain unclear. The use of topical agents, tourniquet and drains remains at the discretion of the surgeon. Anaesthetic techniques include correct patient positioning, avoidance of hypothermia and regional anaesthesia. Permissive hypotension may be beneficial in select cases. Promising haemostatic strategies include pharmacological agents such as desmopressin, prothrombin complex concentrate and fibrinogen concentrate, and use of viscoelastic haemostatic assays but further evidence of benefit is required.

Conclusions: Reducing perioperative blood requires a multimodal and multidisciplinary approach. Although high-quality evidence exists in certain areas, the overall evidence base for reducing intraoperative blood loss remains limited.

Introduction

Approximately 313 million surgical procedures are performed worldwide each year[1]. Recent estimates show that at least 4.2 million people die within 30 days of surgery each year, which accounts for 7.7% of all deaths globally[2]. Estimates of postoperative complications and morbidity are even higher[3,4]. Perioperative bleeding remains a major complication during and after surgery, and is associated with a high risk of death, complications, and healthcare resource use[5-8].

The mechanisms contributing to non-vascular, non-traumatic, intraoperative bleeding are complex and include pre-existing co-morbidity, type of surgical procedure, activation of fibrinolytic and inflammatory pathways[9-11], and acquired haemostatic impairment secondary to haemodilution, consumption[12], medications (e.g. anticoagulants, antiplatelets), hypothermia and acidosis[13].

Advances in anaesthesia, surgery and transfusion medicine over the past decade has led to the development of 'Patient Blood Management' – a multi-modal, evidence-based strategy consisting of three pillars: treating anaemia; reducing perioperative blood loss; and improving tolerance to anaemia (*Fig. 1*)[14]. In this review article, we will discuss the organisational and *intraoperative* surgical, anaesthetic and haemostatic strategies that can be used to minimise blood loss and improve patient outcomes (*Table 1*). The management of major haemorrhage, perioperative anaemia and transfusion thresholds are beyond the scope of this review and are described elsewhere[15-19].

Methods

We searched MEDLINE, PubMed, EMBASE, Transfusion Evidence Library, and Cochrane Central Register of Controlled Trials. The search strategy included "surgery" in combination with the terms "transfusion", "blood management", "blood conservation", "blood loss", "haemoglobin", "hemoglobin". Titles and abstracts were screened. We checked references of all identified trials, relevant review articles and current treatment guidelines for further relevant literature. We restricted our search to literature from 1st January 2000, but older important publications were not excluded. Relevant topics beyond the scope of this review were referenced by relevant narrative reviews, systematic reviews or clinical guidelines, where applicable.

Organisational strategies

Organisational considerations for minimising intraoperative bleeding begin in the preoperative period and include identifying patients at risk, followed by triggering pathways and initiating appropriate interventions to minimise that risk.

- **Pre-operative history**

Current UK and European guidelines recommend taking a structured bleeding history before surgery, which takes into account previous excessive surgical bleeding, response to haemostatic challenges, family history and the use of antiplatelet and anticoagulant therapy[20,21]. In the presence of a negative history, routine coagulation testing is not recommended as the predictive value for bleeding of these tests is poor[22]. For patients with a positive bleeding history, a more quantitative description of symptoms should be obtained along with a referral to a haematologist with an interest in haemostasis for further assessment. Quantification of bleeding risk can also help in decision making for stopping anticoagulation and plan requirements for any bridging therapy that may be required. Examples of bleeding assessment tools include the International Society on Thrombosis and Haemostasis Bleeding Assessment Tool[23], the Vicenza Bleeding Score[24] and the Pediatric Bleeding Questionnaire[25]. Although none of these have been prospectively validated in a large population of general surgical patients, the benefit of asking precise questions is likely to be more superior than an unstructured bleeding history[26].

