Practice Guidelines for Perioperative Blood Management

An Updated Report by the American Society of Anesthesiologists Task Force on Perioperative Blood Management[*]

PRACTICE guidelines are systematically developed recommendations that assist the practitioner and patient in making decisions about health care. These recommendations may be adopted, modified, or rejected according to clinical needs and constraints, and are not intended to replace local institutional policies. In addition, practice guidelines developed by the American Society of Anesthesiologists (ASA) are not intended as standards or absolute requirements, and their use cannot guarantee any specific outcome. Practice guidelines are subject to revision as warranted by the evolution of medical knowledge, technology, and practice. They provide basic recommendations that are supported by a synthesis and analysis of the current literature, expert and practitioner opinion, open forum commentary, and clinical feasibility data.

This document updates the "Practice Guidelines for Perioperative Blood Transfusion and Adjuvant Therapies: an Updated Report by the American Society of Anesthesiologists Task Force on Perioperative Blood Transfusion and Adjuvant Therapies," adopted by the ASA in 2005 and published in 2006.[†]

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Address correspondence to the American Society of Anesthesiologists: 520 N. Northwest Highway, Park Ridge, Illinois 60068-2573. These Practice Guidelines, as well as all ASA Practice Parameters, may be obtained at no cost through the Journal Web site, www.anesthesiology.org.

[†] American Society of Anesthesiologists: Practice Guidelines for Perioperative Blood Transfusion and Adjuvant Therapies: An Updated Report. *ANESTHESIOLOGY 2006;105:198-208*

Methodology

A. Definition of Perioperative Blood Management

Perioperative blood management refers to perioperative blood transfusion and adjuvant therapies. Perioperative blood transfusion addresses the preoperative, intraoperative, and postoperative administration of blood and blood components (*e.g.*, allogeneic or autologous blood, red blood cells, platelets, cryoprecipitate, and plasma products (*e.g.*, FFP, PF24 or Thawed Plasma).[‡] Adjuvant therapies refer to drugs and techniques to reduce or prevent blood loss and the need for transfusion of allogeneic blood.

B. Purpose of the Guidelines

The purposes of these updated Guidelines are to improve the perioperative management of blood transfusion and adjuvant therapies and to reduce the risk of adverse outcomes associated with transfusions, bleeding, or anemia.

C. Focus

These Guidelines focus on the perioperative management of patients undergoing surgery or other invasive procedures in which significant blood loss occurs or is expected. This includes but is not limited to: (1) patients undergoing cardiopulmonary bypass or cardiac surgery, urgent or emergent procedures, obstetric procedures, organ transplantation, and non-cardiac surgery; (2) patients with preexisting blood disorders or acquired coagulation deficiency; (3) critically-ill patients undergoing surgical or other interventional procedures; and (4) patients who elect not to undergo perioperative transfusion. Excluded from the focus of these Guidelines are neonates, infants, children weighing less than 35 kg, and patients who are not undergoing procedures.

The Task Force recognizes that the physiology of bleeding may be influenced by the

[‡] FFP refers to plasma frozen within 8 hr after Phlebotomy, PF24 refers to plasma frozen within 24 hr after Phlebotomy, and Thawed Plasma refers to FFP stored up to 5 days at 1-6 C after thawing. In the USA, it is common practice to use these terms interchangeably. Throughout this document, the term FFP will refer to the use of any of these plasma products.

vasodilatory effects of anesthetics; therefore for some clinical presentations or surgical situations, the recommendations in these Guidelines may not apply. Practitioners will need to use their judgment of the clinical situation in applying the more generalized recommendations contained in these Guidelines.

D. Application

These Guidelines apply to both inpatient and outpatient surgical settings, and to interventional procedures performed in operating rooms as well as in other locations (*e.g.*, interventional radiology, critical care units) where blood transfusion or other adjuvant therapy is indicated. They are directly applicable to care administered by anesthesiologists and individuals who deliver care under the medical direction or supervision of an anesthesiologist. They are also intended to serve as a resource for other physicians and patient care personnel who are involved in the perioperative care of these patients.

E. Task Force Members and Consultants

In 2012, the ASA Committee on Standards and Practice Parameters requested that the updated Guidelines published in 2006 be re-evaluated. This current update consists of a literature evaluation, and an evaluation of new survey findings of expert consultants and ASA members. A summary of recommendations is found in Appendix 1.

This update was developed by an ASA appointed Task Force of 10 members, consisting of anesthesiologists in both private and academic practices from various geographic areas of the United States, a pathologist specializing in transfusion medicine, and two consulting methodologists from the ASA Committee on Standards and Practice Parameters.

The Task Force developed the Guidelines by means of a seven-step process. First, they reached consensus on the criteria for evidence of effective blood transfusion and adjuvant therapies. Second, original published research studies from peer-reviewed journals relevant to

the perioperative management of patients undergoing blood transfusions were reviewed. Third, a panel of expert consultants was asked to (1) participate in opinion surveys on the effectiveness of various perioperative management strategies and (2) review and comment on a draft of the Guidelines developed by the Task Force. Fourth, survey opinions about the Guideline recommendations were solicited from a random sample of active members of the ASA. Fifth, the Task Force held open forums at two major national meetings to solicit input on its draft recommendations.[§] National organizations representing specialties whose members typically care for patients undergoing perioperative transfusion were invited to participate in the open forums. Sixth, the consultants were surveyed to assess their opinions on the feasibility of implementing the Guidelines. Seventh, all available information was used to build consensus within the Task Force to finalize the Guidelines.

F. Availability and Strength of Evidence

Preparation of these updated Guidelines followed a rigorous methodological process. Evidence was obtained from two principal sources: scientific evidence and opinion-based evidence *(Appendix 2).*

Scientific Evidence:

Scientific evidence used in the development of these updated Guidelines is based on cumulative findings from literature published in peer-reviewed journals. Literature citations are obtained from PubMed and other healthcare databases, direct internet searches, Task Force members, liaisons with other organizations and from manual searches of references located in reviewed articles.

Findings from the aggregated literature are reported in the text of the Guidelines by evidence category, level, and direction. Evidence categories refer specifically to the strength and quality

[§] International Anesthesia Research Society 2014 Annual Meeting and International Science Symposium, Montreal, Canada, May 19, 2014; and 36th Annual Meeting of the Society of Cardiovascular Anesthesiologists, March 31, 2014, New Orleans, Louisiana.

of the *research design* of the studies. Category A evidence represents results obtained from randomized controlled trials (RCTs), and Category B evidence represents observational results obtained from non-randomized study designs or RCTs without pertinent comparison groups. When available, Category A evidence is given precedence over Category B evidence in the reporting of results. These evidence categories are further divided into evidence levels. Evidence levels refer specifically to the strength and quality of the summarized study *findings* (*i.e.*, statistical findings, type of data, and the number of studies reporting/replicating the findings) within the two evidence categories. For this document, only the highest level of evidence is included in the summary report for each intervention, including a directional designation of benefit, harm, or equivocality for each outcome.

Category A: RCTs report comparative findings between clinical interventions for specified outcomes. Statistically significant ($p < 0.01$) outcomes are designated as either beneficial (B) or harmful (H) for the patient; statistically non-significant findings are designated as equivocal (E).

Level 1: The literature contains a sufficient number of RCTs to conduct meta-analysis,[**] and meta-analytic findings from these aggregated studies are reported as evidence.

Level 2: The literature contains multiple RCTs, but the number of RCTs is not sufficient to conduct a viable meta-analysis for the purpose of these updated Guidelines. Findings from these RCTs are reported as evidence.

Level 3: The literature contains a single RCT, and findings from this study are reported as evidence.

Category B: Observational studies or RCTs without pertinent comparison groups may permit *inference* of beneficial or harmful relationships among clinical interventions and outcomes. Inferred findings are given a directional designation of beneficial (B), harmful (H) or

[**] All meta-analyses are conducted by the ASA methodology group. Meta-analyses from other sources are reviewed but not included as evidence in this document.

equivocal (E). For studies that report statistical findings, the threshold for significance is $p < 0.01$.

Level 1: The literature contains observational comparisons (*e.g.,* cohort, case-control research designs) between clinical interventions for a specified outcome.

Level 2: The literature contains observational studies with associative statistics (*e.g.,* relative risk, correlation, sensitivity/specificity).

Level 3: The literature contains non-comparative observational studies with descriptive statistics (*e.g.,* frequencies, percentages).

Level 4: The literature contains case reports.

Insufficient Literature: The *lack* of sufficient scientific evidence in the literature may occur when the evidence is either unavailable (*i.e.,* no pertinent studies found) or inadequate. Inadequate literature cannot be used to assess relationships among clinical interventions and outcomes, since such literature does not permit a clear interpretation of findings due to methodological concerns (*e.g.,* confounding in study design or implementation) or does not meet the criteria for content as defined in the "Focus" of the Guidelines.

Opinion-Based Evidence:

All opinion-based evidence (*e.g.,* survey data, open-forum testimony, internet-based comments, letters, and editorials) relevant to each topic was considered in the development of these updated Guidelines. However, only the findings obtained from formal surveys are reported.

Opinion surveys were developed for this update by the Task Force to address each clinical intervention identified in the document. Identical surveys were distributed to expert consultants and a random sample of ASA members.

Category A: Expert Opinion. Survey responses from Task Force-appointed expert consultants are reported in summary form in the text, with a complete listing of consultant survey responses reported in Appendix 2.

Category B: Membership Opinion. Survey responses from active ASA members are reported in summary form in the text, with a complete listing of ASA member survey responses reported in Appendix 2.

Survey responses from expert and membership sources are recorded using a 5-point scale and summarized based on median values.[††]

Strongly Agree:	Median score of 5 (At least 50% of the responses are 5)
Agree:	Median score of 4 (At least 50% of the responses are 4 or 4 and 5)
Equivocal:	Median score of 3 (At least 50% of the responses are 3, or no other response category or combination of similar categories contain at least 50% of the responses)
Disagree:	Median score of 2 (At least 50% of responses are 2 or 1 and 2)
Strongly Disagree:	Median score of 1 (At least 50% of responses are 1)

Category C: Informal Opinion. Open-forum testimony obtained during development of the original Guidelines, Internet-based comments, letters and editorials are all informally evaluated and discussed during the formulation of Guideline recommendations. When warranted, the Task Force may add educational information or cautionary notes based on this information.

Guidelines

I. Patient Evaluation.

Preoperative evaluation of a patient to identify risk factors for requiring a blood transfusion or adjuvant therapy includes: (1) reviewing previous medical records, (2) conducting a patient or family interview, (3) reviewing existing laboratory test results, and (4) ordering additional laboratory tests when indicated.

[††] When an equal number of categorically distinct responses are obtained, the median value is determined by calculating the arithmetic mean of the two middle values. Ties are calculated by a predetermined formula.

Literature findings: Although it is well accepted clinical practice to review medical records and conduct a patient interview, comparative studies are insufficient to evaluate the impact of these practices. Observational studies and case reports indicate that certain congenital or acquired conditions (*e.g.,* sickle-cell anemia, clotting factor deficiency, hemophilia, and liver disease) may be associated with blood transfusion complications *(Category B3/B4-H evidence)*[1-20] In addition, observational studies indicate that findings from pertinent preoperative laboratory tests (*e.g.*, hemoglobin, hematocrit, coagulation tests) may be predictive of perioperative blood loss, the risk of transfusion, or other adverse events (*e.g.,* acute kidney injury) associated with transfusion *(Category B2-B evidence).*[21-41]

Survey findings: The consultants and ASA members both strongly agree to (1) a review of previous medical records and interview the patient or family to identify prior blood transfusion, history of drug- induced coagulopathy, presence of congenital coagulopathy, history of thrombotic events, and risk factors for organ ischemia and (2) a review available laboratory test results including hemoglobin, hematocrit, and coagulation profiles and order additional laboratory tests depending on a patient's medical condition (e.g., coagulopathy, anemia). The ASA members agree and the consultants strongly agree regarding (1) informing patients of the potential risks versus benefits of blood transfusion and elicit their preferences and (2) conducting a physical examination of the patient (e.g., ecchymoses, petechiae, pallor).

