Operative Techniques in
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Multimodal Perioperative Blood Management for Spinal Surgery

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Blood loss remains a major consideration in all spinal surgery. With increasing rates of complex spinal deformity surgery in North America combined with mounting evidence for the association of adverse outcomes with allogenic blood transfusion, there has been a renewed emphasis on transfusion prevention and alternative blood management protocols. Blood management begins with preoperative evaluation and treatment of preoperative anemia. Antiplatelet and anticoagulants must be optimized prior to surgery; a plan for thrombosis prevention and prophylaxis must be in place during the perioperative period. Intraoperative adjuncts such as tranexamic acid should be used unless contraindications exist. Addressing blood loss during the procedure and minimizing ongoing losses in the immediate post-op period remains the domain of the surgical team and is essential in minimizing allogenic blood transfusion.
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Introduction

Blood loss remains a major consideration in spine surgery.[1] Due to the increasing evidence for the association of adverse outcomes with allogenic blood transfusion, there has been a shift toward transfusion prevention and alternatives.[2] The World Health Organization (WHO) emphasized the importance of using transfusion alternatives and implementing individualized patient blood management to reduce blood transfusion needs.[3] The 3 pillars of patient blood management are (1) detection and treatment of preoperative anemia, (2) minimizing perioperative blood loss, and (3) harnessing and optimizing the patient-specific physiological tolerance of anemia.[4-8] The purpose of this review is to discuss these pillars focusing on the perioperative blood management of patients undergoing spine surgery.

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Preoperative Evaluation

Patient Evaluation

Preoperative evaluation involves obtaining a complete history to identify any risk factors predisposing a patient for requiring blood transfusion or its alternatives. This is done through review of the patient's chart, taking a full history from the patient or a family member, and reviewing laboratory tests.[9,10] A thorough review of medical records and obtaining a detailed history can help identify the need for previous transfusion, history of thrombotic events, history of drug induced or congenital coagulopathies, and risk of organ ischemia.[9] Some studies have shown an association between some congenital or acquired hematologic conditions with blood transfusion complications.[11-13] Identifying patients with risk factors can help predict the requirement of transfusions and guide the risk/benefit discussion with the patient in the preoperative assessment.

Detection and Treatment of Preoperative Anemia

The prevalence of preoperative anemia (hemoglobin equal to or less than 12 g/dL in women and equal to or less than 13 g/dL in men) among patients undergoing orthopaedic

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procedures is estimated to be between 20% and 50%.[14] Preoperative anemia is a strong predictor of perioperative blood transfusion which carries a significant risk of adverse events.[15] Furthermore, the cause of anemia in up to 33% of these patients is iron deficiency.[16] Ideally, patients undergoing major spine surgery should be tested for anemia months before surgery in order to maximize the effectiveness of any attempted treatment. Optimizing red blood cell (RBC) mass preoperatively has been associated with improved outcomes after 90 days in patients undergoing hip and knee surgery.[17] Our institution is currently attempting similar efforts in all major spine procedures.

The implementation of a patient blood management program has been shown to reduce the rate of preoperative anemia and blood transfusion.[18] Assessment of patients as little as 3-8 weeks preoperatively can provide enough time for treatment to take effect.[19,20] If iron deficiency anemia is diagnosed, initiating iron supplementation to correct iron levels prior to surgery is recommended.[19,20] Oral iron supplementation is well tolerated by a majority of patients with minimal side effects.[21] However, Lin et al conducted a systematic review and concluded that patients with preoperative anemia may have a quicker and more robust recovery in hemoglobin with intravenous iron supplementation when compared with oral iron supplementation.[22]

When other causes of anemia have been either excluded or treated, but decreased hemoglobin levels remain, erythropoietin-stimulating agents are recommended. In hip and knee surgery, the use of preoperative erythropoietin-stimulating agents has been reported to significantly reduce autologous transfusion and increase hemoglobin levels compared to control groups.[23]

In our institution, patients scheduled for elective spine surgery are evaluated within 9 months of surgery for anemia and other risks. Once a patient is diagnosed with anemia, further investigations are ordered to identify the etiology. If iron deficiency is identified as the underlying pathology, therapy with oral iron 150 mg/d, folic acid 2 mg/d, vitamin C 500 mg/d, and vitamin B12 1000 mcg/d are initiated. Patients are then referred to the patient blood management program for follow-up blood work, to arrange for intravenous iron and erythropoietin-stimulating agents as necessary, and for consideration toward delaying surgery until anemia is corrected. Erythropoietin-stimulating agents are avoided in patients with a history of thrombotic events (deep vein thrombosis, pulmonary embolism).

Managing Antiplatelet Agents and Anticoagulants

Low platelets, low fibrinogen concentration, and factor XIII deficiency are predictive of bleeding complications in major spine surgery.[10] The current literature is insufficient to evaluate the benefit of stopping aspirin preoperatively.[9] However, 2 randomized controlled trials have shown equivocal results for perioperative blood loss, rate of transfusion, or postoperative adverse events (eg, myocardial infarction, major bleeding, or death) when comparing aspirin with placebo when administered preoperatively.[24,25] If withholding aspirin preoperatively, there is a strong recommendation, albeit with low-quality evidence, for interruption 3 days prior to the planned procedure.[10] When aspirin is stopped preoperatively, it should be resumed as soon as possible postoperatively, given the increased risk of thrombotic events.[10]

