

# Strategies to minimize intraoperative blood loss during major surgery

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

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

**Results:** Interventions can begin early in the preoperative phase through identification of patients at high risk of bleeding. Directly acting anticoagulants can be stopped 48 h before most surgery in the presence of normal renal function. Aspirin can be continued for most procedures. Intraoperative cell salvage is recommended when anticipated blood loss is greater than 500 ml and this can be continued after surgery in certain situations. Tranexamic acid is safe, cheap and effective, 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 selected patients. Promising haemostatic strategies include use of pharmacological agents such as desmopressin, prothrombin complex concentrate and fibrinogen concentrate, and use of viscoelastic haemostatic assays.

**Conclusion:** Reducing perioperative blood loss 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.

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## Introduction

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

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<sup>9–11</sup>, and acquired haemostatic impairment

secondary to haemodilution, consumption<sup>12</sup>, medications (such as anticoagulants and antiplatelets), hypothermia and acidosis<sup>13</sup>.

Advances in anaesthesia, surgery and transfusion medicine over the past decade have led to the development of 'patient blood management', a multimodal, evidence-based strategy consisting of three pillars: treating anaemia, reducing perioperative blood loss and improving tolerance to anaemia (*Fig. 1*)<sup>14</sup>. This review article discusses the organizational and intraoperative surgical, anaesthetic and haemostatic strategies that can be used to minimize blood loss and improve patient outcomes (*Table 1*). The management of major haemorrhage, perioperative anaemia and transfusion thresholds is beyond the scope of this review and is described elsewhere<sup>15–19</sup>.

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

	First pillar: optimize erythropoiesis	Second pillar: minimize blood loss and bleeding	Third pillar: harness and optimize physiological reserve of anaemia
Preoperative	Detect, investigate and treat anaemia Treat iron deficiency Treat other haematinic deficiencies	Preoperative history Risk stratification Managing anticoagulation and antiplatelet therapies	Optimize physiological reserve and other risk factors Formulate patient-specific plans to minimize blood loss, optimize red cell mass and reduce anaemia
Intraoperative	Schedule surgery with haematological optimization	Cell salvage Anaesthetic blood conservation strategies Blood-sparing surgical techniques Meticulous surgery Pharmacological agents	Optimize cardiac output, ventilation and oxygenation Restrictive transfusion thresholds
Postoperative	Stimulate erythropoiesis Be aware of drug interactions that can increase anaemia	Vigilance for postoperative bleeding Maintain normothermia Manage anticoagulation Treat infection promptly Postoperative cell salvage	Optimize anaemia reserve Minimize oxygen consumption Avoid unnecessary phlebotomy Restrictive transfusion thresholds

**Table 1 Strategies to minimize intraoperative blood loss**

Organizational	Surgical	Anaesthetic	Haemostatic
Preoperative history	Tourniquet	Permissive hypotension	Desmopressin
Risk stratification	Antifibrinolytics	Neuraxial anaesthesia	Procoagulant factors
Management of antiplatelet and anticoagulant therapies	Cell salvage Drains Surgical technique Diathermy Topical agents	Patient positioning Normothermia Adequate ventilation	Viscoelastic haemostatic assays

## Methods

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

## Organizational strategies

Organizational considerations for minimizing intraoperative bleeding begin in the preoperative phase, and include

identifying patients at risk, followed by triggering pathways and initiating appropriate interventions to minimize that risk.

## Preoperative history

Current UK<sup>20</sup> and European<sup>21</sup> guidelines recommend taking a structured history about bleeding before surgery, which takes into account previous excessive surgical bleeding, response to haemostatic challenges, family history, and the use of antiplatelet and anticoagulant therapy. In the presence of a negative history, routine coagulation testing is not recommended as the predictive value of these tests for bleeding is poor<sup>22</sup>. For patients with a positive history of bleeding, a more quantitative description of symptoms should be obtained, along with 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 planning requirements for any bridging anticoagulant

therapy that may be required. Examples of bleeding assessment tools include the International Society on Thrombosis and Haemostasis Bleeding Assessment Tool<sup>23</sup>, the Vicenza Bleeding Score<sup>24</sup> and the Pediatric Bleeding Questionnaire<sup>25</sup>. Although none of these has been validated prospectively in a large population of general surgical patients, asking precise questions is likely to be superior to an unstructured bleeding history<sup>26</sup>.