Recommendations for patient evaluation:

- Review previous medical records and interview the patient or family to identify:
    - Prior blood transfusion
    - History of drug-induced coagulopathy (*e.g.*, warfarin, clopidogrel, aspirin and other anticoagulants, as well as vitamins or herbal supplements that may affect coagulation *[Appendix 3]*)

- The presence of congenital coagulopathy
- History of thrombotic events (*e.g.*, deep vein thrombosis, pulmonary embolism)
- Risk factors for organ ischemia (*e.g.*, cardiorespiratory disease) which may influence the ultimate transfusion trigger for red blood cells (*e.g.*, hemoglobin level)

- Inform patients of the potential risks *versus* benefits of blood transfusion and elicit their preferences.
- Review available laboratory test results including hemoglobin, hematocrit and coagulation profiles.
- Order additional laboratory tests depending on a patient's medical condition (*e.g.*, coagulopathy, anemia).
- Conduct a physical examination of the patient (*e.g.*, ecchymosis, petechiae, pallor).
- If possible, perform the preoperative evaluation well enough in advance (*e.g.*, several days to weeks) to allow for proper patient preparation.

II. Preadmission Patient Preparation.

Preadmission patient preparation includes (1) treatment of anemia, (2) discontinuation of anticoagulants and antiplatelet agents, (3) preadmission autologous blood collection.

Treatment of anemia: The World Health Organization identifies anemia as hemoglobin thresholds of 11.0 g/dl for children 0.50-4.99 years,[‡‡] 11.5 g/dl for children 5.0-11.99 years, 12.0 g/dl for children 12.0-14.99 years, and non-pregnant women ≥ 15.0 years, 11.0 g/dl for pregnant women and 13.0 g/dl for men ≥ 15.0 years.[42,43] Preadmission treatment of anemia includes the administration of erythropoietin and/or iron to improve preoperative hemoglobin levels.

[‡‡] [‡‡] Neonates, infants, and children weighing less than 35 kg are excluded from the focus of these ASA Guidelines.

Literature findings: Meta-analyses of placebo-controlled RCTs indicate that erythropoietin with or without iron is effective in reducing the number of patients requiring allogeneic transfusions as well as reducing the volume of allogeneic blood transfused *(Category A1-B evidence*).[44-58] The literature is insufficient to evaluate the efficacy of erythropoietin with iron compared with erythropoietin without iron. RCTs report equivocal findings when preadmission oral iron is compared with either placebo or no iron regarding preoperative hemoglobin levels or perioperative allogeneic blood transfused *(Category A2-E evidence).*[59-61]

Survey findings: Both the consultants and ASA members agree that erythropoietin with or without iron may be administered when possible to reduce the need for allogeneic blood in select patient populations (e.g., renal insufficiency, anemia of chronic disease, refusal of transfusion); and both the consultants and ASA members strongly agree regarding the administration of iron to patients with iron deficiency anemia if time permits.

Discontinuation of anticoagulants and antiplatelet agents:

Literature findings: One nonrandomized comparative observational study is equivocal regarding the effect of discontinuing warfarin and replacing it with low-molecular weight heparin on blood transfusion requirements when compared with patients not on warfarin.[62] Observational studies report blood loss volumes ranging from 265-756 ml, and blood transfusion requirements ranging from a mean of 0.08 to 0.5 units when clopidogrel is discontinued preoperatively.[63-65] The literature is insufficient to evaluate the effects of discontinuing aspirin before surgery, although two RCTs comparing the administration of aspirin with placebo before surgery report equivocal findings ($p > 0.01$) for perioperative blood loss, transfusion requirements or postoperative adverse events (*e.g.*, myocardial infarction, major bleeding or death).[66,67]

Survey findings: Both the consultants and ASA members strongly agree regarding (1) discontinuing anticoagulation therapy (e,g,. warafin, anti-Xa drugs, anti-thrombin agents) for elective surgery, in consultation with an appropriate specialist; (2) if clinically possible, discontinuing non-aspirin antiplatelet agents (*e.g.*, thienopyridines such as clopidogrel, ticagrelor, or prasugrel) for a sufficient time in advance of surgery, except for patients with a history of percutaneous coronary interventions; and (3) that the risk of thrombosis versus the risk of increased bleeding should be considered when altering anticoagulation status.

Preadmission autologous blood donation:

Literature findings: RCTs indicate that the preadmission donation of autologous blood reduces the number of patients requiring allogeneic transfusions and the volume of allogeneic blood transfused per patient *(Category A2-B evidence).*[68-73§§]

Survey findings: The consultants and ASA members both strongly agree regarding assuring that blood and blood components are available for patients when significant blood loss or transfusion is expected; they both agree that when autologous blood is preferred, the patient should be offered the opportunity to donate blood before admission only if there is adequate time for erythropoietic reconstitution.

Recommendations for preadmission patient preparation:

- Erythropoietin with or without iron may be administered when possible to reduce the need for allogeneic blood in selected patient populations (*e.g.*, renal insufficiency, anemia of chronic disease, refusal of transfusion).[***]
- Administer iron to patients with iron deficiency anemia if time permits.
- In consultation with an appropriate specialist, discontinue anticoagulation therapy

§§ The Task Force notes that certain adverse outcomes (*e.g.*, transfusion reaction due to clerical errors, bacterial contamination) may still occur with the use of autologous blood.

*** The Task Force recognizes that erythropoietin administration is perceived as being expensive and requires time (in weeks) to induce a significant increase in hemoglobin concentration.

(*e.g.*, warfarin, anti-Xa drugs, antithrombin agents) for elective surgery.

- Transition to a shorter acting drug (*e.g.*, heparin, low molecular weight heparin) may be appropriate in selected patients.

- If clinically possible, discontinue non-aspirin antiplatelet agents (*e.g.*, thienopyridines such as clopidogrel, ticagrelor, or prasugrel) for a sufficient time in advance of surgery, except for patients with a history of percutaneous coronary interventions.[†††]
  - Aspirin may be continued on a case-by-case basis.
- The risk of thrombosis *versus* the risk of increased bleeding should be considered when altering anticoagulation status.
- Assure that blood and blood components are available for patients when significant blood loss or transfusion is expected.
- When autologous blood is preferred, the patient may be offered the opportunity to donate blood before admission only if there is adequate time for erythropoietic reconstitution.[‡‡‡]

III. Preprocedure Preparation.

Preprocedure patient preparation includes the following strategies for reducing intraoperative allogeneic transfusion: (1) use of blood management protocols, (2) reversal of anticoagulants, (3) administration of antifibrinolytics for prophylaxis of excessive blood loss,[§§§] (4) use of acute normovolemic hemodilution, and conversely (5) pre-procedure transfusion of red blood cells.

[†††] The Task Force cautions that clopidogrel and aspirin should not be stopped prior to surgery in patients with coronary stents placed in the last 3 months for bare metal stents and 1 year for drug eluting stents due to the risk of perioperative myocardial infarction. See "American Society of Anesthesiologists Committee on Standards and Practice Parameters: Practice alert for the perioperative management of patients with coronary artery stents: a report by the American Society of Anesthesiologists Committee on Standards and Practice Parameters. Anesthesiology. 2009; 110:22-23. Additional information may be found in: American College of Cardiology/American Heart Association: 2014 ACC/AHA guideline on perioperative cardiovascular evaluation and management of patients undergoing noncardiac surgery. (in press).

[‡‡‡] The Task Force cautions that preadmission blood donation may induce preoperative anemia, increase total intraoperative (autologous or allogeneic) transfusions, and increase costs.

[§§§] Antifibrinolytics for prophylaxis of blood loss refers to preoperative and/or intraoperative administration.

Blood management protocols: Protocols for perioperative blood management include: (1) multimodal protocols or algorithms, (2) liberal versus restrictive transfusion criteria, (3) avoidance of transfusion, (4) a massive (*i.e.*, hemorrhage) transfusion protocol, and (5) maximal surgical blood order schedules.

Multimodal protocols or algorithms: Multimodal protocols are strategies that typically consist of a predetermined "bundle" of interventions intended to reduce blood loss and transfusion requirements. The bundle components may include consultation with multiple medical specialties, institutional support, using transfusion algorithms, and point-of-care testing in addition to other perioperative blood conservation interventions. Algorithms are intended to identify decision points or "pathways" during a procedure whereby certain interventions should be employed.

Literature findings: RCTs comparing multimodal protocols or algorithms using coagulation tests or hemoglobin concentrations with routine blood management practices report variable findings regarding blood and blood product transfusions when such protocols are implemented *(Category A2-E evidence)*.[74-76] RCTs demonstrate reduced blood transfusions and percentage of patients transfused when TEG-guided protocols or algorithms are compared with standard laboratory coagulation testing in cardiac surgery patients. *(Category A2-B evidence)*.[77-79] An RCT reports reductions in allogeneic blood product requirements when comparing a rotational thromboelastometry-guided algorithm with no algorithm for bleeding burn patients. *(Category A1-B evidence)*.[80] The above studies report protocols or algorithms that contain a large variety of interventional components and the impact of any single component on outcome is not reported.

Survey findings: The consultants and ASA members both strongly agree regarding employment of multimodal protocols or algorithms as strategies to reduce the utilization of blood products.

Restrictive versus liberal transfusion strategy: Definitions for a restrictive versus liberal strategy for blood transfusion vary in the literature, although hemoglobin criteria for transfusion below 8 g/dL and hematocrit values below 25% are typically reported as restrictive.

Literature findings: Meta-analysis of RCTs comparing restrictive with liberal transfusion criteria report fewer red blood cell transfusions when restrictive transfusion strategies are employed *(Category A1-B evidence).*[81-85] RCT findings for mortality, cardiac, neurologic or pulmonary complications, and length of hospital stay were equivocal *(Category A2-E evidence).*[81-89]

Survey findings: The ASA members agree and the consultants strongly agree that a restrictive red blood cell transfusion strategy may be used to reduce transfusion requirements.

Avoidance of transfusion: A protocol to avoid transfusion or to reduce the volume of blood lost may be preferred in certain selected cases.

Literature findings: Studies with observational findings report low blood loss volumes for certain cardiac or other major procedures when these protocols are implemented *(Category B3-B evidence).*[90-95]

Survey findings: Both the consultants and ASA members strongly agree that a protocol for avoidance of transfusion may be used as a strategy to reduce blood loss for patients in whom transfusion is refused or is not possible.

Massive transfusion protocols: Massive transfusion protocols are implemented in cases of life-threatening hemorrhage after trauma and/or during a procedure, and are intended to minimize the adverse effects of hypovolemia and dilutional coagulopathy. These protocols

require the availability of large amounts of allogeneic blood and blood products. They often prescribe the transfusion FFP and platelets in a higher (*e.g.*, 1:1) ratio with the transfusion of red blood cells.

Literature findings: An observational study indicates that the ratio of FFP to RBCs is higher following the implementation of a massive transfusion protocol *(Category B3-E evidence).*[96]

Survey findings: The consultants and ASA members both strongly agree regarding use of a massive transfusion protocol when available as a strategy to optimize the delivery of blood products to massively bleeding patients.

Maximal surgical blood order schedule:

Literature findings: Observational studies indicate that implementing a maximal surgical blood order schedule or surgical blood order equation may improve the efficiency of blood ordering practices *(Category B2-B evidence).*[97-106] An RCT comparing a surgical blood order equation with a maximal surgical blood order schedule demonstrated an improved crossmatch-to-transfusion ratio for SBOE *(Category A3-B evidence)*[107]

Survey findings: The consultants and ASA members both agree regarding the use of a maximal surgical blood order schedule, when available and in accordance with institutional policy, as a strategy to improve the efficiency of blood ordering practices.