With regards to P2Y12 inhibitors (clopidogrel, prasugrel, and ticagrelor), it is recommended to hold ticagrelor and clopidogrel for at least 5 days and prasugrel for at least 7 days before any planned procedure.[10,26] Patients with new-generation coronary stent implants are usually placed on dual antiplatelet therapy for 3-6 months.[27,28] It is recommended to delay any elective surgery until dual antiplatelet therapy is completed and if possible, perform surgery without the discontinuation of aspirin.[29]

Vitamin K antagonists (VKA) such as warfarin are not an uncommon anticoagulant encountered in patients undergoing surgery. In order to determine a perioperative anticoagulation plan, each patient should be assessed by specialists and risk stratified for their thrombotic risk and surgical related bleeding risk.[30] In patients undergoing major spine surgery with low to moderate risk of a thrombotic event, it is recommended to stop VKA 5 days prior to surgery with no bridging needed.[10,30] Patients with high risk of thrombotic events should be bridged with low molecular weight heparin (LMWH) with the last dose given 24 hours prior to surgery.[10,31] In patients with low risk of bleeding, it is recommended to resume VKA the night of or the day after surgery concomitant with LMWH until the target INR is reached.[10] In patients with moderate to high risk of bleeding, it is recommended to give a prophylactic dose of LMWH or unfractionated heparin the evening of the procedure for 48-72 hours then resume therapeutic LMWH and VKA until the target INR is achieved and then discontinue the LMWH.[10]

Other anticoagulants encountered include direct oral anticoagulants, including Rivaroxaban, Apixaban, and Edoxaban. The European Society of Anesthesiology strongly recommends (with low-quality evidence) to stop these direct anticoagulants 2 days before an intervention with moderate to high risk of bleeding.[10,32] Furthermore, they recommend stopping Dabigatran 3 days before surgery without the need for any bridging.[10,32,33]

Management of Intraoperative Blood Loss

Intraoperatively, the anesthetist plays a vital role in minimizing perioperative blood loss. Apart from meticulous surgical technique, successful management of blood loss during spine surgery involves several components: establishing peripheral or central access for fluid management, careful attention to monitoring and measuring volume changes, blood conservation strategies, and safe delivery to the appropriate level of postoperative care.

Peripheral and Central Venous Access

Obtaining venous access can often be difficult in the supine position, with the level of difficulty increasing dramatically with a patient in the lateral, or prone position. It is advisable to place all lines necessary to accommodate any and all perioperative needs prior to finalizing patient positioning. The use of peripheral vs central access is determined by several factors: ease and quality of available peripheral access, the type and length of surgery, expected blood loss, anticipated fluid requirements and shifts, and potential need for pressor support.

Central lines are valuable for both access and monitoring. Indications for placement may include patients with peripheral vascular disease, ischemic heart disease, congestive heart failure, severe valvular disease, symptomatic dysrhythmia, metabolic disorders, or the need for prolonged postoperative access. Unfortunately, central venous pressure, as measured through a central line, is not a validated measure in the prone position and may not accurately predict fluid responsiveness.[34,35]

Whether central or peripheral vascular access is desired, both expose the patient to risk, as noted in the Closed Claims Project (USA) and NAP4 study (UK). Complications related to peripheral venous access include fluid extravasation, drug extravasation, scarring, peripheral nerve injuries, and compartment syndrome. Central line insertion carries the risk of wire embolization, pneumo/hemothorax, carotid artery injury, stroke, nerve injury, cardiac injury, and death. While the incidence of major complications is very low, the use of central and peripheral access should remain purposeful.

Monitoring

Monitoring of blood pressure, and indirectly perfusion of the spinal cord, is mandatory in avoiding nerve, end organ, or spinal cord ischemia. In addition to the standard monitors of pulse oximetry, noninvasive blood pressure monitors, and ECG, arterial access is frequently used for beat-to-beat blood pressure monitoring (stroke volume variation or SVV) as well as to draw labs in longer cases. The noninvasive blood pressure cuff running every 5 minutes can result in muscle pain, skin bruising, peripheral nerve injury, and compartment syndrome.[36] Prolonged surgery should itself be considered an indication for placement of an arterial line. Other indications for invasive monitoring include cases of deliberately induced hypotension, prolonged surgical procedures, anticipated heavy blood loss, significant cardiopulmonary or renal disease, or when single lung ventilation is required.

Waveform analyses of arterial line tracings have been employed to determine characteristics of cardiac function and optimal fluid management. By measuring the change in mean arterial pressure (MAP) through SVV, it is possible to estimate a patient's fluid responsiveness. Caution with respect to interpretation should be exercised in the prone position due to the associated change in pressurization of the abdominal and thoracic cavities. Although SVV is still in the process of being validated for the prone position,[37] these measures can at the least provide a trend, which in turn can serve as an indication of responsiveness to interventions undertaken.