- **Risk stratification**

Consideration should be given to the type of surgery being undertaken. Cardiac surgery, where rates of bleeding and blood product use are high, has been at the forefront for developing surgery-specific risk scores to predict bleeding and the need for transfusion. The Papworth Bleeding Risk Score was developed in 2010, and subsequently validated in 2015, to identify patients at risk of excessive blood loss after cardiac surgery[27]. This score has a high negative predictive value but the positive predictive value is low; only 15% of patients who were classed as high risk actually suffered from increased postoperative bleeding[28]. More recently, the ACTA-PORT score has been demonstrated to be a valid, simple and accurate predictor of the risk of transfusion for patients undergoing cardiac surgery[29]. Components of the score include age, sex, body surface area, logistic EUROSCORE, preoperative haemoglobin and creatinine, and type of surgery. Such scoring systems have the potential to identify modifiable risk factors, quantify risk prior to surgery, allocate resources (e.g. cell salvage) and better guide blood service inventory management.

- **Managing anticoagulant and antiplatelet therapies**

Increasing numbers of patients are continuing antiplatelet (e.g. aspirin, clopidogrel) and anticoagulant (e.g. warfarin, direct oral anticoagulants (DOACs)) therapy into the perioperative period to reduce the risk of major cardiovascular and thrombotic events. These risks must be balanced with the procedure-related risks of bleeding on an individual patient basis and may require discussions with the patient, surgeon, haematologist and anaesthetist. Detailed reviews on the pharmacology and perioperative management of these agents can be found elsewhere[30-33], but in summary:

(i) Aspirin can be continued for most procedures;

(ii) Bridging therapy for warfarin should only be considered in patients with the highest risk of thrombosis (e.g. mechanical heart valves, venous thromboembolism within the previous three months);

(iii) Post-operative bridging should not be started until at least 48 hours after high bleeding risk surgery;

(iv) DOACs, due to their predictable pharmacokinetics, can be stopped 48 hours prior to most surgery in the presence of normal hepatic and renal function (*Fig. 2*);

(v) ADP-receptor antagonists, such as clopidogrel, should be stopped 5-7 days pre-operatively;

(vi) Consider the use of tranexamic acid in patients with urgent high-risk bleeding surgery in patients on antiplatelet agents or where a residual anticoagulant effect of DOACs is suspected.

Surgical strategies

- **Tourniquet**

Tourniquets are widely used during lower limb surgery. Although tourniquets reduce intraoperative blood loss, meta-analyses of studies suggest there is no difference in overall blood loss[34,35]. The release of inflammatory mediators as a result of limb ischemia may even increase blood loss[36]. Interpretation of studies is often limited by surgeons inflating tourniquets to different pressures and for different portions of the procedure. Currently, the decision to use a tourniquet is dictated by factors other than blood management such as visibility of the surgical field[37]. Disadvantages of tourniquet use include increased postoperative pain, impaired quadriceps function and increased risk of thombotic events[34,38,39].

- **Antifibrinolytics**

Antifibrinolytics, such a tranexamic acid, are synthetic lysine analogues that inhibit plasminogen activation and provide clot stabilisation. In the UK. it is recommended for all surgery where blood loss is expected to be greater than 500 mls[40, 41]. Tranexamic acid is not approved by the Food and Drug Administration for this purpose and epsilon-aminocaproic acid (aprotinin) may be used as an alternative. Aprotinin has been associated with increased postoperative mortality rates[42].

A number of studies have investigated the safety and efficacy of tranexamic acid and the majority demonstrate a reduction in blood loss and transfusion requirements. Most studies have been carried out in orthopaedic surgery where tranexamic acid has been shown to reduce the rate of allogeneic blood transfusion by up to 69%[43] after hip and knee surgery, without increased risk of complications, including thromboembolic events[44]. When considering all surgical procedures, tranexamic acid has been shown to reduce blood loss by approximately one third[45]. Tranexamic acid has specifically been shown to reduce blood loss and the rate of allogeneic blood transfusions after coronary artery surgery[46], spinal surgery[47], orthopaedic fracture surgery[48], prostate surgery[49], caesarean section or hysterectomy[50], and plastic surgery procedures[51].

The salient area of uncertainty is the optimal route, dose, and timing of tranexamic acid administration. Protocols in studies to date are extremely heterogeneous. Tranexamic acid administration can be intravenous, intra-articular, oral, or in combination. Doses may be weight-adjusted and usually range from 10mg/kg to 20mg/kg. Administration may be repeated during the intraoperative and postoperative periods[41]. Network meta-analyses are underway to determine an optimal dosing regimen to standardise clinical care and guide comparators for future research[52]. Potential advantages of topical delivery are that it may overcome contraindications such as renal disease due to lower plasma levels[60]. Repeat doses may play a greater role for a prolonged duration of surgery or large volume blood loss to maintain therapeutic levels.