Reversal of anticoagulants*:* Reversal of anticoagulants includes the topics of: (1) preprocedure administration of prothrombin complex concentrates (PCCs), (2) administration of FFP, and (3) pre-procedure administration of vitamin K.

Literature findings: Observational studies and case reports indicate that 4 factor-PCCs administered preoperatively are followed by a reduction in INR values, with thromboembolic events reported at 0.003% following patient infusions *(Category B3/4-B evidence).*[108-110] The

literature is insufficient to evaluate the impact of the use of FFP with reversal of anticoagulants. One retrospective study comparing vitamin K administered immediately before surgery with no vitamin K administered reports equivocal findings for transfusion requirements.[111]

Survey findings: Both the consultants and ASA members strongly agree that for urgent reversal of warafin, administer prothrombin complex concentrates (PCCs) in consultation with the appropriate specialist, or administer FFP. The ASA members agree and the consultants strongly agree regarding administration of vitamin K for non-urgent reversal of warfarin, except when rapid restoration of anticoagulation after surgery is required.

Antifibrinolytics for prophylaxis of excessive blood loss:

Literature findings:

ε-Aminocaproic acid: Meta-analysis of placebo-controlled RCTs indicate that the use of ε-aminocaproic acid administered before and/or during a procedure is effective in reducing total perioperative blood loss and the number of patients transfused in major cardiac, orthopedic, or liver surgery *(Category A1-B evidence)*; equivocal findings are reported for the volume of blood transfused *(Category A1-E evidence).*[112-121] An RCT comparing ε-aminocaproic acid with placebo reports less blood loss and lower RBC transfusion requirements when ε-aminocaproic acid is administered for prophylaxis of excessive bleeding after total knee replacement surgery and before tourniquet deflation *(Category A3-B evidence).*[122]

Tranexamic acid: Meta-analysis of placebo-controlled RCTs indicate that tranexamic acid for prophylaxis of excessive bleeding administered before and/or during a procedure is effective in reducing perioperative blood loss, the number of patients transfused, and the volume of blood products transfused *(CategoryA1-B evidence).*[123-146] Randomized trials comparing tranexamic acid with placebo or no tranexamic acid controls report no differences for stroke, myocardial infarction, renal failure, reoperation for bleeding, or mortality *(Category A2-B evidence).*[147-153]

Meta-analysis of placebo-controlled RCTs indicate that tranexamic acid for prophylaxis of excessive bleeding initiated after a knee and hip arthroplasty and before tourniquet deflation compared with placebo also reported lower blood loss volumes *(Category A1-B evidence)*.[122.154-159] One RCT did not show efficacy when tranexamic acid was administered after cardiac surgery and continued for 12 hours *(Category A3-E evidence)*.[160]

Survey findings: The consultants and ASA members both agree regarding use of prophylactic antifibrinolytic therapy to reduce bleeding and the risk of transfusion for patients at risk of excessive bleeding. The consultants and ASA members both agree regarding use of antifibrinolytic therapy to reduce allogeneic blood transfusion in patients undergoing cardiopulmonary bypass. They also both agree regarding the consideration of using antifibrinolytic therapy in other clinical circumstances at high-risk for excessive bleeding.

Acute normovolemic hemodilution (ANH):

Literature findings: Meta-analyses of RCTs indicate that ANH is effective in reducing the volume of allogeneic blood transfused and the number of patients transfused with allogeneic blood for major cardiac, orthopedic, thoracic, or liver surgery *(CategoryA1-B evidence)*.[161-174] Additional meta-analyses of RCTs indicate that ANH combined with intraoperative red blood cell recovery compared with intraoperative red blood cell recovery alone is effective in reducing the volume of allogeneic blood transfused *(CategoryA1-B evidence)* and is equivocal regarding the number of patients transfused with allogeneic blood *(CategoryA1-E evidence)*.[175-184]

Survey findings: Both the consultants and ASA members agree regarding use of ANH to reduce allogeneic blood transfusion in patients at high-risk for excessive bleeding (*e.g.*, major cardiac, orthopedic, thoracic, or liver surgery), if possible.

Recommendations for preprocedure preparation:

Blood management protocols:

- Multimodal protocols or algorithms may be employed as strategies to reduce the utilization of blood products. However, no single algorithm or protocol can be recommended at this time.
- A restrictive red blood cell transfusion strategy may be safely used to reduce transfusion administration.[****]
    - The determination of whether hemoglobin concentrations between 6 and 10 g/dl justify or require red blood cell transfusion should be based on potential or actual ongoing bleeding (rate and magnitude), intravascular volume status, signs of organ ischemia, and adequacy of cardiopulmonary reserve.
    - Red blood cells should be administered unit-by-unit, when possible, with interval reevaluation.
- A protocol for avoidance of transfusion may be used as a strategy to reduce blood loss for patients in whom transfusion is refused or is not possible.
- A massive (*i.e.*, hemorrhagic) transfusion protocol may be used when available as a strategy to optimize the delivery of blood products to massively bleeding patients.
- Use a maximal surgical blood order schedule, when available and in accordance with your institutional policy, as a strategy to improve the efficiency of blood ordering practices.

Reversal of anticoagulants:

- For urgent reversal of warfarin, administer prothrombin complex concentrates (PCCs) in consultation with the appropriate specialist, or administer FFP.

[****] Red blood cells refers to all red blood cell containing components. Transfusion of red blood cells is rarely necessary when the hemoglobin concentration is more than 10 g/dl.

- Administer vitamin K for selected patients for non-urgent reversal of warfarin, except when rapid restoration of anticoagulation after surgery is required.

Antifibrinolytics for prophylaxis of excessive blood loss:

- Use antifibrinolytic therapy for prophylaxis of the use of allogeneic blood transfusion in patients undergoing cardiopulmonary bypass.
    - Consider using antifibrinolytic therapy for prophylaxis in certain orthopedic procedures such as knee replacement surgery.
    - Consider using antifibrinolytic therapy for prophylaxis in liver surgery and other clinical circumstances at high-risk for excessive bleeding.[††††]

Acute normovolemic hemodilution (ANH):

- Consider ANH to reduce allogeneic blood transfusion in patients at high-risk for excessive bleeding (*e.g.*, major cardiac, orthopedic, thoracic, or liver surgery), if possible.[‡‡‡‡]

IV. Intraoperative and Postoperative Management of Blood Loss.

Intraoperative and postoperative interventions include: (1) allogeneic red blood cell transfusion, (2) autologous blood cell transfusion, (3) intraoperative and postoperative patient monitoring, and (4) management of coagulopathy and excessive bleeding.

Allogeneic red blood cell transfusion: Transfusion of allogeneic blood includes the topics of (1) the age of stored blood, and (2) leukocyte reduction.

Age of stored blood:

Literature findings: Nonrandomized comparative studies are equivocal regarding the effects of newer versus older stored blood on in-hospital mortality, 30 days postdischarge

[††††] The safety of antifibrinolytics has not been established in hypercoagulable patients (*e.g.*, pregnancy)
[‡‡‡‡] ANH may not be possible due to preexisting patient factors such as small blood volume, low hemoglobin, or presence of ischemic disease.

mortality, infectious complications, and length of stay in the ICU or hospital *(Category B1-E evidence).*[185-194]

Survey findings: The consultants are equivocal and ASA members disagree regarding the administration of blood without consideration of duration of storage.

Leukocyte reduction:

Literature findings: RCTs are equivocal regarding postoperative infections and infectious complications when leukocyte RBC depletion is compared with non-leukocyte depletion *(Category A2-B evidence).*[195-201]

Survey findings: The ASA members agree and the consultants strongly agree that leukocyte reduced blood may be used for transfusion for the purpose of reducing complications associated with allogeneic blood transfusion.

Reinfusion of recovered red blood cells:

Intraoperative red blood cell recovery:

Literature findings: Meta-analyses of RCTs indicate that intraoperative red blood cell recovery compared with conventional transfusion (*i.e.*, non-blood cell recovery) is effective in reducing the volume of allogeneic blood transfused *(CategoryA1-B evidence).*[202-213]

Postoperative red blood cell recovery:

Literature findings: RCTs indicate that postoperative blood recovery and reinfusion with recovered red blood cells reduces the frequency of allogeneic blood transfusions *(Category A2-B evidence)* in patients undergoing major orthopedic surgery.[214-216]

Survey findings: The consultants and ASA members both strongly agree regarding the reinfusion of recovered red blood cells as a blood-sparing intervention in the intraoperative and/or postoperative period.

Intraoperative and postoperative patient monitoring:

Intraoperative and postoperative monitoring consists of monitoring for: (1) blood loss, (2) perfusion of vital organs, (3) anemia, (4) coagulopathy, and (5) adverse effects of transfusion.

Monitoring for blood loss:

Blood loss monitoring consists of visual assessment of the surgical field, including the extent of blood present, presence of microvascular bleeding, surgical sponges, clot size and shape, and volume in suction canister.

Literature findings: The literature is insufficient to evaluate the impact of periodically assessing the surgical field for the extent of blood present, the presence of excessive microvascular bleeding (*i.e.*, coagulopathy) or observing surgical sponges, clot size and shape, or the volume of blood in the suction canister to measure blood loss.[§§§§]

Survey findings: Both the consultants and ASA members strongly agree regarding: (1) periodically conducting a visual assessment of the surgical field jointly with the surgeon to assess the presence of surgical or excessive microvascular (*i.e.*, coagulopathy) bleeding and (2) use of standard methods for quantitative measurement of blood loss including checking suction canisters, surgical sponges, and surgical drains.

Monitoring for perfusion of vital organs:

Monitoring for perfusion of vital organs includes standard ASA monitoring. Additional monitoring may include echocardiography, renal monitoring (urine output), cerebral monitoring (*i.e.*, cerebral oximetry and near infrared spectroscopy), analysis of arterial blood gasses, and mixed venous oxygen saturation.

Literature findings: The literature is insufficient to evaluate the efficacy of the above monitoring techniques on clinical outcomes associated with blood transfusion.

[§§§§] The risk of underestimating blood loss may be reduced by adopting more precise volumetric and gravimetric measurement techniques.

Survey findings: Both the consultants and ASA members strongly agree regarding: (1) monitoring for perfusion of vital organs using standard ASA monitors (*i.e.,* blood pressure, heart rate, oxygen saturation, electrocardiography) in addition to observing clinical symptoms and physical exam features and (2) that additional monitoring may include echocardiography, renal monitoring (urine output), cerebral monitoring (*i.e.,* cerebral oximetry and near infrared spectroscopy), analysis of arterial blood gasses, and mixed venous oxygen saturation.

Monitoring for anemia:

Monitoring for anemia includes hemoglobin/hematocrit monitoring.

Literature findings: The literature is insufficient to evaluate the efficacy of perioperative monitoring for anemia.

Survey findings: The consultants and ASA members both strongly agree that if anemia is suspected, monitor hemoglobin/hematocrit values based on estimated blood loss and clinical signs.

Monitoring for coagulopathy:

Monitoring for coagulopathy includes standard coagulation tests (*e.g.*, International Normalized Ratio (INR), activated partial thromboplastin time (aPTT), fibrinogen concentration), as well as platelet count. Additional monitoring for coagulopathy may include tests of platelet function, and viscoelastic assays (*e.g.*, thromboelastrography [TEG], ROTEM.