Arterial lines do pose a risk of radial nerve injury, arterial wall injury or dissection, and hand ischemia in the case of single artery perfusion of the palmar arch. Performing an Allen's test prior to cannulation and the use of ultrasound for placement are advised. In the hands of a skilled anesthesiologist, the rate of complications is low. In a large retrospective study, only 21 patients out of 62,626 (7.8:10,000) who underwent radial artery catherization in the operating room suffered from a complication.[38]

Hemodynamic Goals

Blood pressure goals for spine surgery are debatable; permissive hypotension may decrease surgical bleeding but can cause ischemic damage to sensitive organs such as the brain, spinal cord tissue, myocardium, and optic nerves.[39] Although permissive hypotension has been validated in the pediatric population, these studies are not considered widely generalizable in adult patients.[40]

Hypotension decreases physiologic reserves and puts patients at higher risk of cardiac arrest should significant surgical bleeding or tension pneumothorax occur.[41] Even relative hypotension should generally be avoided in patients with risk factors for developing intraoperative cardiac ischemia such as existing coronary artery disease, advanced age, diabetes, atherosclerosis, and longstanding history of hypertension.[41]

Hypertension is an independent predictor of cardiac adverse events in noncardiac surgery.[42] Intraoperative hypotension on the other hand is one of the most encountered factors associated with deaths related to anesthesia.[43] Guidelines advanced by multiple anesthesiology groups including the American Society of Anesthesiologists Task Force on Perioperative Visual Loss, the North American Neuro-Ophthalmology Society, and the Society for Neuroscience in Anesthesiology and Critical Care strongly state that deliberate hypotension should be a multidisciplinary decision and that it should be reserved for essential cases only.[44] Patients with pre-existing hypertension should maintain an intraoperative MAP within 25% of baseline. In the setting of acute hypertension, the treatment goal is to decrease blood pressure by no more than 25%.[45]

Hypertension may be beneficial in reducing secondary injury in traumatic spine injuries. Areas of injury experience a focal loss of autoregulation. In his article, Hadley recommended a MAP at 85 or greater.[46] In a multivariate analysis of risk factors for perioperative complications in men who underwent noncardiac surgery, the presence of preoperative hypertension increased the odds ratio for postoperative death to 3.8 times that of normotensives.[42]

Fluid goals are a balance between supporting intravascular volume, ensuring adequate tissue oxygenation and perfusion to organs, and preventing fluid overload. During prolonged surgery in the prone position, dependent areas such as the head, neck, and face can become overly edematous, causing potential airway obstruction if postoperative extubation is performed, and can necessitate a prolonged course of mechanical ventilation through a protected airway. It is necessary to strike a delicate balance between hypotension to minimize blood loss and hypertension for maintaining tissue oxygenation.

Hemostasis and Coagulation

Significant intraoperative blood loss is a concern in major spine surgery. Although many patient and surgical factors contribute to the amount of blood lost, one systematic review reports an average blood loss of 650-2839 mL during spine fusion.[47] In concert with the high prevalence of preoperative anemia, patients undergoing spinal fusion are at high risk of requiring allogenic blood transfusions. Indeed, 50%-81% of patients undergoing spine fusion require a transfusion.[47] Mitigating the hazards of allogenic blood transfusions include using a fluid warmer for packed red blood cells and plasma, avoiding dilutional coagulopathy by monitoring and replacing blood products in appropriate ratios, and replacing calcium to counteract citrate used in the preservation of blood products.

Factors that increase risk of blood loss include a higher BMI, advanced age, pre-existing bleeding diathesis, higher number of spinal levels operated on, and increased intra-abdominal pressure.[48] Meticulous surgical technique, an experienced surgeon, and staged procedures can reduce surgical bleeding. Medical management of bleeding and the avoidance of physiological factors that increase bleeding can significantly reduce intraoperative blood loss. Even mild hypothermia can induce a coagulopathy and worsen bleeding; a reduction of 1°C can increase bleeding by 16% and increase the risk of blood transfusions by 22%.[49,50]

Transmitted pressures from the abdominal and thoracic cavities can increase vena cava pressures, causing venous engorgement and increased bleeding. Careful positioning can prevent unnecessary abdominal and thoracic compression and reduce blood loss.[51] Modes of ventilation can affect intrathoracic pressures and bleeding in spine surgeries. Kang et al demonstrated that pressure control ventilation reduces bleeding when compared to volume control ventilation in posterior lumbar interbody fusion operations due to the ability to deliver the same ventilatory volume with less pressure.[52]

Antifibrinolytic agents, such as aprotinin, aminocaproic acid, and tranexamic acid (TXA), prevent the lysis of clots and thereby reduce intraoperative bleeding. This class of drug has been increasingly used in operations with a high risk of bleeding. TXA has been shown to be safe in multiple studies and does not produce complications related to hypercoagulability. In spine surgery, TXA has been well studied in the pediatric population but optimal dosing has yet to be established in adults. Although no protocols have been established, doses as low as 1 mg/kg/h exhibit hemostatic benefits.[53] Multiple studies that vary in the loading dose (0-100 mg/kg) and infusion rates (1-2 mg/kg/h) all show less blood loss and seem to require less blood transfusions when compared to placebo.[54-56] Aminocaproic acid, an older agent, is more costly than TXA and does not provide superior outcomes.[57]

Monitoring for Coagulopathy

The etiology of intraoperative coagulopathy is most frequently either a consumptive or dilutional process. Monitoring the function of the coagulation system and maintaining its homeostasis will avoid unnecessary blood loss and help prevent disseminated intravascular coagulation.