A further uncertainty is whether the risk of thromboembolic events has been adequately addressed in high risk subgroups, although tranexamic acid was not associated with an increased rate of adverse events in patients undergoing major surgery for malignancy [53]. The favourable side-effect profile, cost and ease of availability of tranexamic acid means it should be considered for all surgical procedures where moderate blood loss is anticipated [40].

- **Cell salvage**

Cell salvage is a method of recovering blood from the surgical field during the intraoperative or immediately postoperative period that is then reinfused to the patient (*Fig. 3*). The National Institute for Health and Care Excellence (NICE) recommends the use of cell salvage for procedures when a very high volume of blood loss is anticipated[40], which the recent Association of Anaesthetists guidance consider to be greater than 500ml[54,55]. The key principle is to use cell salvage in combination with other blood conservation strategies, when it is expected to reduce the likelihood of allogeneic blood transfusion and/or severe postoperative anaemia[55].

Intraoperative blood collection is through a suction system whereas postoperative blood collection is through surgical drains. Collected blood is anticoagulated and filtered prior to reinfusion. Blood collected intraoperative is typically washed and resuspended in normal saline prior to reinfusion, whereas blood collected postoperatively through drains is typically unwashed. Current technology requires approximately 500 mls of collected blood to produce a clinically valuable volume of blood for reinfusion after processing[55]. Cell salvage reduces the risk of exposure to allogeneic blood by 54% across all surgical specialities[56,57].

Procedures with significant variation in volume of blood loss make it difficult to anticipate whether sufficient blood will be collected to permit reinfusion. In this setting cell salvage can be used in 'collect only' mode and only processed for reinfusion if more than 500 mls is collected. When procedures with high volume blood loss are performed under tourniquet, postoperative rather than intraoperative cell salvage should be considered. For example, blood loss from revision knee arthroplasty reliably exceeds 500 ml, but if performed under tourniquet there is limited intraoperative blood loss[37]. There remain controversies as to which patients benefit from cell salvage, and it is not currently recommended for routine use during caesarean section[55,58,59].

Infection and malignancy were traditionally contraindications to cell salvage, however, there is increasing evidence to support the use of cell salvage in these settings. With the use of a leucocyte depletion filter (40 microns), there is a 99% reduction in bacterial contamination in blood resuspended in 0.9% saline[60]. The potential increased risks of bacterial contamination must be weighted again the increased risk of infection through immunomodulation secondary to allogeneic blood transfusion[61]. Similarly, studies have not identified any association between the use of cell salvage and increased risk of metastasis during cancer surgery and reinfused tumour cells do not have metastatic potential[62]. When surgery requires revision of metalwork, leucocyte depletion filters do not remove small metal fragments so selective suctioning should be employed so that the most contaminated blood is not collected[63].

- **Drains**

Surgical site drains are often used with the aim of reducing haematomas, surgical site infection, and depending on the procedure performed, incidence fistula development. There are a limited number of robust studies investigating the effectiveness of drains in preventing postoperative complications, and many do not demonstrate any benefit of drain insertion over drain omission[64-67]. In orthopaedic surgery, conventional suction drains can increase postoperative blood loss[68].

In procedures with continuing postoperative blood loss there may be a role of autologous reinfusion drains (cell salvage). After knee arthroplasty surgery, autologous reinfusion drains can reduce blood loss and allogeneic red blood cell transfusion rates compared with conventional suction drains or no drain [69,70]. The value of drains is specific to each procedure. Given increasing the increasing number of studies that suggest drains do not confer improved clinical outcomes and may increase blood loss, the use of drains may warrant revisiting for where they are currently employed routinely.

- **Surgical technique**

Surgical developments include the introduction of laparoscopic and robotic surgery, driven by a number of outcomes, but they may also reduce blood loss. In a study of transanal mesorectal excision for rectal cancer, operative blood loss was lower with laparoscopic compared with open, and with robotic compared with laparoscopic surgery[71]. Similar findings have been reported in other surgical specialties [72-75].