Literature findings: An observational study examining point-of-care measurement of activated partial thromboplastin time and prothrombin time by a portable laser photometer reports shorter times for obtaining test results with point-of-care monitoring *(Category B2-B evidence).*[217] Significant correlations were reported between photometer and traditional laboratory test findings. An observational study examining platelet count during

cardiopulmonary bypass to predict excessive blood loss reports a sensitivity value of 83% and a specificity value of 58% *(Category B2 evidence).*[218] An RCT reported equivocal findings for blood loss and transfusion requirements when TEG is compared with standard laboratory coagulation tests *(Category A3-E evidence).*[219] An RCT reported equivocal findings with ROTEM versus no fibrinolysis monitoring for RBC, FFP and platelet transfusion requirements *(Category A3-E evidence).*[220] Note that TEG and ROTEM-guided algorithms are shown to be effective in reducing blood transfusion requirements (see multimodal protocols or algorithms above). For ROTEM, a sensitivity finding for blood loss was reported to be 13%, specificity values ranged from 52%-80%, and a positive predictive value of 45% *(Category B2 evidence).*[221,222] Nonrandomized correlational studies reported significant correlations ($p < 0.01$) with standard coagulation tests for fibrinogen level and platelet count, while correlations between ROTEM and PT and aPTT measures were not statistically significant *(Category B2 evidence).*[223-228]

Survey findings: Both the consultants and ASA members agree that if coagulopathy is suspected, obtain viscoelastic assays (*e.g.,* thromboelastography [TEG] and rotational thromboelastometry [ROTEM]), when available, as well as platelet count. They both strongly agree that if viscoelastic assays are not available, obtain standard coagulation tests (*e.g.,* International Normalized Ratio [INR], aPTT, fibrinogen concentration), as well as platelet count for monitoring.

Monitoring for adverse effects of transfusions:

Monitoring for adverse effects of transfusions includes periodic checking for signs of ABO incompatibility such as hyperthermia, hemoglobinuria, or microvascular bleeding; signs of transfusion-related acute lung injury (TRALI) or transfusion-associated circulatory overload (TACO) such as hypoxemia, respiratory distress and elevated peak airway pressure;

signs of bacterial contamination such as hyperthermia and hypotension; signs of allergic reaction such as urticaria; and signs of citrate toxicity such as hypocalcemia *(Appendix 4).*

Literature findings: Nonrandomized comparative studies report higher risk of infection after RBC transfusion *(Category B1-H evidence),*[229-232] and case reports indicate that adverse outcomes including TRALI and delayed hemolytic transfusion reaction may occur after transfusion *(Category B4-H evidence).*[233-235] The literature is insufficient to recommend specific monitoring practices to identify these adverse transfusion effects.

Survey findings: Both the consultants and ASA members strongly agree that (1) during and after transfusion, periodically check for hyperthermia, hemoglobinuria, microvascular bleeding, hypoxemia, respiratory distress, elevated peak airway pressure, urticaria, hypotension, and signs of hypocalcemia and (2) before instituting therapy for transfusion reactions, stop the blood transfusion and order appropriate diagnostic testing.

Treatment of excessive bleeding:

Intraoperative and postoperative treatment of excessive bleeding includes: (1) transfusion of platelets, (2) transfusion of FFP, (3) transfusion of cryoprecipitate, and (4) pharmacologic treatment of excessive bleeding.

Transfusion of platelets:

Literature findings: Recent literature is insufficient to evaluate the impact of platelet transfusion on resolution of coagulopathy.

Survey findings: The consultants and ASA members both agree regarding obtaining a platelet count before transfusion of platelets, if possible; however, the ASA members agree and the consultants are equivocal regarding obtaining a test of platelet function, if available, in patients with suspected or drug-induced (*e.g.*, clopidogrel) platelet dysfunction.

Transfusion of FFP:

Literature findings: RCTs report inconsistent findings regarding blood loss and RBC transfusion requirements when FFP transfusion is compared with non-FFP transfusion, *(Category A2-E evidence).*[236,237]

Survey findings: The consultants and ASA members both agree that, in patients with excessive bleeding, obtain coagulation tests (*i.e.,* PT or INR and aPTT) before transfusion of FFP, if possible.

Transfusion of cryoprecipitate:

Literature findings: The literature is insufficient to evaluate the intraoperative or postoperative transfusion of cryoprecipitate to manage actual or potential coagulopathy.

Survey findings: The ASA members agree and the consultants strongly agree that, in patients with excessive bleeding, assess fibrinogen levels before the administration of cryoprecipitate, if possible.

Pharmacologic treatment of excessive bleeding:

Pharmacologic treatments for excessive bleeding include: (1) desmopressin, (2) antifibrinolytics *(i.e.,* ε-aminocaproic acid, tranexamic acid), (3) topical hemostatics (*i.e.,* fibrin glue, thrombin gel), (4) prothrombin complex concentrates, (5) coagulation factor concentrates (recombinant factor VIIa), and (6) treatments for hypofibrinogenemia (cryoprecipitate, fibrinogen concentrate).

Desmopressin:

Literature findings: Meta-analysis of placebo-controlled RCTs indicate that desmopressin is effective in reducing the volume of postoperative blood loss *(Category A1-B evidence).*[238-244]

Survey findings: Both the consultants and ASA members agree that, in patients with excessive bleeding and platelet dysfunction, consider the use of desmopressin.

Antifibrinolytics:

Literature findings: An RCT is equivocal regarding blood loss and RBC transfusion requirements when ε-aminocaproic acid is compared with placebo to treat postoperative blood loss (*i.e.,* patients with chest drainage of 100 mL/hr or more *(Category A3-E evidence).*[245] The literature is insufficient to evaluate the postoperative administration of tranexamic acid for treatment of excessive blood loss.

Survey findings: The consultants and ASA members both agree that, in patients with excessive bleeding, consider the use of antifibrinolytics (*i.e.,* ε-aminocaproic acid, tranexamic acid), if not already being used.

Topical hemostatics:

Literature findings: Meta-analysis of RCTs indicates that fibrin glue is effective in reducing the volume of perioperative blood loss and the number of patients transfused when compared with no fibrin glue *(Category A1-B evidence).*[246-257] RCTs indicate that thrombin gel is effective in reducing perioperative blood loss and time to hemostasis *(Category A2-B evidence).*[258-260]

Survey findings: The consultants and ASA members both agree that, in patients with excessive bleeding, consider topical hemostatics such as fibrin glue or thrombin gel.

PCCs:

Literature findings: Observational studies and case reports indicate that intraoperative administration of 4 factor-PCCs are followed by a reduction in blood loss and normalization of INR values. *(Category B3/4-B evidence).*[261-264]

Survey findings: The consultants and ASA members both agree that, in patients with excessive bleeding and elevated INR, consider the use of prothrombin complex concentrates.

Coagulation factor concentrates:

Literature findings: Meta-analysis of placebo-controlled RCTs of recombinant activated factor VII reports equivocal findings regarding the volume of blood loss, the volume of blood transfused, and the number of patients transfused *(CategoryA1-E evidence)*.[265-271]

Survey findings: Both the consultants and ASA members agree that, when traditional options for treating excessive bleeding due to coagulopathy have been exhausted, consider administering recombinant activated factor VII.

Treatments for hypofibrinogenemia:

Literature findings: The literature is insufficient to evaluate the intraoperative or postoperative transfusion of cryoprecipitate to manage hypofibrinogenemia. RCTs comparing fibrinogen concentrate with placebo report a lower volume of RBC transfusion and a reduced frequency of patients transfused when fibrinogen concentrate is administered intraoperatively *(Category A2-B evidence)*.[272,273]

Survey findings: The consultants and ASA members both agree that, in patients with excessive bleeding, consider the use of fibrinogen concentrate.

Recommendations for Intraoperative and Postoperative Management of Blood Loss:

Allogeneic red blood cell transfusion:

- Administer blood without consideration of duration of storage.
- Leukocyte reduced blood may be used for transfusion for the purpose of reducing complications associated with allogeneic blood transfusion.

Reinfusion of recovered red blood cells:

- Reinfuse recovered red blood cells as a blood-sparing intervention in the intraoperative period, when appropriate.

Intraoperative and postoperative patient monitoring:

- Periodically conduct a visual assessment of the surgical field jointly with the surgeon to assess the presence of excessive microvascular (*i.e.*, coagulopathy) or surgical bleeding.
- Use standard methods for quantitative measurement of blood loss, including checking suction canisters, surgical sponges, and surgical drains.
- Monitor for perfusion of vital organs using standard ASA monitors (i.*e.*, blood pressure, heart rate, oxygen saturation, electrocardiography) in addition to observing clinical symptoms and physical exam features.[*****]
    - Additional monitoring may include echocardiography, renal monitoring (urine output), cerebral monitoring (*i.e.*, cerebral oximetry and near infrared spectroscopy), analysis of arterial blood gasses, and mixed venous oxygen saturation.
- If anemia is suspected, monitor hemoglobin/hematocrit values based on estimated blood loss and clinical signs.
- If coagulopathy is suspected, obtain standard coagulation tests (*e.g.*, International Normalized Ratio [INR], aPTT, fibrinogen concentration) or viscoelastic assays *(e.g.*, thromboelastography [TEG] and rotational thromboelastometry [ROTEM]), if available, as well as platelet count.
- During and after transfusion, periodically check for signs of a transfusion reaction including hyperthermia, hemoglobinuria, microvascular bleeding, hypoxemia, respiratory distress, elevated peak airway pressure, urticaria, hypotension and signs of hypocalcemia.

[*****] American Society of Anesthesiologists: Standards for Basic Anesthetic Monitoring (last amended October 20, 2010, effective date July 1, 2011).

- If signs of a transfusion reaction are apparent, immediately stop the transfusion, give supportive therapy, and initiate supportive care.
- Notify the blood bank of the transfusion reaction case.

Treatment of excessive bleeding:

In patients with excessive bleeding, the following recommendations are made based upon the evidence for each of these interventions when studied singly or when compared with placebo. The impact of combinations of these interventions is not addressed in these Guidelines.

- Obtain a platelet count before transfusion of platelets, if possible (see Table 1 for suggested transfusion criteria for platelets).[†††††] In addition, obtain a test of platelet function, if available, in patients with suspected or drug-induced (*e.g.*, clopidogrel) platelet dysfunction.
- Obtain coagulation tests (*i.e.*, PT or INR and aPTT) before transfusion of FFP, if possible (see Table 1 for suggested transfusion criteria for FFP).[‡‡‡‡‡]
- Assess fibrinogen levels before the administration of cryoprecipitate, if possible (see Table 1 for suggested transfusion criteria for cryoprecipitate).
- Desmopressin may be used in patients with excessive bleeding and platelet dysfunction.
- Consider topical hemostatics such as fibrin glue or thrombin gel.
- Consider the use of antifibrinolytics *(i.e.,* ε-aminocaproic acid, tranexamic acid) if fibrinolysis us documented or suspected and if these agents are not already being used.

[†††††] A platelet count is not necessary when a massive transfusion protocol is utilized.
[‡‡‡‡‡] Coagulation tests are not necessary when a massive transfusion protocol is utilized.

- Prothrombin complex concentrates may be used in patients with excessive bleeding and elevated INR.
- Consider recombinant activated factor VII when traditional options for treating excessive bleeding due to coagulopathy have been exhausted. §§§§§
- Fibrinogen concentrate may be used.

§§§§§ The Task Force cautions that there may be a risk of arterial thrombosis with the use of activated factor VII that can result in a myocardial infarction, especially in older patients.

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Table 1: Suggested Criteria for Perioperative Transfusion of Non-RBC Blood Products[******]

Platelets

- Platelet transfusion may be indicated despite an apparently adequate platelet count or in the absence of a platelet count if there is known or suspected platelet dysfunction (*e.g.*, the presence of potent antiplatelet agents, cardiopulmonary bypass, congenital platelet dysfunction) and bleeding.[††††††]
- In surgical or obstetric patients, platelet transfusion is rarely indicated if the platelet count is known to be greater than 100×10^9 /L and is usually indicated when the count is below 50×10^9 /L in the presence of excessive bleeding.