### 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 of the development of surgery-specific risk scores to predict bleeding and the need for transfusion. The Papworth Bleeding Risk Score<sup>27</sup> was developed in 2010, and subsequently validated in 2015, to identify patients at risk of excessive blood loss after cardiac surgery. This score has a high negative predictive value but the positive predictive value is low: only 15 per cent of patients who were classed as high risk actually had increased postoperative bleeding<sup>28</sup>. More recently, the ACTA-PORT score<sup>29</sup> has been demonstrated to be a valid, simple and accurate predictor of the risk of transfusion in patients undergoing cardiac surgery. Components of the score include: age, sex, body surface area, logistic EUROSCORE, preoperative haemoglobin and creatinine levels, and type of surgery. Such scoring systems have the potential to identify modifiable risk factors, quantify risk before surgery, allocate resources (such as cell salvage) and better guide blood service inventory management.

### Managing anticoagulant and antiplatelet therapies

Increasing numbers of patients are continuing antiplatelet (for example, aspirin, clopidogrel) and anticoagulant (such as warfarin, direct oral anticoagulants (DOACs)) therapy into the perioperative phase to reduce the risk of major cardiovascular and thrombotic events. These risks must be balanced against the procedure-related risks of bleeding for an individual patient, and may require discussions with the patient, surgeon, haematologist and anaesthetist. Detailed reviews<sup>30–33</sup> of the pharmacology and perioperative management of these agents can be found elsewhere, but in summary: aspirin can be continued for most procedures; bridging therapy for warfarin should be considered only in patients with the highest risk of thrombosis (for example, those with mechanical heart valves or venous thromboembolism within the previous 3 months); postoperative bridging should not be started until at least 48 h after surgery

with a high bleeding risk; DOACs, owing to their predictable pharmacokinetics, can be stopped 48 h before most operations in the presence of normal hepatic and renal function (*Fig. 2*); adenosine 5'-diphosphate receptor antagonists, such as clopidogrel, should be stopped 5–7 days before operation; and the use of tranexamic acid should be considered in patients undergoing urgent surgery with a high risk of bleeding who are on antiplatelet agents or where a residual anticoagulant effect of DOACs is suspected.