- **Diathermy**

Monopolar and bipolar radiofrequency electrosurgery are key tools for achieving haemostasis during surgery. A number of new devices are available, often in the form of bipolar sealing systems, proposed to result in less damage to adjacent healthy tissue, but there is limited evidence that they reduce blood loss[76] and factors such as surgical technique are likely to be more important.

- **Topical agents**

Topical agents including fibrin sealants (fibrinogen and thrombin), gelatine-thrombin matrices, and oxidised cellulose may be applied to bleeding tissues intraoperatively as a haemostatic strategy. However, these agents are expensive and despite numerous studies across different surgical specialities, there is only weak evidence to suggest they offer a clinically important reduction in blood loss[77,78].

Anaesthetic strategies

- **Permissive hypotension**

Permissive hypotension consists of using pharmacological agents to lower intraoperative mean arterial pressure to values between 50 and 65 mm Hg to reduce blood flow to the surgical field. The intention is to reduce blood loss, whilst also improving the quality of the surgical field. This has to be balanced with the risks of organ hypoperfusion such as delayed awakening, permanent cerebral damage, myocardial and kidney injury, and death[79]. Therefore, this technique should be avoided in patients with coronary artery disease, poorly controlled hypotension and cerebrovascular disease.

Permissive hypotension can be achieved through a reduction in cardiac output, blood pressure or a combination of these depending on the technique used. Techniques, some of which will be discussed in this review, include patient positioning, central neuraxial anaesthesia, intravenous anaesthetics (e.g. propofol), opioids (e.g. remifentanil), directly acting vasodilators (e.g. nitroglycerine), selective β-blockers (e.g. esmolol), selective α-blocker (e.g. dexmedetomidine), combined α and β-blocker (e.g. labetalol) and volatile anaesthetics (e.g. sevoflurane). Systematic reviews and randomised controlled trials have demonstrated that permissive hypotension reduces blood loss in patients undergoing orthopaedic, maxillofacial, spinal and radical prostatectomy surgery[80-83]. This translated into a reduction in transfusion requirements only in orthopaedic surgery. However, all of the included studies were small, low quality, and more importantly, did not evaluate harm. If permissive hypotension is to be undertaken, adequate patient selection is paramount and hypotension must be closely monitoring to ensure adequate organ perfusion.

- **Central neuraxial anaesthesia**

Anaesthetic techniques play an important role in minimising intra-operative blood loss. Central neuraxial blockade (i.e. subarachnoid / epidural anaesthesia) results in blockade of preganglionic sympathetic nerve fibres, arterial hypotension and reduced peripheral venous pressures. These result in less arterial, and perhaps more noticeably, less venous oozing from the surgical site. Blockade of sympathetic nerve fibres also results in the attenuation of the surgical 'stress response', which in turn is associated with stabilisation of clotting factors and reduced fibrinolysis[84,85].

Early meta-analyses of randomised trials, conducted in a range of surgical specialties (abdominal, thoracic, pelvic, lower extremity), demonstrated that the use of neuraxial anaesthesia was associated with significant decreases in intra-operative blood loss and allogeneic red blood cell transfusion requirements [86,87]. However, more recent meta-analyses have demonstrated no difference in blood loss or red blood cell requirements [88,89]. These conflicting results should be interpreted in the context of widespread adoption of restrictive transfusion practices since much of the original research was undertaken, along with the implementation of other simultaneous blood conservation strategies as part of patient blood management.

- **Patient positioning**

Correct patient positioning is a simple and effective intervention to reduce intraoperative blood loss. This is particularly important in patients undergoing surgery in the prone position (e.g. lumbar surgery). Incorrect positioning can lead to compression of the inferior vena cava with subsequent obstruction of venous return. The increase in hydrostatic pressure diverts blood towards the epidural venous plexus causing vessel engorgement and bleeding at the surgical site [90]. Changes to intra-abdominal pressure may also be associated with blood loss [91]. In the supine position, the patient may be slightly titled to the left to avoid inferior vena cava compression. Correct reverse Trendelenburg and lateral positions have also been demonstrated to reduce blood loss in patients undergoing endoscopic sinus surgery [92] and hip arthroplasty [93], respectively. In addition, where possible the site of surgery should be elevated above the level of the right atrium to facilitate venous drainage and reduce venous pressures.