Plasma products (*e.g.*, FFP, PF24 or Thawed Plasma).[‡‡‡‡‡]

- FFP is indicated:
  - For correction of excessive microvascular bleeding (*i.e.*, coagulopathy) in the presence of an INR greater than 2.0, in the absence of heparin
  - For correction of excessive microvascular bleeding secondary to coagulation factor deficiency in patients transfused with more than one blood volume (approximately 70ml/kg) and when PT or INR and aPTT cannot be obtained in a timely fashion
  - For urgent reversal of warfarin therapy when PCCs are not available
  - For correction of known coagulation factor deficiencies for which specific concentrates are unavailable.
- FFP is not indicated:
  - If PT or INR and aPTT are normal.
  - Solely for augmentation of plasma volume or albumin concentration.
- Administer FFP in doses calculated to achieve a minimum of 30% of plasma factor concentration. Four to five platelet concentrates, 1 unit single-donor apheresis platelets, or 1 unit fresh whole blood[§§§§§§] provide a quantity of coagulation factors similar to that contained in one unit FFP.

Cryoprecipitate

- Cryoprecipitate is indicated:
  - When a test of fibrinogen activity indicates a fibrinolysis.
  - When the fibrinogen concentration is less than 80-100 mg/dl in the presence of

[******] This table displays some transfusion criteria that may suggest when to transfuse with the above blood products. The decision to apply some or all of the criteria shown in this table is dependent upon the clinical context and judgment of the practitioner. The table is not intended as a mandatory or exhaustive list. Scientific evidence is insufficient to evaluate the perioperative benefit of applying the above suggested criteria.

[††††††] The proper dose of platelets should be based on recommendations of the local institutional transfusion committee

[‡‡‡‡‡] FFP refers to plasma frozen within 8 hr after Phlebotomy, PF24 refers to plasma frozen within 24 hr after Phlebotomy, and Thawed Plasma refers to FFP stored up to 5 days at 1-6 C after thawing. In the USA, it is common practice to use these terms interchangeably. In this table, the term FFP refers to the use of any of these plasma products.

[§§§§§§] Many institutions in the United States no longer have fresh whole blood available from the blood bank.

excessive bleeding.[*******]
    - As an adjunct in massively transfused patients when fibrinogen concentrations cannot be measured in a timely fashion.
    - For patients with congenital fibrinogen deficiencies.
    - Whenever possible, decisions regarding patients with congenital fibrinogen deficiencies should be made in consultation with the patient's hematologist.
- Transfusion of cryoprecipitate is rarely indicated if fibrinogen concentration is greater than 150 mg/dl in non-pregnant patients.
- Treat bleeding patients with von Willebrand disease types 1 and 2A with desmopressin and subsequently with specific VWF/FVIII concentrate, if available. Cryoprecipate should be administered if there is no response to or availability of desmopressin or VWF/FVIII concentrate.
- Treat bleeding patients with von Willebrand disease types 2B, 2M, 2N and 3 with specific VWF/FVIII concentrate, if available. If VWF/FVIII concentrate is not available, cryoprecipitate is indicated.

[*******] Cryoprecipitate may be indicated at a higher fibrinogen concentration in actively bleeding obstetric patients.

Appendix I: Summary of Recommendations

I. Patient Evaluation

- Review previous medical records and interview the patient or family to identify:
  - Prior blood transfusion
  - History of drug-induced coagulopathy (*e.g.*, warfarin, clopidogrel, aspirin and other anticoagulants, as well as vitamins or herbal supplements that may affect coagulation *[Appendix 3]*)
  - The presence of congenital coagulopathy
  - History of thrombotic events (*e.g.*, deep vein thrombosis, pulmonary embolism)
  - Risk factors for organ ischemia (*e.g.*, cardiorespiratory disease) which may influence the ultimate transfusion trigger for red blood cells (*e.g.*, hemoglobin level)
- Inform patients of the potential risks *versus* benefits of blood transfusion and elicit their preferences.
- Review available laboratory test results including hemoglobin, hematocrit and coagulation profiles.
- Order additional laboratory tests depending on a patient's medical condition (*e.g.*, coagulopathy, anemia).
- Conduct a physical examination of the patient (*e.g.*, ecchymosis, petechiae, pallor).
- If possible, perform the preoperative evaluation well enough in advance (*e.g.*, several days to weeks) to allow for proper patient preparation.

II. Preadmission Patient Preparation

- Erythropoietin with or without iron may be administered when possible to reduce the need for allogeneic blood in selected patient populations (*e.g.*, renal insufficiency, anemia of chronic disease, refusal of transfusion).[†††††††]
- Administer iron to patients with iron deficiency anemia if time permits.
- In consultation with an appropriate specialist, discontinue anticoagulation therapy (*e.g.*, warfarin, anti-Xa drugs, antithrombin agents) for elective surgery.
  - Transition to a shorter acting drug (*e.g.*, heparin, low molecular weight heparin) may be appropriate in selected patients.
- If clinically possible, discontinue non-aspirin antiplatelet agents (*e.g.*, thienopyridines such as clopidogrel, ticagrelor, or prasugrel) for a sufficient time in advance of surgery, except for patients with a history of percutaneous coronary interventions.[‡‡‡‡‡‡‡]
  - Aspirin may be continued on a case-by-case basis.
- The risk of thrombosis *versus* the risk of increased bleeding should be considered when altering anticoagulation status.

[†††††††] The Task Force recognizes that erythropoietin administration is perceived as being expensive and requires time (in weeks) to induce a significant increase in hemoglobin concentration.

[‡‡‡‡‡‡‡] The Task Force cautions that clopidogrel and aspirin should not be stopped prior to surgery in patients with coronary stents placed in the last 3 months for bare metal stents and 1 year for drug eluting stents due to the risk of perioperative myocardial infarction. See "American Society of Anesthesiologists Committee on Standards and Practice Parameters: Practice alert for the perioperative management of patients with coronary artery stents: a report by the American Society of Anesthesiologists Committee on Standards and Practice Parameters. Anesthesiology 2009; 110:22-23.

- Assure that blood and blood components are available for patients when significant blood loss or transfusion is expected.
- When autologous blood is preferred, the patient may be offered the opportunity to donate blood before admission only if there is adequate time for erythropoietic reconstitution.[§§§§§§§]

III. Preprocedure Preparation

Blood management protocols:

- Multimodal protocols or algorithms may be employed as strategies to reduce the utilization of blood products. However, no single algorithm or protocol can be recommended at this time.
- A restrictive red blood cell transfusion strategy may be safely used to reduce transfusion administration.[********]
    - The determination of whether hemoglobin concentrations between 6 and 10 g/dl justify or require red blood cell transfusion should be based on potential or actual ongoing bleeding (rate and magnitude), intravascular volume status, signs of organ ischemia, and adequacy of cardiopulmonary reserve.
    - Red blood cells should be administered unit-by-unit, when possible, with interval reevaluation.
- A protocol for avoidance of transfusion may be used as a strategy to reduce blood loss for patients in whom transfusion is refused or is not possible.
- A massive (*i.e.*, hemorrhagic) transfusion protocol may be used when available as a strategy to optimize the delivery of blood products to massively bleeding patients.
- Use a maximal surgical blood order schedule, when available and in accordance with your institutional policy, as a strategy to improve the efficiency of blood ordering practices.

Reversal of anticoagulants:

- For urgent reversal of warfarin, administer prothrombin complex concentrates (PCCs) in consultation with the appropriate specialist, or administer FFP.
- Administer vitamin K for selected patients for non-urgent reversal of warfarin, except when rapid restoration of anticoagulation after surgery is required.

Antifibrinolytics for prophylaxis of excessive blood loss:

- Use antifibrinolytic therapy for prophylaxis of the use of allogeneic blood transfusion in patients undergoing cardiopulmonary bypass.
- Consider using antifibrinolytic therapy for prophylaxis in certain orthopedic surgery.
    - Consider using antifibrinolytic therapy for prophylaxis in liver surgery and other clinical circumstances at high-risk for excessive bleeding.[††††††††]

Acute normovolemic hemodilution (ANH):

- Consider ANH to reduce allogeneic blood transfusion in patients at high-risk for excessive bleeding (*e.g.*, major cardiac, orthopedic, thoracic, or liver surgery), if possible.[‡‡‡‡‡‡‡]

[§§§§§§§] The Task Force cautions that preadmission blood donation may induce preoperative anemia, increase total intraoperative (autologous or allogeneic) transfusions, and increase costs.

[********] Red blood cells refers to all red blood cell containing components. Transfusion of red blood cells is rarely necessary when the hemoglobin concentration is more than 10 g/dl.

[††††††††] The safety of antifibrinolytics has not been established in hypercoagulable patients (*e.g.*, pregnancy)

IV. Intraoperative and Postoperative Management of Blood Loss

Allogeneic red blood cell transfusion:

- Administer blood without consideration of duration of storage.
- Leukocyte reduced blood may be used for transfusion for the purpose of reducing complications associated with allogeneic blood transfusion.

Reinfusion of recovered red blood cells:

- Reinfuse recovered red blood cells as a blood-sparing intervention in the intraoperative period, when appropriate.

Intraoperative and postoperative patient monitoring:

- Periodically conduct a visual assessment of the surgical field jointly with the surgeon to assess the presence of excessive microvascular (*i.e.*, coagulopathy) or surgical bleeding.
- Use standard methods for quantitative measurement of blood loss, including checking suction canisters, surgical sponges, and surgical drains.
- Monitor for perfusion of vital organs using standard ASA monitors (i.*e.*, blood pressure, heart rate, oxygen saturation, electrocardiography) in addition to observing clinical symptoms and physical exam features.[§§§§§§§§]
    - Additional monitoring may include echocardiography, renal monitoring (urine output), cerebral monitoring (*i.e.*, cerebral oximetry and near infrared spectroscopy), analysis of arterial blood gasses, and mixed venous oxygen saturation.
- If anemia is suspected, monitor hemoglobin/hematocrit values based on estimated blood loss and clinical signs.
- If coagulopathy is suspected, obtain standard coagulation tests (*e.g.*, International Normalized Ratio [INR], aPTT, fibrinogen concentration) or viscoelastic assays *(e.g.*, thromboelastography [TEG] and rotational thromboelastometry [ROTEM]), if available, as well as platelet count.
- During and after transfusion, periodically check for signs of a transfusion reaction includin hyperthermia, hemoglobinuria, microvascular bleeding, hypoxemia, respiratory distress, elevated peak airway pressure, urticaria, hypotension and signs of hypocalcemia.
    - If signs of a transfusion reaction are apparent, immediately stop the transfusion, give supportive therapy, and initiate supportive care.
    - Notify the blood bank of the transfusion reaction case.

Treatment of excessive bleeding:

In patients with excessive bleeding, the following recommendations are made based upon the evidence for each of these interventions when studied singly or when compared with placebo. The impact of combinations of these interventions is not addressed in these Guidelines.

- Obtain a platelet count before transfusion of platelets, if possible (see Table 1 for suggested transfusion criteria for platelets).[*********] In addition, obtain a test of

[‡‡‡‡‡‡‡‡] ANH may not be possible due to preexisting patient factors such as small blood volume, low hemoglobin, or presence of ischemic disease.

[§§§§§§§§] American Society of Anesthesiologists: Standards for Basic Anesthetic Monitoring (last amended October 20, 2010, effective date July 1, 2011).

[*********] A platelet count is not necessary when a massive transfusion protocol is utilized.

platelet function, if available, in patients with suspected or drug-induced (*e.g.*, clopidogrel) platelet dysfunction.

- Obtain coagulation tests (*i.e.*, PT or INR and aPTT) before transfusion of FFP, if possible (see Table 1 for suggested transfusion criteria for FFP).[†††††††††]
- Assess fibrinogen levels before the administration of cryoprecipitate, if possible (see Table 1 for suggested transfusion criteria for cryoprecipitate).
- Desmopressin may be used in patients with excessive bleeding and platelet dysfunction.
- Consider topical hemostatics such as fibrin glue or thrombin gel.
- Consider the use of antifibrinolytics *(i.e.*, ε-aminocaproic acid, tranexamic acid) if fibrinolysis is documented or suspected and if these agents are not already being used.
- Prothrombin complex concentrates may be used in patients with excessive bleeding and elevated INR.
- Consider recombinant activated factor VII when traditional options for treating excessive bleeding due to coagulopathy have been exhausted. [‡‡‡‡‡‡‡‡]
- Fibrinogen concentrate may be used.