### Surgical strategies

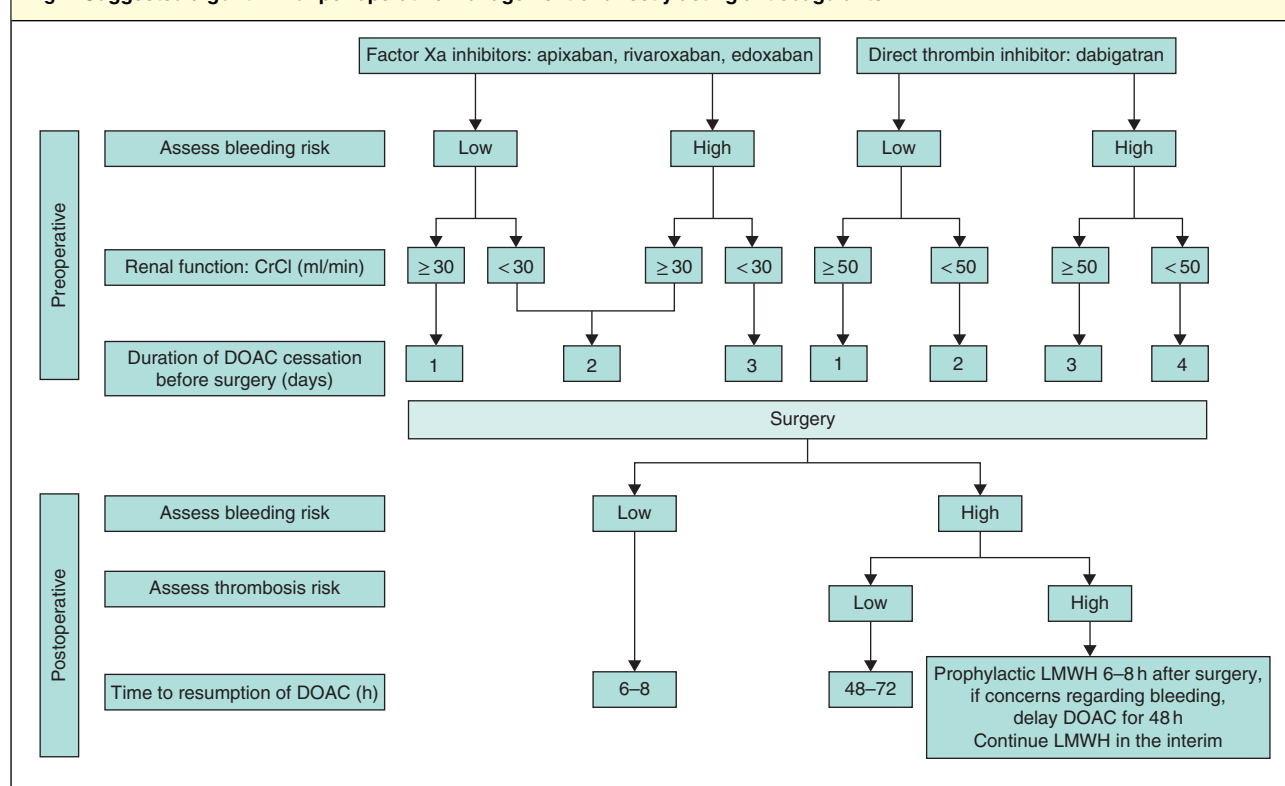
#### Tourniquet

Tourniquets are used widely during limb surgery. Although they reduce intraoperative blood loss, meta-analyses<sup>34,35</sup> of studies suggest that there is no difference in overall blood loss. The release of inflammatory mediators as a result of limb ischaemia may even increase blood loss<sup>36</sup>. 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<sup>37</sup>. Disadvantages of tourniquet use include increased postoperative pain, impaired quadriceps function and increased risk of thrombotic events<sup>34,38,39</sup>.

#### Antifibrinolytics

Antifibrinolytics, such as tranexamic acid, are synthetic lysine analogues that inhibit plasminogen activation and provide clot stabilization. In the UK, tranexamic acid is recommended for all surgery where blood loss is expected to be greater than 500 ml<sup>40,41</sup>. Tranexamic acid is not approved by the US 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<sup>42</sup>.

A number of studies have investigated the safety and efficacy of tranexamic acid, with the majority demonstrating 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 per cent<sup>43</sup> after hip and knee surgery, without increased risk of complications, including thromboembolic events<sup>44</sup>. Considering all surgical procedures, tranexamic acid has been shown to reduce blood loss by approximately one-third<sup>45</sup>. It has been shown specifically to reduce blood loss, and the rate of allogeneic blood transfusions after coronary artery surgery<sup>46</sup>,

**Fig. 2 Suggested algorithm for perioperative management of directly acting anticoagulants**

CrCl, creatinine clearance; DOAC, directly acting anticoagulant; LMWH, low molecular weight heparin.

spinal surgery<sup>47</sup>, orthopaedic fracture surgery<sup>48</sup>, prostate surgery<sup>49</sup>, caesarean section or hysterectomy<sup>50</sup> and plastic surgery procedures<sup>51</sup>.

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 10 to 20 mg/kg. Administration may be repeated during the intraoperative and postoperative phases<sup>41</sup>. Network meta-analyses are under way to determine an optimal dosing regimen to standardize clinical care and guide comparators for future research<sup>52</sup>. Potential advantages of topical delivery are that it may overcome contraindications such as renal disease owing to lower plasma levels<sup>52</sup>. Repeat doses to maintain therapeutic levels may play a greater role in prolonged surgery or where a large volume of blood is lost.