Several institutional policies around the monitoring of coagulopathy and blood loss have been shown to be effective in guiding intraoperative resuscitation. The protocol published by Halpin et al includes a recommendation for complete blood count, PT, PTT, fibrinogen, and calcium drawn every 2 hours for the first 6 hours and then every 1 hour after that and provided guidelines for temperature management, blood product management, and positioning.[58] A follow-up retrospective study by Zeeni et al showed that adhering to the protocol resulted in a statistically significant savings of 1 unit of packed red blood cells and 1.1 units of total red blood cells compared to lab work based on the attending anesthesiologist's discretion.[59]

New point of care coagulation testing will likely change the paradigm of resuscitation with blood products. Rotem and thromboelastography are based on the formation of a clot and the resistance it generates in a rotating pin-cup apparatus. These technologies can diagnose issues within the coagulation process (platelet adhesion, clot stability, and fibrinolysis) and allow the anesthesiology team to tailor blood products specific to the requirements of the patient.[60] Naik et al demonstrated that the use of this technology decreased the amount of blood products required during a major spine surgery.[61]

Replacement

The mainstay of treatment for surgical bleeding is the transfusion of blood products. Due to its ability to replenish the oxygen-carrying capacity and increase the factors required for coagulation in a correct balance, the transfusion of whole blood is thought to be best.[62] Unfortunately, whole blood is not readily available due to storage issues. By providing a balanced ratio of packed RBC, fresh frozen plasma, and platelets, it is possible to mimic whole blood and prevent dilutional coagulopathies. Ratios beside the commonly used 1:1:1 have been discussed in the literature but have not been found to be superior.[63] As point-of-care testing for hemostasis becomes more prevalent, anesthesiologists will be able to address the specific defects and replace the required factors, thereby reducing the amount of blood products required.[61]

The threshold for transfusion of RBC has been studied extensively. The TRICC trial, a multicenter ICU study, established a hemoglobin threshold of 70 g/L. This guideline is frequently employed across multiple clinical settings.[64] However, 70 g/L as a threshold for transfusion should be used cautiously in the setting of major spine surgery. The tissues of the spinal cord may be more sensitive to hypoxia than previously suspected. Studies in mice show that neural tissue undergoes hypoxic changes at a hemoglobin level as low as 89 g/L.[65] Other complications from lower hemoglobin include higher rates of postoperative delirium.[66] Using a restrictive hemoglobin transfusion threshold of 100 g/L intraoperatively and 80 g/L postoperatively has been linked to lower mortality rates, shorter hospital stay, lower infection rate, lower thrombotic events, and lower rates of organ ischemia.[67]

Acute normovolemic hemodilution (ANH) is a technique where whole blood is taken from the patient prior to the initial incision. The volume that is drawn off and stored is then replaced with crystalloid to maintain a normal intravascular volume. As bleeding occurs, the patient's own blood can be transfused back during the operation. This technique reduces the viscosity of the blood, thereby increasing flow through terminal capillaries and includes a mild hypercoagulable state.[68] It has been found to decrease the percentage of patients requiring autologous blood transfusion in major spine surgeries.[69] While this technique has benefits, ANH should only be used in appropriately selected patients.[70] Patients should have an initial hemoglobin above 120 g/L, be free of any coronary, pulmonary, renal disease, liver disease, or severe hypertension and should not have an active infection. Despite its benefits, studies have found that ANH is often a costly intervention and that the stored blood is often not used.[39]

Intraoperative blood salvaging is a technique where blood lost intraoperatively is recovered and transfused back to the patient. This technique requires specialized equipment that collects lost blood, mixes it with an anticoagulant, and finally washes and concentrates the blood. The processed blood is then transfusion back into the patient at a hematocrit approaching 60%. Due to the anticoagulation process, an induced coagulopathy from residual anticoagulant used during the salvaging process can occur and appropriate hemostatic monitoring should be used. Intraoperative blood salvaging is acceptable in the use of major spine surgeries and is most cost effective when blood loss is expected to be greater than 2000 mL.[71,72] A recent Cochrane review demonstrated that cell salvage is effective in spine procedures and reduces transfusion rate.[73] In fact, the review shows that cell salvage can reduce transfusion rates by 39%.[73] However, another study demonstrated that cell salvage in lumbar spine surgery was associated with increased blood loss and adds controversy to the effectiveness of cell salvage techniques.[74] Others voice concern about using cell salvage in patients with infection or cancer to avoid spreading disease. A more recent study has shown that cell salvage can reduce transfusion without decreased long-term survival in patients with metastatic disease undergoing spine surgery.[75] Therefore, the role of cell salvage can become useful in decreasing transfusion rates after spine surgery. Due to the high associated cost, intraoperative blood salvaging is not effective in single-level spine surgeries and does not alter the number of blood products required in these cases.[76]

Optimizing Patient-Specific Physiological Tolerance of Anemia Postoperatively

Complex spine surgery and blood management go hand in hand. With average blood loss values as high as 1.5 L in complex spine surgery reported in the literature,[77] strategies to minimize this loss and optimize patients' postoperative need for transfusion become very important. This optimization can also help decrease the requirements for blood transfusion postoperatively. Any reduction in postoperative blood transfusion rate helps to decrease both cost and complications associated with postoperative care, as transfusion has been associated with such complications as increased risk of wound infection and increased length of stay in hospital.[78]

The need for postoperative blood transfusion may still persist, despite preoperative correction of anemia.[49] The ideal indications for postoperative transfusion therefore become difficult to determine. In fact, de Araujo et al[79] showed that severe anemia in Jehovah's witness patients, as low as 1.4 g/dL, can recover without complications, without the need for blood transfusion. Although these cases demonstrate extreme instances, restrictive transfusion triggers can be adequate and even beneficial.[49] Lower transfusion triggers can help limit transfusion rate without affecting patient outcomes. In addition, some animal trials showed that anemia tolerance changes for different organs and showed that major organs can tolerate hemoglobin levels as low as 4 g/dL.[80] Thus, although studies show that lower hemoglobin level can be well tolerated, the optimal threshold for transfusion is difficult to determine from the literature. Our institution does not set a fixed threshold for postoperative transfusion. Transfusion is recommended on a symptomatic basis, and in the absence of active bleeding, restricted to a single unit of packed RBC prior to clinical reassessment.