- **Avoidance of hypothermia**

Intraoperative hypothermia, defined as a core body temperature less than 36 degrees Celsius, can result from many factors such as low operating theatre temperatures, evaporation from body cavities, cold intravenous fluids and anaesthetic gases, reduced metabolic activity and loss of thermal regulation and responses due to anaesthesia (e.g. shivering). Patients at risk of developing hypothermia include those at extremes of age, undergoing combined regional and general anaesthesia, major surgery, prolonged surgery and higher American Society of Anaesthesiology status.

The reversible adverse effects of hypothermia on platelet function and the coagulation-cascade, as a result of impairment of temperature-dependent enzymatic reactions, are well recognised[94,95]. Even mild hypothermia has been associated with an increase in blood loss by 16% and relative risk for red blood cell transfusion by 22%[96,97]. In addition, hypothermia can also lead to increased rates of wound infection[98], cardiovascular events[99], and prolonged recovery[100]. As a result, NICE has issued guidance on the prevention and management of hypothermia in patients undergoing surgery [101]. Examples of strategies used to avoid intra-operative warming include regular temperature monitoring every 30 minutes, ensuring the ambient theatre temperature is at least 21 degrees Celsius, using active forced air warming devices and administering intravenous fluids through fluid warmers.

- **Ventilation strategies**

Positive pressure ventilation with minimal use of positive end-expiratory pressure (PEEP) and low tidal volumes has been previously advocated to reduce blood loss as it promotes venous return[102]. However, this is not supported by high quality evidence and needs to be balanced with the benefits of PEEP, such as alveolar recruitment.

A recent secondary analysis, of a previously published trial comparing the effect of a lung-protective strategy in patients undergoing major abdominal surgery[103], evaluated the effect of PEEP between 6 and 8 cmH_2O versus zero PEEP specifically in patients undergoing hepatic resection surgery[104]. The authors found that using PEEP, when compared to a zero PEEP strategy, was not associated with increased bleeding.

<u>**Haemostatic strategies**</u>

- **Desmopressin**

Desmopressin is a synthetic analogue of the naturally occurring antidiuretic hormone vasopressin. It causes a transient rise in plasma levels Factor VIII and von Willebrand factor, and has been used for the treatment of mild to moderate haemophilia A and von Willebrand disease for more than 40 years [105]. It can be given subcutaneously or intravenously at a dose of 0.3 ug/kg. Safety considerations include the risk of developing arterial or venous thromboses and in rare cases, desmopressin may be associated with hyponatraemia and seizures.

Recently, its use has been expanded to other potential indications. In trauma, European guidelines recommend desmopressin be administered in patients on anti-platelet agents[106]. In the perioperative setting, guidelines suggest using desmopressin where there is demonstrable evidence of acquired platelet dysfunction secondary to drugs, uraemia or cardiopulmonary bypass[107,108].

However, the evidence for desmopressin to reduce perioperative transfusion requirements and blood loss is weak. A recent Cochrane review of 65 trials with 3874 participants undergoing surgery found no overall benefit of desmopressin[109]. Small reductions in blood loss and transfusion requirements were observed in patients undergoing cardiac surgery but these were judged not to be clinically important. Many of the included trials were at high risk of bias and the overall quality of evidence ranged from very low to moderate. Any potential benefits may be seen in specific subgroups of patients such as those with acquired platelet dysfunction or on anti-platelet therapy[110].

- **Procoagulant factors**

There is growing interest in the targeted use of procoagulant haemostatic factors, mainly driven by the demonstrable lack of efficacy and safety concerns regarding fresh frozen plasma[111,112]. These can be derived from plasma as concentrates or developed as specific recombinant factors. The potential advantages of this include more rapid availability in the emergency situation, as the current processes for thawing plasma would not apply, and better efficacy as a more concentrated source of factors is being administered. This would, in turn, lead to quicker and stronger fibrin clot formation.

Concentrates can contain multiple factors, for example prothrombin complex concentrates, which contain three or four Vitamin K-dependent factors at high concentrations. The main indication for prothrombin complex is in patients on anticoagulant therapy, such as warfarin, with significant bleeding or who require emergency surgery [113]. Conversely, single procoagulant factors are also available and the most notable one is fibrinogen concentrate. As with desmopressin, these agents have the potential to increase the rates of thrombotic events. This has been clearly shown in clinical trials of using recombinant Factor VIIa in unselected patients [114].