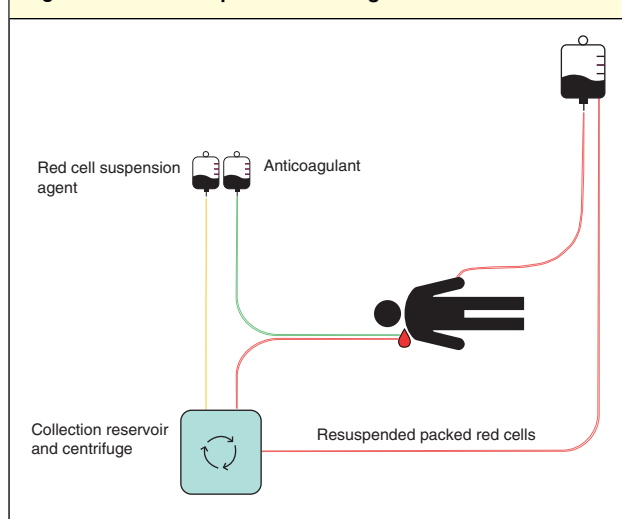
A further uncertainty is whether the risk of thromboembolic events has been adequately addressed in high-risk subgroups, although tranexamic acid was not associated with an increased rate of adverse events in patients undergoing major surgery for malignancy<sup>53</sup>. The favourable

side-effect profile, cost and ready availability of tranexamic acid mean that it should be considered for all surgical procedures where moderate blood loss is anticipated<sup>40</sup>.

## Cell salvage

Cell salvage is a method of recovering blood from the surgical field during the intraoperative or immediate postoperative phase that is then reinfused to the patient (Fig. 3). The National Institute for Health and Care Excellence (NICE)<sup>40</sup> recommends the use of cell salvage for procedures when a very high volume of blood loss is anticipated, which the recent Association of Anaesthetists guidance<sup>54,55</sup> considers to be greater than 500 ml. 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<sup>55</sup>.

Intraoperative blood collection is through a suction system, whereas postoperative blood collection is through surgical drains. Collected blood is anticoagulated and filtered before reinfusion. Blood collected during surgery is typically washed and resuspended in normal saline

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

before reinfusion, whereas blood collected after operation through drains is typically unwashed. Current technology requires approximately 500 ml collected blood to produce a clinically valuable volume of blood for reinfusion after processing<sup>55</sup>. Cell salvage reduces the risk of exposure to allogeneic blood by 54 per cent across all surgical specialties<sup>56,57</sup>.

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 processed for reinfusion only if more than 500 ml 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 revisional knee arthroplasty reliably exceeds 500 ml but, if performed under tourniquet, there is limited intraoperative blood loss<sup>37</sup>. There remain controversies regarding which patients benefit from cell salvage, and it is not currently recommended for routine use during caesarean section<sup>55,58,59</sup>.

Infection and malignancy were traditionally contraindications to cell salvage, but there is increasing evidence to support its use in these settings. With the use of a leucocyte depletion filter (40 µm), there is a 99 per cent reduction in bacterial contamination in blood resuspended in 0.9 per cent saline<sup>60</sup>. The potentially increased risks of bacterial contamination must be weighed against the increased risk of infection through immunomodulation secondary to allogeneic blood transfusion<sup>61</sup>. 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<sup>62</sup>.

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<sup>63</sup>.

## Drains

Surgical-site drains are often used with the aim of reducing haematomas and surgical-site infection. A limited number of robust studies have investigated the effectiveness of drains in preventing postoperative complications, and many did not demonstrate any benefit of drain insertion over no drain<sup>64–67</sup>. In orthopaedic surgery, conventional suction drains can increase postoperative blood loss<sup>68</sup>.

In procedures with continuing postoperative blood loss, there may be a role for 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<sup>69,70</sup>. The value of drains is specific to each procedure. Given the increasing number of studies suggesting that drains do not confer improved clinical outcomes (and may increase blood loss), the use of drains may warrant revisiting where they are currently employed routinely.

## Surgical technique

Surgical developments, including the introduction of laparoscopic and robotic surgery, are driven by a number of outcomes, but they may also reduce blood loss. In a study<sup>71</sup> of transanal mesorectal excision for rectal cancer, operative blood loss was lower with laparoscopic than open operations, and with robotic compared with laparoscopic surgery. Similar findings have been reported in other surgical specialties<sup>72–75</sup>.