Perioperative fluid therapy regimens have been proposed in the literature to improve patient outcomes and limit blood transfusion rate. The regimens presented in the literature do not qualify as general recommendations according to the European Society of Anaesthesiology, given the limited power of the studies and limited generalizability of the results.[10] Goal-directed fluid therapy has however been demonstrated in recent meta analyses[81-83] to show benefit in maintaining tissue perfusion based on hemodynamic monitoring, especially in complex patient scenarios, avoiding some major postoperative complications. The role of goal-directed therapy in spine surgery may be important and can potentially help decrease the need for postoperative transfusion.

Autologous predonation has been widely investigated to determine if it is effective in decreasing the need for postoperative blood transfusion. Recent studies have shown no benefit in predonation with respect to blood loss and transfusion requirements.[84] Therefore, this technique has been abandoned in the majority of centers due to its lack of postoperative benefits.

Conclusion

Appropriate perioperative blood management requires a multidisciplinary approach. Preoperative optimization, including treatment of iron deficiency anemia is crucial to decreasing the requirement for transfusion. Intraoperative management guidelines exist to minimize the complications associated with transfusion and help mitigate intraoperative blood loss. Appropriate ratios of blood product replacement, maintenance of patient temperature, and optimization of hemostasis and coagulation can all improve patient outcomes. Careful attention to specific patient needs postoperatively is likely indicated over specific transfusion thresholds.