[†††††††††] Coagulation tests are not necessary when a massive transfusion protocol is utilized.

[‡‡‡‡‡‡‡‡] The Task Force cautions that there may be a risk of arterial thrombosis with the use of activated factor VII that can result in a myocardial infarction, especially in older patients.

Appendix 2: Methods and Analyses

A. State of the Literature.

For these updated Guidelines, a review of studies used in the development of previous update was combined with studies published subsequent to approval of the update in 2005.[§§§§§§§§§] The scientific assessment of these Guidelines was based on evidence linkages or statements regarding potential relationships between clinical interventions and outcomes. The interventions listed below were examined to assess their relationship to a variety of outcomes related to the perioperative blood transfusion and adjuvant therapies.

Patient Evaluation:

- Reviewing medical records (checking for acquired or congenital conditions, previous lab tests)
- Conducting a patient interview
- Conducting/ordering new laboratory tests when indicated
    - Hemoglobin or hematocrit (to identify preoperative anemia)
    - Coagulation profile (PT, aPTT, ACT, TEG)
    - Type and cross versus type and screen
    - Maximum surgical blood ordering schedule for elective procedures

Preadmission Patient Preparation:

- Prevention or reduction of perioperative anemia
    - Erythropoietin
    - Iron
- Discontinuation of anticoagulants
    - Warfarin
- Discontinuation of anti-thrombotic agents
    - Clopidogrel, Ticagralor, Prasugrel or other thienopyridines
    - Aspirin
- Preadmission autologous blood donation (PAD)
    - PAD *versus* allogeneic blood or blood products
    - PAD *versus* preprocedure acute normovolemic hemodilution (ANH)
    - PAD *versus* intraoperative or postoperative blood recovery

Preprocedure preparation:

- Blood management protocol
    - Multimodality protocol or algorithm
    - Liberal versus restrictive transfusion protocol

[§§§§§§§§§] American Society of Anesthesiologists: Practice Guidelines for Perioperative Blood Transfusion and Adjuvant Therapies: An Updated Report. *ANESTHESIOLOGY 2006;105:198-208*

    - Non-transfusion protocol (*i.e.*, bloodless surgery)
    - Massive transfusion protocol
    - Maximum surgical blood ordering schedule for elective procedures
- Reversal of anticoagulants
    - Prothrombin complex concentrates (PCC)
        - Bebulin
        - Profilnin
        - Kcentra (Beriplex, Confidex)
    - Vitamin K
- Antifibrinolytics for prophylaxis of excessive blood loss
    - ε-Aminocaproic acid
    - Tranexamic acid
- Acute normovolemic hemodilution (ANH)
    - ANH versus no ANH
    - ANH combined with intraoperative blood recovery (ICSB) versus either ANH or ISCB

Intraoperative and Postoperative Interventions:

- Allogeneic red blood cell transfusion:
    - Age of stored RBCs
    - Leukocyte reduction
- Autologous red blood cell transfusion:
    - Intraoperative blood recovery
        - Cell salvage
        - Whole blood (WB)
    - Postoperative blood recovery
        - Cell salvage
        - Whole blood (WB)
- Intraoperative and postoperative patient monitoring:
    - Monitoring blood loss:
        - Visual assessment of the surgical field
            - Extent of blood present
            - Presence of microvascular bleeding
            - Surgical sponges
            - Clot size and shape
            - Volume in suction canister
    - Monitoring for inadequate perfusion and oxygenation of vital organs
        - Cardiac monitoring (blood pressure, heart rate, oxygen saturation)
        - Renal monitoring (urine output)
        - Cerebral monitoring
            - Cerebral oximetry
            - Near infrared spectroscopy (NIRS)
        - Arterial blood gas measurement
        - Mixed venous oxygen saturation
    - Monitoring for non-RBC transfusion – coagulopathy
        - Platelet function monitoring
        - Viscoelastic haemostatic assays (VHA)

878 - Thromboelastrography (TEG)
879 - Rotational thromboelastometry (ROTEM)
880 - Monitoring (periodic checking) for adverse effects of transfusions
881 - Transfusion-related acute lung injury (TRALI)
882 - Hemolytic *(ABO incompatibility)* transfusion reactions
883 - Citrate toxicity (hypocalcemia*)*
884 - Transfusion-associated circulatory overload (TACO)
885 - Bacterial contamination
886 - Immunomodulation (*e.g.*, graft versus host disease [GVHD], infection)
887 - Treatment of excessive bleeding
888 - Transfusion treatments:
889 - Platelet transfusion
890 - Fresh frozen plasma transfusion
891 - Cryoprecipitate
892 - Pharmacologic treatments:
893 - Desmopressin (DDAVP)
894 - Antifibrinolytics
895 - ε-Aminocaproic acid
896 - Tranexamic acid
897 - Topical hemostatics
898 - Fibrin glue
899 - Thrombin gel
900 - Prothrombin complex concentrates (PCC)
901 - PCC versus FFP
902 - Bebulin
903 - Profilnin
904 - Kcentra (Beriplex, Confidex)
905 - Coagulation factor concentrates
906 - Recombinant Factor VIIa
907 - Treatments for hypofibrinogenemia:
908 - Cryoprecipitate
909 - Fibrinogen concentrate (Riastap)

910 For the literature review, potentially relevant clinical studies were identified *via* electronic
911 and manual searches of the literature. The updated searches covered an 11-year period from
912 2004 through 2014. Over 1800 new citations that addressed topics related to the evidence
913 linkages were identified. These articles were reviewed and those meeting the appropriate criteria
914 as outlined in the "Focus" section above were combined with pre-2005 articles used in the
915 previous update, resulting in a total of 520 articles that contained direct linkage-related evidence.
916 A complete bibliography used to develop these Guidelines, organized by section, is available as
917 Supplemental Digital Content 2, http://links.lww.com/ALN/___.

Initially, each pertinent study finding was classified and summarized to determine meta-analysis potential. Literature pertaining to eleven evidence linkages contained enough studies with well-defined experimental designs and statistical information sufficient for meta-analyses. These linkages were (1) erythropoietin *versus* placebo, (2) ε-aminocaproic acid *versus* placebo; (3) tranexamic acid *versus* placebo administered before or during surgery, (4) acute normovolemic hemodilution (ANH) *versus* no acute normovolemic hemodilution; (5) ANH with intraoperative red blood cell recovery *versus* red blood cell recovery alone, (6) restrictive versus liberal transfusion strategy, (7) intraoperative red blood cell recovery *versus*conventional transfusion, (8) desmopressin *versus* placebo, (9) tranexamic acid *versus* placebo administered after surgery, (10) fibrin glue *versu*s no fibrin glue, and (11) recombinant activated factor VII *versus* placebo *(Table 2).*

General variance-based effect-size estimates or combined probability tests were obtained for continuous outcome measures, and Mantel-Haenszel odds-ratios were obtained for dichotomous outcome measures. Two combined probability tests were employed as follows: (1) the Fisher combined test, producing chi-square values based on logarithmic transformations of the reported P values from the independent studies, and (2) the Stouffer combined test, providing weighted representation of the studies by weighting each of the standard normal deviates by the size of the sample. An odds-ratio procedure based on the Mantel-Haenszel method for combining study results using 2 x 2 tables was used with outcome frequency information. An acceptable significance level was set at $P < 0.01$ (one-tailed). Tests for heterogeneity of the independent studies were conducted to assure consistency among the study results. DerSimonian-Laird random-effects odds ratios were obtained when significant heterogeneity was found ($P < 0.01$). To control for potential publishing bias, a "fail-safe n" value was calculated. No search for unpublished studies was conducted, and no reliability tests for locating research results were

done. To be accepted as significant findings, Mantel-Haenszel odds-ratios must agree with combined test results whenever both types of data are assessed. In the absence of Mantel-Haenszel odds-ratios, findings from both the Fisher and weighted Stouffer combined tests must agree with each other to be acceptable as significant.

For the previous update, interobserver agreement among Task Force members and two methodologists was established by interrater reliability testing. Agreement levels using a kappa (k) statistic for two-rater agreement pairs were as follows: (1) type of study design, k = 0.83-0.94; (2) type of analysis, k = 0.87-0.94; (3) evidence linkage assignment, k = 0.89-0.96; and (4) literature inclusion for database, k = 0.44-0.78. Three-rater chance-corrected agreement values were: (1) study design, Sav = 0.89, Var (Sav) = 0.004; (2) type of analysis, Sav = 0.88, Var (Sav) = 0.004; (3) linkage assignment, Sav = 0.92 Var (Sav) = 0.002; (4) literature database inclusion, Sav = 0.58 Var (Sav) = 0.054. These values represent moderate to high levels of agreement.

B. Consensus-Based Evidence.

For the previous update, consensus was obtained from multiple sources, including: (1) survey opinion from consultants who were selected based on their knowledge or expertise in perioperative blood transfusion and adjuvant therapies, (2) survey opinions from a randomly selected sample of active members of the ASA, (3) testimony from attendees of two publicly-held open forums at two national anesthesia meetings,[**********] (4) Internet commentary, and (5) Task Force opinion and interpretation. The survey rate of return was 31% (n = 21 of 67) for consultants, and 29% (n = 87 of 300) for membership respondents. Survey results are reported in Tables 3 and 4, and summarized in the text of the Guidelines.

For the previous update, the consultants were asked to indicate which, if any, of the evidence linkages would change their clinical practices if the Guidelines were instituted. The rate of

[**********] 79th Clinical and Scientific Congress of the International Anesthesia Research Society, March 12, 2005, Honolulu, Hawaii, and 27th Annual Meeting of the Society of Cardiovascular Anesthesiologists, May 14, 2005, Baltimore, Maryland.

return was 24% (n = 16 of 67). The percent of responding consultants expecting *no change* associated with each linkage were as follows: preoperative evaluation - 75%; discontinuation of anticoagulation and delay of surgery- 94%; drugs to manage perioperative anemia - 75%; drugs to promote coagulation and minimize blood loss - 81%; preoperative autologous blood collection - 88%; monitoring for inadequate perfusion and oxygenation - 94%; monitoring for transfusion indications - 88%; transfusion of allogeneic red blood cells - 94%, transfusion of autologous blood - 100%; transfusion of platelets - 88%; transfusion of frozen plasma - 88%; transfusion of cryoprecipitate - 94%; treatment of excessive bleeding - 88%; and monitoring and laboratory testing for transfusion reactions - 88%. Eighty-eight percent of the respondents indicated that the Guidelines would have *no effect* on the amount of time spent on a typical case. Two respondents (12%) indicated that there would be an increase in the amount of time they would spend on a typical case with the implementation of these Guidelines. The amount of increased time anticipated by these respondents ranged from 5-10 min.