## 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, suggested to result in less damage to adjacent healthy tissue. There is limited evidence that they reduce blood loss<sup>76</sup> 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 oxidized cellulose may be applied to bleeding tissues during surgery



as a haemostatic strategy. However, these agents are expensive and, despite numerous studies across different surgical specialties, there is only weak evidence to suggest that they offer a clinically important reduction in blood loss<sup>77,78</sup>.

## Anaesthetic strategies

### Permissive hypotension

Permissive hypotension consists of using pharmacological agents to lower intraoperative mean arterial BP to values between 50 and 65 mmHg to reduce blood flow to the surgical field. The intention is to reduce blood loss, while also improving visibility in the surgical field. This has to be balanced against the risks of organ hypoperfusion, such as delayed awakening, permanent cerebral damage, myocardial and kidney injury, and death<sup>79</sup>. Therefore, this technique should be avoided in patients with coronary artery disease, poorly controlled hypotension or cerebrovascular disease.

Permissive hypotension can be achieved through a reduction in cardiac output, BP or a combination of these, depending on the method used. Techniques, some of which will be discussed in this review, include patient positioning, central neuraxial anaesthesia, intravenous anaesthetics (such as propofol), opioids (remifentanyl), directly acting vasodilators (nitroglycerine), selective beta-blockers (esmolol), selective  $\alpha$ -blocker (dexmedetomidine), combined  $\alpha$ - and beta-blocker (labetalol) and volatile anaesthetics (sevoflurane). Systematic reviews and RCTs<sup>80–83</sup> have demonstrated that permissive hypotension reduces blood loss in patients undergoing orthopaedic, maxillofacial, spinal and radical prostatectomy surgery. This translated into a reduction in transfusion requirements only in orthopaedic surgery. However, all of the included studies were small, of 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 monitored closely to ensure adequate organ perfusion.

### Central neuraxial anaesthesia

Anaesthetic techniques play an important role in minimizing intraoperative blood loss. Central neuraxial blockade (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 attenuation of the surgical stress

response, which in turn is associated with stabilization of clotting factors and reduced fibrinolysis<sup>84,85</sup>.

Early meta-analyses<sup>86,87</sup> of RCTs, 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 intraoperative blood loss and allogeneic red blood cell transfusion requirements. However, more recent meta-analyses<sup>88,89</sup> have demonstrated no difference in blood loss or red blood cell requirements. 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 (for example 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<sup>90</sup>. Changes to intra-abdominal pressure may also be associated with blood loss<sup>91</sup>. In the supine position, the patient may be slightly tilted 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<sup>92</sup> and hip arthroplasty<sup>93</sup> 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 below 36°C, can result from many factors such as low operating theatre temperatures, evaporation from body cavities, use of cold intravenous fluids and anaesthetic gases, reduced metabolic activity, and loss of thermal regulation and responses owing to anaesthesia (such as shivering). Patients at risk of developing hypothermia include those at extremes of age, undergoing combined regional and general anaesthesia, major surgery, prolonged surgery and with higher ASA fitness grade.

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 recognized<sup>94,95</sup>. Even mild hypothermia has been associated with an increase in blood loss of 16 per cent, and increase in relative risk of red blood cell transfusion by 22 per cent<sup>96,97</sup>. In addition, hypothermia can also lead to increased rates of wound infection<sup>98</sup> and cardiovascular events<sup>99</sup>, and prolonged recovery<sup>100</sup>. As a result, NICE<sup>101</sup> has issued guidance on the prevention and management of hypothermia in patients undergoing surgery. Examples of strategies used to avoid intraoperative cooling include regular temperature monitoring every 30 min, ensuring that the ambient theatre temperature is at least 21°C, using active forced air warming devices and administering intravenous fluids through a fluid warmer.

## Ventilation strategies

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

A recent secondary analysis, of a previously published trial<sup>103</sup> comparing the effect of a lung-protective strategy in patients undergoing major abdominal surgery, evaluated the effect of PEEP between 6 and 8 cmH<sub>2</sub>O *versus* zero PEEP in patients undergoing hepatic resection surgery<sup>104</sup>. The authors found that using PEEP, compared with a zero PEEP strategy, was not associated with increased bleeding.