Fibrinogen depletion, secondary to haemodulition and/or consumption, is thought to occur before deficiencies of other coagulation factors become apparent during haemorrhage[115]. Hypofibrinogenaemia is a risk factor for haemorrhage in orthopaedic surgery[116], cardiac surgery[117] and trauma[115]. In obstetric haemorrhage, a fibrinogen level of <2 g/l has a 100% predictive value for progression for progression from moderate to severe haemorrhage[118]. Fibrinogen concentrate is currently not licenced for acquired hypofibrinogenaemia in the UK, but is used widely in Europe. UK guidelines recommend using cryoprecipitate as the source of fibrinogen[119]. However, off-label use has been reported with small studies showing reduced red cell and fresh frozen plasma transfusion requirements[120].

Despite the physiological promise of procoagulant factors, high quality data to guide safe and effective use are lacking. A recent systematic review was unable to draw any conclusions due to a paucity of data[121]. However, the review identified 22 ongoing trials so more definitive evidence regarding the safety, efficacy and cost effectiveness of procoagulant factors is likely to be available in the future.

- **Viscoelastic haemostatic assays**

Viscoelastic assays are increasingly being used in the management of severe bleeding. The two commonest assays are thromboelastography (TEG) and rotational thromboelastometry (ROTEM). The main advantage of these assays is the quick turnaround time, with an assessment of all stages of clot formation available in a few minutes. Standard laboratory tests such as prothrombin time can have a turn-around time of up to 77 minutes, which is not useful in a rapidly evolving situation[122].

In brief, TEG/ROTEM measure the physical properties of clot formation in whole blood via a pin suspended in a cup heated to 37 degrees Celsius. The pin is connected to a torsion wire connected to a transducer. The strength (or lack) of the developing clot alters the rotation of the pin, which is then converted into an electrical signal to generate a graphical output. Defects in particular parameters of clot formation allow for more targeted haemostatic therapy. For example, prolonged clot initiation ('R time') on TEG is suggestive of global depletion of coagulation factors and/or warfarin therapy. A detailed review on assay machine mechanics, quality assurance and test accuracy can be found elsewhere[123].

Current NICE guidelines recommend the use of these assays only in patients undergoing cardiac and liver surgery, where robust cost-effective data exist to support their use [124]. More recent guidance from the British Society of Haematology, also suggests that TEG/ROTEM may have a role in the management of trauma and obstetric haemorrhage[123,125,126].

Conclusion

The potential for major intraoperative blood loss remains a key concern for clinicians. Strategies to mitigate this, such as identification and management of high-risk patients, can be implemented early in the preoperative period. Intraoperatively, meticulous surgical techniques and local haemostasis are fundamental measures in the control of bleeding. Cell salvage is a valuable adjunct. Tranexamic acid reduces blood loss but the optimal route, dose or timing of administration remains unclear. Additional anaesthetic techniques, such as regional anaesthesia, can also help to reduce blood loss. Other key considerations include avoidance of hypothermia, acidosis and excessive haemodilution along with early identification of coagulopathy using viscoelastic haemostatic assays. The optimal use of haemostatic therapies such as desmopressin and procoagulant factors is unclear at present but represents an important area of ongoing research *(Table 2).* Close collaboration between anaesthetists, surgeons, haematologists and laboratory personnel is vital.

Conflicts of interest / Disclosures

A.S. is currently being supported by an NIHR Doctoral Research Fellowship (DRF-2017-10-094) and is the Trainee Fellow on the editorial board of *Anaesthesia*. A.K. is the Editor-in-Chief of *Anaesthesia*. A.K. or his employer has received educational grant funding from or honoraria from CSL Behring, Haemonetics, Pharmacosmos, Fisher and Paykel, Massimo and Vifor Pharma. No other conflicts of interest declared.

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Figure Legends

Fig 1. The three-pillar, nine-field matrix of perioperative patient blood management.

Fig 2. Suggested algorithm for the perioperative management of direct acting anticoagulants.

Fig 3. Standard set-up of a cell salvage circuit.