Table 2. Meta-Analysis Summary

Linkages	N	Fisher Chi-square	p	Weighted Stouffer Zc	p	Effect Size	Mantel-Haenszel OR	CI	Heterogeneity Significance	Heterogeneity Effect Size
Preadmission patient preparation										
Prevent or reduction of perioperative anemia										
Erythropoietin vs. placebo [1]										
Blood volume transfused	8	67.93	0.001	-4.80	0.001	0.21	-	-	0.001	0.003
Patients transfused	15	-	-	-	-	-	0.38	0.27-0.53	-	0.039
Pts. transfused (without iron)	7	-	-	-	-	-	0.45	0.26-0.78	-	0.038
Pts. transfused (with iron)	8	-	-	-	-	-	0.34	0.23-0.52	-	0.179
Preadmission patient preparation										
Antifibrinolytics for Prophylaxis of Excessive Bleeding										
ε-Aminocaproic acid vs. placebo (administered before or during surgery) [1]										
Total blood loss	7	58.34	0.001	-5.35	0.001	-0.28	-	-	0.490	0.597
Patients transfused	9	-	-	-	-	-	0.58	0.33-0.96	-	0.043
Tranexamic acid vs. placebo (administered before or during surgery) [1]										
Intraoperative blood loss	10	68.83	0.001	-4.41	0.001	-0.19	-	-	0.343	0.340
Postoperative blood loss	12	172.51	0.001	-10.20	0.001	-0.36	-	-	0.001	0.001
Total blood loss	13	180.64	0.001	-6.22	0.001	-0.30	-	-	0.051	0.002
Patients transfused [2]	13	-	-	-	-	-	0.29	0.13-0.86	-	0.005
Tranexamic acid vs. placebo (administered after surgery) [1]										
Total blood loss	5	91.77	0.001	-10.84	0.001	-0.59	-	-	0.043	0.001
Patients transfused [2]	6	-	-	-	-	-	0.33	0.49-2.38	-	0.001

Acute Normovolemic Hemodilution (ANH)										
ANH vs. no ANH										
Volume transfused with allogeneic blood	7	60.84	0.001	-2.79	0.003	-0.21	-	-	0.003	0.001
Patients transfused with allogeneic blood	11	-	-	-	-	-	0.59	0.38-0.90	-	0.308
ANH+intraoperative blood recovery vs. intraoperative blood recovery										
Volume transfused with allogeneic blood	7	64.52	0.001	-5.05	0.001	-0.21	-	-	0.011	0.017
Patients transfused with allogeneic blood	8	-	-	-	-	-	0.71	0.48-1.05	-	0.046
Intraoperative and postoperative interventions										
Restrictive vs. liberal transfusion protocol										
Volume transfused with allogeneic blood	5	49.88	0.001	-3.31	0.001	-0.13	-	-	0.022	0.001
Intraoperative blood recovery vs. conventional transfusion										
Volume transfused with allogeneic blood	7	66.07	0.001	-4.16	0.001	-0.26	-	-	0.036	0.001
Patients transfused with allogeneic blood [2]	9	-	-	-	-	-	0.29	0.10-1.22	-	0.001
Drugs to treat excessive bleeding										
Desmopressin vs. placebo [1]										
Postoperative blood loss	6	51.72	0.001	-2.34	0.010	-0.11	-	-	0.001	0.001
Patients transfused	5	-	-	-	-	-	0.92	0.51-1.66	-	0.125

Topical hemostatics

Fibrin glue vs. no fibrin glue										
Postop/total blood loss	11	145.03	0.001	-4.34	0.001	-0.29	-	-	0.001	0.001
Patients transfused	7	-	-	-	-	-	0.58	0.34-0.97	-	0.012
Factor VII vs. no Factor VII [1]										
Blood volume transfused	5	44.55	0.001	-0.01	0.496	-0.21	-	-	0.075	0.001
Patients transfused [2]	6	-	-	-	-	-	0.16	0.03-2.85	-	0.001

[1] Double-blind studies only.
[2] DerSimonian-Laird random effects odds ratio.

CI = 99% confidence interval; OR = odds ratio; pts = patients

Table 3. Consultant Survey Responses ††††††††††

		Percent Responding to Each Item				
I. Patient Evaluation:	N	Strongly Agree	Agree	Uncertain	Disagree	Strongly Disagree
1. Review previous medical records and interview the patient or family to identify prior blood transfusion, history of drug-induced coagulopathy, presence of congenital coagulopathy, history of thrombotic events, and risk factors for organ ischema	74	68.9*	24.3	2.7	4.1	0.0
2. Inform patients of the potential risks vs. benefits of blood transfusion and elicit their preferences	74	75.7*	12.2	8.1	4.1	0.0
3. Review available laboratory test results including hemoglobin, hematocrit, and coagulation profiles and order additional laboratory tests depending on a patient's medical condition (*e.g.*, coagulopathy, anemia)	74	91.9*	6.8	1.4	0.0	0.0
4. Conduct a physical examination of the patient (*e.g.*, ecchymoses, petechiae, pallor)	74	58.1*	29.7	10.8	1.4	0.0
II. Preadmission Patient Preparation:						
5. Erythropoietin with or without iron may be administered when possible to reduce the need for allogeneic blood in select patient populations (*e.g.*, renal insufficiency, anemia of chronic disease, refusal of transmission)	72	43.2	30.6*	19.4	5.6	1.4
6. Administer iron to patients with iron deficiency anemia if time permits	71	63.4*	31.0	2.8	2.8	0.0
7. In consultation with an appropriate specialist, discontinue anticoagulation therapy (*e,g,*. warafin, anti-Xa drugs, anti-thrombin agents) for elective surgery	71	74.6*	14.1	11.3	0.0	0.0
8. If clinically possible, discontinue non-aspirin antiplatelet agents (*e.g.*, thienopyridines such as clopidogrel, ticagrelor, or prasugrel) for a sufficient time in advance of surgery, except for patients with a history of percutaneous coronary interventions)	71	66.2*	18.3	12.7	2.8	0.0
9. The risk of thrombosis vs. the risk of increased bleeding should be considered when altering anticoagulation status	72	88.9*	11.1	0.0	0.0	0.0
10. Assure that blood and blood components are available for patients when significant blood loss or transfusion is expected	72	94.4*	4.2	1.4	0.0	0.0

†††††††††† N = the number of consultants who responded to each item. An asterisk beside a percentage score indicates the median.

11. When autologous blood is preferred, the patient should be offered the opportunity to donate blood before admission only if there is adequate time for erythropoietic reconstitution	71	23.9	31.0*	23.9	11.3	9.9
III. Preprocedure Preparation:						
Blood Management Protocols						
12. Employ multimodal protocols or algorithms as strategies to reduce the utilization of blood products	72	66.7*	27.8	4.2	1.4	0.0
13. A restrictive red blood cell transfusion strategy may be used to reduce transfusion requirements	71	59.2*	35.2	2.8	1.4	1.4
14. A protocol for avoidance of transfusion (*i.e.*, bloodless surgery) may be used as a strategy to reduce blood loss for patients in whom transfusion is refused or is not possible	72	69.4*	25.0	5.6	0.0	0.0
15. Use massive transfusion protocol when available as a strategy to optimize the delivery of blood products to massively bleeding patients	71	78.9*	15.5	4.2	1.4	0.0
16. Use a maximal surgical blood order schedule, when available and in accordance with your institutional policy, as a strategy to improve the efficiency of blood ordering practices	72	44.4	30.6*	23.6	1.4	0.0
Reversal of Anticoagulants						
17. For urgent reversal of warafin, administer prothrombin complex concentrates (PCCs) in consultation with the appropriate specialist, or administer fresh frozen plasma (FFP)	71	53.5*	35.2	4.2	4.2	2.8
18. Administer vitamin K for non-urgent reversal of warafin, except when rapid restoration of anticoagulation after surgery is required	71	60.6*	28.2	5.6	1.4	4.2
Antifibrinolytics for prophylaxis of excessive bleeding						
19. In patients at risk for excessive bleeding, use prophylactic antifibrinolytic therapy to reduce the bleeding and risk of transfusion	71	28.2	39.4*	16.9	11.3	4.2
20. Use antifibrinolytic therapy to reduce allogeneic blood transfusion in patients undergoing cardiopulmonary bypass	71	46.5	35.2*	15.5	2.8	0.0
21. Consider using antifibrinolytic therapy in other clinical circumstances at high-risk for excessive bleeding	69	30.4	49.3*	17.4	2.9	0.0

Acute Normovolemic Hemodilution						
22. Use acute normovolemic hemodilution (ANH) to reduce allogeneic blood transfusion in patients at high-risk for excessive bleeding (*e.g.*, major cardiac, orthopedic, thoracic, or liver surgery), if possible	72	22.2	30.6*	25.0	18.1	4.2
IV. Intraoperative and Postoperative Management of Blood Loss and Transfusions:						
Allogeneic Red Blood Cell Transfusion						
23. Administer blood without consideration of duration of storage	72	15.3	26.4	29.2*	18.1	11.1
24. Leukocyte reduced blood may be used for transfusion for the purpose of reducing complications associated with allogeneic blood transfusion	72	50.0*	33.3	11.1	5.6	0.0
Reinfusion of Recovered Red Blood Cells						
25. Reinfuse recovered red blood cells as a blood-sparing intervention in the intraoperative and/or postoperative period	72	65.3*	23.6	9.7	1.4	0.0
Intraoperative and Postoperative Patient Monitoring						
26. Periodically conduct a visual assessment of the surgical field jointly with the surgeon to assess the presence of excessive microvascular (i.e., coagulopathy) or surgical bleeding	72	72.2*	19.4	8.3	0.0	0.0
27. Use standard methods for quantitative measurement of blood loss including checking suction canisters, surgical sponges, and surgical drains	72	68.1*	27.8	4.2	0.0	0.0
28. Monitor for perfusion of vital organs using standard ASA monitors (i.e., blood pressure, heart rate, oxygen saturation, electro-cardiography) in addition to observing clinical symptoms and physical exam features	71	81.7*	12.7	5.6	0.0	0.0
29. Additional monitoring may include echocardiography, renal monitoring (urine output), cerebral monitoring (i.e., cerebral oximetry and near infrared spectroscopy), analysis of arterial blood gasses, and mixed venous oxygen saturation	72	69.4*	26.4	4.2	0.0	0.0
30. If anemia is suspected, monitor hemoglobin /hematocrit values based on estimated blood loss and clinical signs	72	73.6*	18.1	8.3	0.0	0.0
31. If coagulopathy is suspected, obtain viscoelastic assays (*e.g.*, thromboelastography and rotational thromboelastometry, when available, as well as platelet count	70	48.6	25.7*	14.3	7.1	4.3

32. If viscoelastic assays are not available, obtain standard coagulation tests (*e.g.,* International Normalized Ratio [INR], aPTT, fibrinogen concentration), as well as platelet count for monitoring	70	68.6*	28.6	1.4	1.4	0.0
33. During and after transfusion, periodically check for hyperthermia, hemoglobinuria, microvascular bleeding, hypoxemia, respiratory distress, elevated peak airway pressure, urticaria, hypotension, and signs of hypocalcemia	71	73.2*	25.4	1.4	0.0	0.0
34. Before instituting therapy for transfusion reactions, stop the blood transfusion and order appropriate diagnostic testing	71	64.8*	23.9	7.0	2.8	1.4
Treatment of Excessive Bleeding						
35. In patients with excessive bleeding:						
a) obtain a platelet count before transfusion of platelets if possible	70	47.1	31.4*	7.1	11.4	2.9
b) in addition, obtain a test of platelet function, if available, in patients with suspected or drug-induced (e.g., clopidogrel) platelet dysfunction	70	27.1	17.1	22.9*	27.1	5.7
36. In patients with excessive bleeding, obtain coagulation tests (*i.e.,* PT or INR and aPTT) before transfusion of FFP, if possible	71	47.9	31.0*	9.9	7.0	4.2
37. In patients with excessive bleeding, assess fibrinogen levels before the administration of cryoprecipitate, if possible	70	50.0*	34.3	10.0	2.9	2.9
38. In patients with excessive bleeding and platelet dysfunction, consider the use of desmopressin	70	32.9	38.6*	22.9	4.3	1.4
39. In patients with excessive bleeding, consider topical hemostatics such as fibrin glue or thrombin gel	70	45.7	34.3*	17.1	2.9	0.0
40. In patients with excessive bleeding, consider the use of antifibrinolytics (*i.e.,* ε-aminocaproic acid, tranexamic acid), if not already being used	70	47.1	40.0*	11.4	1.4	0.0
41. In patients with excessive bleeding and elevated INR, consider the use of prothrombin complex concentrates (PCCs)	70	30.0	38.6*	24.3	1.4	5.7
42. In patients with excessive bleeding, consider the use of fibrinogen concentrate	70	22.9	37.1*	30.0	4.3	5.7
43. When traditional options for treating excessive bleeding due to coagulopathy have been exhausted, consider administering recombinant activated factor VII	71	22.5	49.3*	16.9	5.6	5.6