References

1. Hu SS: Blood loss in adult spinal surgery. Eur Spine J 13(Suppl 1):S3-S5, 2004. https://doi.org/10.1007/s00586-004-0753-x
2. Blumberg N: Deleterious clinical effects of transfusion immunomodulation: Proven beyond a reasonable doubt. Transfusion 45:33S-39S, 2005; discussion 39S-40S. https://doi.org/10.1111/j.1537-2995.2005.00529.x
3. World Health Organization (2010) Availability, safety and quality of blood products. www.who.int/bloodsafety/resolutions/en/
4. Carson JL, Carless PA, Hebert PC: Transfusion thresholds and other strategies for guiding allogeneic red blood cell transfusion. Cochrane Database Syst Rev 10:CD002042, 2012. https://doi.org/10.1002/14651858.CD002042.pub3
5. Goodnough LT, Shander A: Patient blood management. Anesthesiology 116:1367-1376, 2012. https://doi.org/10.1097/ALN.0b013e318254d1a3
6. Shander A, Hofmann A, Isbister J, et al: Patient blood management—The new frontier. Best Pract Res Clin Anaesthesiol 27:5-10, 2013. https://doi.org/10.1016/j.bpa.2013.01.001
7. Spahn DR, Goodnough LT: Alternatives to blood transfusion. Lancet 381:1855-1865, 2013. https://doi.org/10.1016/S0140-6736(13)60808-9
8. Williamson LM, Devine DV: Challenges in the management of the blood supply. Lancet 381:1866-1875, 2013. https://doi.org/10.1016/S0140-6736(13)60631-5
9. American Society of Anesthesiologists Task Force on Perioperative Blood Management: Practice guidelines for perioperative blood management: An updated report by the American Society of Anesthesiologists Task Force on Perioperative Blood Management. Anesthesiology 122:241-275, 2015. https://doi.org/10.1097/ALN.0000000000000463
10. Kozek-Langenecker SA, Ahmed AB, Afshari A, et al: Management of severe perioperative bleeding: Guidelines from the European Society of Anaesthesiology: First update 2016. Eur J Anaesthesiol 34:332-395, 2017. https://doi.org/10.1097/EJA.0000000000000630
11. Bocchieri KA, Scheinerman SJ, Graver LM: Exchange transfusion before cardiopulmonary bypass in sickle cell disease. Ann Thorac Surg 90:323-324, 2010
12. Cash KL, Brown T, Sausais L, et al: Severe delayed hemolytic transfusion reaction secondary to anti-At(a). Transfusion 39:834-837, 1999
13. Gerrah R, Shargal Y, Elami A: Impaired oxygenation and increased hemolysis after cardiopulmonary bypass in patients with glucose-6-phosphate dehydrogenase deficiency. Ann Thorac Surg 76:523-527, 2003. https://doi.org/10.1016/s0003-4975(03)00351-5
14. Kendoff D, Tomeczkowski J, Fritze J, et al: Preoperative anemia in orthopedic surgery: Clinical impact, diagnostics and treatment. Der Orthopade 40:1018-1020, 1023-1015, 1027-1018, 2011. https://doi.org/10.1007/s00132-011-1789-3
15. Schiergens TS, Rentsch M, Kasparek MS, et al: Impact of perioperative allogeneic red blood cell transfusion on recurrence and overall survival after resection of colorectal liver metastases. Dis Colon Rectum 58:74-82, 2015
16. Theusinger OM, Leyvraz PF, Schanz U, et al: Treatment of iron deficiency anemia in orthopedic surgery with intravenous iron: Efficacy and limits: A prospective study. Anesthesiology 107:923-927, 2007. https://doi.org/10.1097/01.anes.0000291441.10704.82
17. Kotze A, Carter LA, Scally AJ: Effect of a patient blood management programme on preoperative anaemia, transfusion rate, and outcome after primary hip or knee arthroplasty: A quality improvement cycle. Br J Anaesth 108:943-952, 2012. https://doi.org/10.1093/bja/aes135
18. Theusinger OM, Kind SL, Seifert B: Patient blood management in orthopaedic surgery: A four-year follow-up of transfusion requirements and blood loss from 2008 to 2011 at the Balgrist University Hospital in Zurich, Switzerland. Blood Transfusion 12:195, 2014
19. Bisbe E, Muñoz M: Management of preoperative anemia: The NATA consensus statements. ISBT Sci Series 7:283-287, 2012
20. Bruce W, Campbell D, Daly D, et al: Practical recommendations for patient blood management and the reduction of perioperative transfusion in joint replacement surgery. ANZ J Surg 83:222-229, 2013. https://doi.org/10.1111/ans.12000
21. Gurusamy KS, Nagendran M, Broadhurst JF, et al: Iron therapy in anaemic adults without chronic kidney disease. Cochrane Database Syst Rev (12):6-37, 2014
22. Lin DM, Lin ES, Tran MH: Efficacy and safety of erythropoietin and intravenous iron in perioperative blood management: A systematic review. Transfus Med Rev 27:221-234, 2013. https://doi.org/10.1016/j.tmrv.2013.09.001
23. Alsaleh K, Alotaibi GS, Almodaimegh HS, et al: The use of preoperative erythropoiesis-stimulating agents (ESAs) in patients who underwent knee or hip arthroplasty: A meta-analysis of randomized clinical trials. J Arthroplasty 28:1463-1472, 2013
24. Devereaux PJ, Mrkobrada M, Sessler DI, et al: Aspirin in patients undergoing noncardiac surgery. N Engl J Med 370:1494-1503, 2014. https://doi.org/10.1056/NEJMoa1401105
25. Oscarsson A, Gupta A, Fredrikson M, et al: To continue or discontinue aspirin in the perioperative period: A randomized, controlled clinical trial. Br J Anaesth 104:305-312, 2010. https://doi.org/10.1093/bja/aeq003
26. Price MJ, Walder JS, Baker BA, et al: Recovery of platelet function after discontinuation of prasugrel or clopidogrel maintenance dosing in aspirin-treated patients with stable coronary disease: The recovery trial. J Am Coll Cardiol 59:2338-2343, 2012
27. Baber U, Mehran R, Sharma SK, et al: Impact of the everolimus-eluting stent on stent thrombosis: A meta-analysis of 13 randomized trials. J Am Coll Cardiol 58:1569-1577, 2011. https://doi.org/10.1016/j.jacc.2011.06.049
28. Feres F, Costa RA, Abizaid A, et al: Three vs twelve months of dual antiplatelet therapy after zotarolimus-eluting stents: The OPTIMIZE randomized trial. JAMA 310:2510-2522, 2013. https://doi.org/10.1001/jama.2013.282183
29. Members ATF, Kristensen SD, Knuuti J, et al: 2014 ESC/ESA Guidelines on non-cardiac surgery: Cardiovascular assessment and management: The Joint Task Force on non-cardiac surgery: Cardiovascular assessment and management of the European Society of Cardiology (ESC) and the European Society of Anaesthesiology (ESA). Eur Heart J 35:2383-2431, 2014
30. Spyropoulos AC, Al-Badri A, Sherwood MW, et al: Periprocedural management of patients receiving a vitamin K antagonist or a direct oral anticoagulant requiring an elective procedure or surgery. J Thromb Haemost 14:875-885, 2016. https://doi.org/10.1111/jth.13305
31. Spyropoulos AC: Bridging of oral anticoagulation therapy for invasive procedures. Curr Hematol Rep 4:405-413, 2005
32. Spyropoulos AC, Douketis JD: How I treat anticoagulated patients undergoing an elective procedure or surgery. Blood 120:2954-2962, 2012
33. Schulman S, Carrier M, Lee AY, et al: Perioperative management of dabigatran: A prospective cohort study. Circulation 132:167-173, 2015. https://doi.org/10.1161/CIRCULATIONAHA.115.015688
34. Soliman D, Maslow A, Bokesch P, et al: Transoesophageal echocardiography during scoliosis repair: Comparison with CVP monitoring. Can J Anaesth 45:925-932, 1998
35. Toyota S, Amaki Y: Hemodynamic evaluation of the prone position by transesophageal echocardiography. J Clin Anesth 10:32-35, 1998
36. Sy WP: Ulnar nerve palsy possibly related to use of automatically cycled blood pressure cuff. Anesth Analg 60:687-688, 1981
37. Yang S-Y, Shim J-K, Song Y, et al: Validation of pulse pressure variation and corrected flow time as predictors of fluid responsiveness in patients in the prone position. Br J Anaesth 110:713-720, 2012
38. Nuttall G, Burckhardt J, Hadley A, et al: Surgical and patient risk factors for severe arterial line complications in adults. Anesthesiology 124:590-597, 2016. https://doi.org/10.1097/ALN.0000000000000967
39. Bible JE, Mirza M, Knaub MA: Blood-loss management in spine surgery. J Am Acad Orthop Surg 26:35-44, 2018. https://doi.org/10.5435/JAAOS-D-16-00184
40. Sum DC, Chung PC, Chen WC: Deliberate hypotensive anesthesia with labetalol in reconstructive surgery for scoliosis. Acta Anaesthesiol Sin 34:203-207, 1996
41. Dutton RP: Controlled hypotension for spinal surgery. Eur Spine J 13 (Suppl 1):S66-S71, 2004. https://doi.org/10.1007/s00586-004-0756-7
42. Browner WS, Li J, Mangano DT: In-hospital and long-term mortality in male veterans following noncardiac surgery. The study of Perioperative Ischemia Research Group. JAMA 268:228-232, 1992
43. Lonjaret L, Lairez O, Minville V, et al: Optimal perioperative management of arterial blood pressure. Integr Blood Press Control 7:49-59, 2014. https://doi.org/10.2147/IBPC.S45292