## Haemostatic strategies

### Desmopressin

Desmopressin is a synthetic analogue of the naturally occurring antidiuretic hormone vasopressin. It causes a transient rise in plasma levels of 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<sup>105</sup>. It can be given subcutaneously or intravenously at a dose of 0.3 µg/kg. Safety considerations include the risk of developing arterial or venous thrombosis 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<sup>106</sup> recommend administration of desmopressin to patients on antiplatelet agents. In the perioperative setting, guidelines<sup>107,108</sup> suggest using desmopressin where there is demonstrable evidence of acquired platelet dysfunction secondary to drugs, uraemia or cardiopulmonary bypass.

However, the evidence for the ability of desmopressin to reduce perioperative transfusion requirements and blood loss is weak. A recent Cochrane review<sup>109</sup> of 65 trials with 3874 participants undergoing surgery found no overall benefit from desmopressin. 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 antiplatelet therapy<sup>110</sup>.

### 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<sup>111,112</sup>. 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 do 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 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<sup>113</sup>. Conversely, single procoagulant factors are also available, most notably fibrinogen concentrate. As with desmopressin, these agents have the potential to increase the rates of thrombotic events. This has been shown clearly in clinical trials of recombinant factor VIIa in unselected patients<sup>114</sup>.

Fibrinogen depletion, secondary to haemodilution and/or consumption, is thought to occur before deficiencies of other coagulation factors become apparent during haemorrhage<sup>115</sup>. Hypofibrinogenaemia is a risk factor for haemorrhage in orthopaedic surgery<sup>116</sup>, cardiac surgery<sup>117</sup> and trauma<sup>115</sup>. In obstetric haemorrhage, a fibrinogen level below 2 g/l has a 100 per cent predictive value for progression from moderate to severe haemorrhage<sup>118</sup>. Fibrinogen concentrate is currently not licensed for acquired hypofibrinogenaemia in the UK, but is used widely in Europe. UK guidelines<sup>119</sup> recommend use of cryoprecipitate as the source of fibrinogen. However, off-label use has

**Table 2 Clinical practice points and research agenda for minimizing intraoperative blood loss**

Clinical practice points	A multimodal strategy should be implemented to minimize intraoperative bleeding in surgical patients
	Preoperative assessment with review and management of preoperative anaemia, and antiplatelet and anticoagulant therapy
	Prophylactic tranexamic administration should be considered for all patients undergoing major cardiac and orthopaedic surgery
	Use of cell salvage and viscoelastic haemostatic assays should be considered in all cases where anticipated blood loss is > 500 ml
	Avoid hypothermia, acidosis and excessive haemodilution.
Research agenda	Close collaboration between anaesthetists, surgeons and haematology is vital
	Cost-effectiveness of viscoelastic haemostatic assays in the management of perioperative bleeding
	Safety and efficacy of haemostatic therapies such as procoagulant factors and desmopressin.
	Optimal dose, route and timing of tranexamic acid

been reported, with small studies showing reduced red cell and fresh frozen plasma transfusion requirements<sup>120</sup>.

Despite the physiological promise of procoagulant factors, high-quality data to guide safe and effective use are lacking. A recent systematic review<sup>121</sup> was unable to draw any conclusions owing to a paucity of data. 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 haemostatic 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 turnaround time of up to 77 min, which is not useful in a rapidly evolving situation<sup>122</sup>.

In brief, TEG and ROTEM measure the physical properties of clot formation in whole blood via a pin suspended in a cup heated to 37°C. The pin is connected to a torsion wire, which is 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 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<sup>123</sup> of assay machine mechanics, quality assurance and test accuracy can be found elsewhere.

Current NICE guidelines recommend the use of these assays only in patients undergoing cardiac and liver surgery, where robust cost-effectiveness data exist to support their use<sup>124</sup>. 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<sup>123,125,126</sup>.

### Conclusion

The potential for major intraoperative blood loss remains a key concern for surgeons and anaesthetists. Strategies to mitigate this, such as identification and management of high-risk patients, can be implemented early in the preoperative phase. During surgery, 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 and timing of administration remain 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.

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