44. Apfelbaum JL, Roth S, Rubin D, et al: Practice advisory for perioperative visual loss associated with spine surgery 2019: An updated report by the American society of anesthesiologists task force on perioperative visual loss, the North American neuro-ophthalmology society, and the society for neuroscience in anesthesiology and critical care. Anesthesiology 130:13-30, 2019
45. Chobanian AV, Bakris GL, Black HR, et al: The seventh report of the joint national committee on prevention, detection, evaluation, and treatment of high blood pressure: The JNC 7 report. JAMA 289:2560-2571, 2003
46. Hadley MN, Walters BC, Grabb PA, et al: Blood pressure management after acute spinal cord injury. Neurosurgery 50:S58-S62, 2002. https://doi.org/10.1097/00006123-200203001-00012
47. Elgafy H, Bransford RJ, McGuire RA, et al: Blood loss in major spine surgery: Are there effective measures to decrease massive hemorrhage in major spine fusion surgery? Spine 35:S47-S56, 2010
48. Mathai KM, Kang JD, Donaldson WF, et al: Prediction of blood loss during surgery on the lumbar spine with the patient supported prone on the Jackson table. Spine J 12:1103-1110, 2012. https://doi.org/10.1016/j.spinee.2012.10.027
49. Theusinger OM, Spahn DR: Perioperative blood conservation strategies for major spine surgery. Best Pract Res Clin Anaesthesiol 30:41-52, 2016. https://doi.org/10.1016/j.bpa.2015.11.007
50. Rajagopalan S, Mascha E, Na J, et al: The effects of mild perioperative hypothermia on blood loss and transfusion requirement. Anesthesiology 108:71-77, 2008. https://doi.org/10.1097/01.anes.0000296719.73450.52
51. Stier GR, Gabriel CL, Cole DJ: Neurosurgical disease and trauma of the spine and spinal cord: anesthetic consideration. Cottrell and Young's Neuroanesthesia. (ed 5). PA: Mosby, 2010
52. Kang WS, Oh CS, Kwon WK, et al: Effect of mechanical ventilation mode type on intra- and postoperative blood loss in patients undergoing posterior lumbar interbody fusion surgery: A randomized controlled trial. Anesthesiology 125:115-123, 2016. https://doi.org/10.1097/ALN.0000000000001131
53. Winter SF, Santaguida C, Wong J, et al: Systemic and topical use of tranexamic acid in spinal surgery: A systematic review. Global Spine J 6:284-295, 2016
54. Raksakietisak M, Sathitkarnmanee B, Srisaen P, et al: Two doses of tranexamic acid reduce blood transfusion in complex spine surgery: A prospective randomized study. Spine 40:E1257-E1263, 2015. https://doi.org/10.1097/BRS.0000000000001063
55. Farrokhi MR, Kazemi AP, Eftekharian HR, et al: Efficacy of prophylactic low dose of tranexamic acid in spinal fixation surgery: A randomized clinical trial. J Neurosurg Anesthesiol 23:290-296, 2011. https://doi.org/10.1097/ANA.0b013e31822914a1
56. Colomina MJ, Koo M, Basora M, et al: Intraoperative tranexamic acid use in major spine surgery in adults: A multicentre, randomized, placebo-controlled trialdagger. Br J Anaesth 118:380-390, 2017. https://doi.org/10.1093/bja/aew434
57. Casati V, Guzzon D, Oppizzi M, et al: Hemostatic effects of aprotinin, tranexamic acid and epsilon-aminocaproic acid in primary cardiac surgery. Ann Thorac Surg 68:2252-2256, 1999; discussion 2256-2257 https://doi.org/10.1016/s0003-4975(99)00866-8
58. Halpin RJ, Sugrue PA, Gould RW, et al: Standardizing care for high-risk patients in spine surgery: The Northwestern high-risk spine protocol. Spine 35:2232-2238, 2010. https://doi.org/10.1097/BRS.0b013e3181e8abb0
59. Zeeni C, Carabini LM, Gould RW, et al: The implementation and efficacy of the Northwestern high risk spine protocol. World Neurosurg 82:e815-e823, 2014
60. Gonzalez E, Moore EE, Moore HB, et al: Goal-directed hemostatic resuscitation of trauma-induced coagulopathy: A pragmatic randomized clinical trial comparing a viscoelastic assay to conventional coagulation assays. Ann Surg 263:1051-1059, 2016. https://doi.org/10.1097/SLA.0000000000001608
61. Naik BI, Pajewski TN, Bogdonoff DI, et al: Rotational thromboelastometry-guided blood product management in major spine surgery. J Neurosurg Spine 23:239-249, 2015. https://doi.org/10.3171/2014.12.SPINE14620
62. Pivalizza EG, Stephens CT, Sridhar S, et al: Whole blood for resuscitation in adult civilian trauma in 2017: A narrative review. Anesth Analg 127:157-162, 2018. https://doi.org/10.1213/ANE.0000000000003427
63. Holcomb JB, Tilley BC, Baraniuk S, et al: Transfusion of plasma, platelets, and red blood cells in a 1:1:1 vs a 1:1:2 ratio and mortality in patients with severe trauma: The PROPPR randomized clinical trial. JAMA 313:471-482, 2015. https://doi.org/10.1001/jama.2015.12
64. Hebert PC, Wells G, Blajchman MA, et al: A multicenter, randomized, controlled clinical trial of transfusion requirements in critical care. Transfusion Requirements in Critical Care Investigators, Canadian Critical Care Trials Group. N Engl J Med 340:409-417, 1999. https://doi.org/10.1056/NEJM199902113400601
65. Mistry N, Mazer CD, Sled JG, et al: Red blood cell antibody-induced anemia causes differential degrees of tissue hypoxia in kidney and brain. Am J Physiol Regul Integr Comp Physiol 314:R611-R622, 2018. https://doi.org/10.1152/ajpregu.00182.2017
66. Kawaguchi Y, Kanamori M, Ishihara H, et al: Postoperative delirium in spine surgery. Spine J 6:164-169, 2006. https://doi.org/10.1016/j.spinee.2005.06.010
67. Purvis TE, Goodwin CR, De la Garza-Ramos R, et al: Effect of liberal blood transfusion on clinical outcomes and cost in spine surgery patients. Spine J 17:1255-1263, 2017
68. Ng KF, Lam CC, Chan LC: In vivo effect of haemodilution with saline on coagulation: A randomized controlled trial. Br J Anaesth 88:475-480, 2002. https://doi.org/10.1093/bja/88.4.475
69. Epstein NE, Peller A, Korsh J, et al: Impact of intraoperative normovolemic hemodilution on transfusion requirements for 68 patients undergoing lumbar laminectomies with instrumented posterolateral fusion. Spine 31:2227-2230, 2006; discussion 2231. https://doi.org/10.1097/01.brs.0000232703.59829.ac
70. Goodnough L, Monk T: Autologous Transfusion: In Miller's Anesthesia. In: Miller RD (ed): 2005 Philadelphia
71. Esper SA, Waters JH: Intra-operative cell salvage: A fresh look at the indications and contraindications. Blood Transfus 9:139, 2011
72. Waters JH: Red blood cell recovery and reinfusion. Anesthesiol Clin North Am 23:283-294. vi, 2005. https://doi.org/10.1016/j.atc.2005.02.001
73. Carless PA, Henry DA, Moxey AJ, et al: Cell salvage for minimising perioperative allogeneic blood transfusion. Cochrane Database Syst Rev 4: CD001888, 2006. https://doi.org/10.1002/14651858.CD001888.pub2
74. Gause PR, Siska PA, Westrick ER, et al: Efficacy of intraoperative cell saver in decreasing postoperative blood transfusions in instrumented posterior lumbar fusion patients. Spine 33:571-575, 2008. https://doi.org/10.1097/BRS.0b013e3181657cc1
75. Gakhar H, Bagouri M, Bommireddy R, et al: Role of intraoperative red cell salvage and autologus transfusion in metastatic spine surgery: A pilot study and review of literature. Asian Spine J 7:167-172, 2013. https://doi.org/10.4184/asj.2013.7.3.167
76. Canan CE, Myers JA, Owens RK, et al: Blood salvage produces higher total blood product costs in single-level lumbar spine surgery. Spine 38:703-708, 2013. https://doi.org/10.1097/BRS.0b013e3182767c8c
77. Möller H, Hedlund R: Instrumented and noninstrumented posterolateral fusion in adult spondylolisthesis: A prospective randomized study: part 2. Spine 25:1716-1721, 2000
78. Fisahn C, Jeyamohan S, Norvell DC, et al: Association between allogeneic blood transfusion and postoperative infection in major spine surgery. Clin Spine Surg 30:E988-E992, 2017
79. de Araujo Azi LM, Lopes FM, Garcia LV: Postoperative management of severe acute anemia in a Jehovah's witness. Transfusion 54:1153-1157, 2014. https://doi.org/10.1111/trf.12424
80. Lauscher P, Kertscho H, Schmidt O, et al: Determination of organ-specific anemia tolerance. Crit Care Med 41:1037-1045, 2013. https://doi.org/10.1097/CCM.0b013e3182746423
81. Abuella G, Corredor C, Arulkumaran N, et al: Meta-analysis of goal directed therapy in high-risk patients undergoing major non-cardiac surgery. Intensive Care Medicine. Springer, 2012 pp. S120-S120
82. Benes J, Giglio M, Brienza N, et al: The effects of goal-directed fluid therapy based on dynamic parameters on post-surgical outcome: A meta-analysis of randomized controlled trials. Crit Care 18:584, 2014
83. Aya HD, Cecconi M, Hamilton M, et al: Goal-directed therapy in cardiac surgery: A systematic review and meta-analysis. Br J Anaesth 110:510-517, 2013. https://doi.org/10.1093/bja/aet020
84. Brookfield KF, Brown MD, Henriques SM, et al: Allogeneic transfusion after predonation of blood for elective spine surgery. Clin Orthop Relat Res 466:1949-1953, 2008. https://doi.org/10.1007/s11999-008-0306-4