Table 4. ASA Membership Survey Responses ‡‡‡‡‡‡‡‡‡

		Percent Responding to Each Item				
I. Patient Evaluation:	N	Strongly Agree	Agree	Uncertain	Disagree	Strongly Disagree
1. Review previous medical records and interview the patient or family to identify prior blood transfusion, history of drug-induced coagulopathy, presence of congenital coagulopathy, history of thrombotic events, and risk factors for organ ischema	386	54.9*	24.1	14.2	4.9	1.8
2. Inform patients of the potential risks vs. benefits of blood transfusion and elicit their preferences	382	47.4	29.3*	17.3	4.2	1.8
3. Review available laboratory test results including hemoglobin, hematocrit, and coagulation profiles and order additional laboratory tests depending on a patient's medical condition (*e.g.*, coagulopathy, anemia)	384	85.2*	12.5	1.6	0.5	0.3
4. Conduct a physical examination of the patient (*e.g.,* ecchymoses, petechiae, pallor)	384	47.4	33.6*	12.5	5.2	1.3
II. Preadmission Patient Preparation:						
5. Erythropoietin with or without iron may be administered when possible to reduce the need for allogeneic blood in select patient populations (*e.g.*, renal insufficiency, anemia of chronic disease, refusal of transmission)	351	39.9	37.3*	16.2	5.4	1.1
6. Administer iron to patients with iron deficiency anemia if time permits	351	53.6*	27.6	13.4	3.1	2.3
7. In consultation with an appropriate specialist, discontinue anticoagulation therapy (*e,g,*. warafin, anti-Xa drugs, anti-thrombin agents) for elective surgery	350	70.9*	22.6	5.7	0.6	0.3
8. If clinically possible, discontinue non-aspirin antiplatelet agents (*e.g.,* thienopyridines such as clopidogrel, ticagrelor, or prasugrel) for a sufficient time in advance of surgery, except for patients with a history of percutaneous coronary interventions)	351	75.2*	19.1	4.0	1.1	0.6
9. The risk of thrombosis vs. the risk of increased bleeding should be considered when altering anticoagulation status	353	85.8*	12.7	1.4	0.0	0.0
10. Assure that blood and blood components are available for patients when significant blood loss or transfusion is expected	348	94.3*	4.6	0.6	0.6	0.0

‡‡‡‡‡‡‡‡‡ N = the number of ASA members who responded to each item. An asterisk beside a percentage score indicates the median.

11. When autologous blood is preferred, the patient should be offered the opportunity to donate blood before admission only if there is adequate time for erythropoietic reconstitution	354	37.9	35.6*	18.4	4.8	3.4
III. Preprocedure Preparation:						
Blood Management Protocols						
12. Employ multimodal protocols or algorithms as strategies to reduce the utilization of blood products	345	57.4*	29.3	9.6	3.8	0.0
13. A restrictive red blood cell transfusion strategy may be used to reduce transfusion requirements	346	42.2	33.8*	18.8	4.6	0.6
14. A protocol for avoidance of transfusion (*i.e.*, bloodless surgery) may be used as a strategy to reduce blood loss for patients in whom transfusion is refused or is not possible	344	54.9*	31.1	11.0	2.6	0.3
15. Use massive transfusion protocol when available as a strategy to optimize the delivery of blood products to massively bleeding patients	345	78.8*	17.7	2.0	1.2	0.3
16. Use a maximal surgical blood order schedule, when available and in accordance with your institutional policy, as a strategy to improve the efficiency of blood ordering practices	342	40.6	29.5*	25.1	3.5	1.2
Reversal of Anticoagulants						
17. For urgent reversal of warafin, administer prothrombin complex concentrates (PCCs) in consultation with the appropriate specialist, or administer fresh frozen plasma (FFP)	345	55.1*	36.2	7.5	0.9	0.3
18. Administer vitamin K for non-urgent reversal of warafin, except when rapid restoration of anticoagulation after surgery is required	344	45.6	41.6*	9.6	2.6	0.6
Antifibrinolytics for prophylaxis of excessive bleeding						
19. In patients at risk for excessive bleeding, use prophylactic antifibrinolytic therapy to reduce the bleeding and risk of transfusion	326	33.1	35.9*	22.7	6.1	2.1
20. Use antifibrinolytic therapy to reduce allogeneic blood transfusion in patients undergoing cardiopulmonary bypass	338	39.1	38.5*	18.6	3.6	0.3
21. Consider using antifibrinolytic therapy in other clinical circumstances at high-risk for excessive bleeding	345	38.6	40.3*	17.1	3.5	0.6

Acute Normovolemic Hemodilution						
22. Use acute normovolemic hemodilution (ANH) to reduce allogeneic blood transfusion in patients at high-risk for excessive bleeding (*e.g.*, major cardiac, orthopedic, thoracic, or liver surgery), if possible	346	24.0	33.2*	26.9	12.1	3.8
IV. Intraoperative and Postoperative Management of Blood Loss and Transfusions:						
Allogeneic Red Blood Cell Transfusion						
23. Administer blood without consideration of duration of storage	328	1.8	10.4	20.7	35.7*	31.4
24. Leukocyte reduced blood may be used for transfusion for the purpose of reducing complications associated with allogeneic blood transfusion	327	36.1	43.7*	15.9	3.1	1.2
Reinfusion of Recovered Red Blood Cells						
25. Reinfuse recovered red blood cells as a blood-sparing intervention in the intraoperative and/or postoperative period	329	67.5*	27.7	3.0	1.5	0.3
Intraoperative and Postoperative Patient Monitoring						
26. Periodically conduct a visual assessment of the surgical field jointly with the surgeon to assess the presence of excessive microvascular (*i.e.*, coagulopathy) or surgical bleeding	329	69.0*	23.7	6.1	1.2	0.0
27. Use standard methods for quantitative measurement of blood loss including checking suction canisters, surgical sponges, and surgical drains	329	73.6*	22.5	3.3	0.0	0.6
28. Monitor for perfusion of vital organs using standard ASA monitors (*i.e.*, blood pressure, heart rate, oxygen saturation, electro-cardiography) in addition to observing clinical symptoms and physical exam features	326	86.5*	12.6	0.9	0.0	0.0
29. Additional monitoring may include echocardiography, renal monitoring (urine output), cerebral monitoring (*i.e.*, cerebral oximetry and near infrared spectroscopy), analysis of arterial blood gasses, and mixed venous oxygen saturation	327	62.7*	28.7	7.0	1.2	0.3
30. If anemia is suspected, monitor hemoglobin /hematocrit values based on estimated blood loss and clinical signs	326	60.7*	30.7	5.2	2.1	1.2
31. If coagulopathy is suspected, obtain viscoelastic assays (*e.g.*, thromboelastography and rotational thromboelastometry) when available, as well as platelet count	326	42.3	33.7*	17.2	6.1	0.6

32. If viscoelastic assays are not available, obtain standard coagulation tests (*e.g.,* International Normalized Ratio [INR], aPTT, fibrinogen concentration), as well as platelet count for monitoring	328	67.4*	26.5	5.8	0.3	0.0
33. During and after transfusion, periodically check for hyperthermia, hemoglobinuria, microvascular bleeding, hypoxemia, respiratory distress, elevated peak airway pressure, urticaria, hypotension, and signs of hypocalcemia	331	71.3*	25.1	3.3	0.3	0.0
34. Before instituting therapy for transfusion reactions, stop the blood transfusion and order appropriate diagnostic testing	330	59.7*	24.5	8.5	5.8	1.5
<u>Treatment of Excessive Bleeding</u>						
35. In patients with excessive bleeding:						
a) obtain a platelet count before transfusion of platelets if possible	331	46.5	25.4*	15.7	9.4	3.0
b) in addition, obtain a test of platelet function, if available, in patients with suspected or drug-induced (e.g., clopidogrel) platelet dysfunction	329	29.2	26.7*	21.0	16.4	6.7
36. In patients with excessive bleeding, obtain coagulation tests (i.e., PT or INR and aPTT) before transfusion of FFP, if possible	329	42.6	32.2*	14.9	7.6	2.7
37. In patients with excessive bleeding, assess fibrinogen levels before the administration of cryoprecipitate, if possible	329	38.6	35.0*	18.5	5.8	2.1
38. In patients with excessive bleeding and platelet dysfunction, consider the use of desmopressin	328	35.1	40.9*	19.2	4.0	0.9
39. In patients with excessive bleeding, consider topical hemostatics such as fibrin glue or thrombin gel	323	48.6	35.3*	12.7	2.2	1.2
40. In patients with excessive bleeding, consider the use of antifibrinolytics (*i.e.,* ε-aminocaproic acid, tranexamic acid), if not already being used	330	39.4	40.0*	16.1	4.2	0.3
41. In patients with excessive bleeding and elevated INR, consider the use of prothrombin complex concentrates (PCCs)	327	33.0	41.6*	20.8	3.7	0.9
42. In patients with excessive bleeding, consider the use of fibrinogen concentrate	327	30.9	44.6*	21.7	2.1	0.6
43. When traditional options for treating excessive bleeding due to coagulopathy have been exhausted, consider administering recombinant activated factor VII	330	37.0	46.7*	13.3	3.0	0.0

Appendix 3. Vitamin and Herbal Supplements that May Affect Blood Loss

Herbal Supplements that Decrease Platelet Aggregation

Bilberry
Bromelain
Dong Quoi
Feverfew
Fish oil
Flax seed oil
Garlic
Ginger
Ginko biloba
Grape seed extract
Saw palmetto

Herbs that Inhibit Clotting

Chamomile
Dandelion root
Dong Quoi
Horse chestnut

Vitamins that Affect Coagulation

Vitamin K
Vitamin E

Appendix 4. Adverse effects associated with transfusion

Acute intravascular hemolytic transfusion reactions occur when red cells break down in the intravascular space due to either a complement mediated immune mechanism (usually secondary to ABO incompatibility) or to physical damage to the red cells (osmotic or temperature related). Both mechanisms result in hemoglobinemia and hemoglobinuria. However, the severe, often fatal complications such as shock and DIC are usually only seen in ABO incompatibility. The frequency of fatalities due to ABO incompatibilities, once the major cause of transfusion-associated fatalities, has markedly decreased over the last decade as strict processes for identifying the patient and the blood units being transfused have been put in place. In the operating room, acute intravascular hemolytic transfusion reactions secondary to ABO incompatibility are manifested by intractable bleeding in the operating field, hypotension and shock, fever, and hemoglobinuria. Treatment consists of stopping the blood transfusion, supportive measures to maintain blood pressure, and aggressive transfusion of platelets, FFP, and cryoprecipitate to counteract the consumptive coagulopathy while maintaining oxygen carrying capacity through transfusion of type O Red Blood Cells.

Transfusion-associated acute lung injury (TRALI) is now the leading cause of transfusion –associated fatalites. It is caused by donor antibodies in plasma-containing blood components (usually FFP or platelets, and occasionally Red Blood Cells) interacting with antigens on the patient's granulocytes (HLA or granulocyte specific) resulting in granulocytes aggregation and complement activation in the lung capillaries. The symptoms (fever, hypoxemia, acute respiratory distress, elevated peak airway pressure) occur within 6 hours after the transfusion. Except for the presence of fever, these symptoms are undistinguishable from those of *transfusion-associated circulatory overload (TACO).* Treatment consists of stopping the transfusion and instituting critical care supportive measures.

Bacterial contamination of blood components is most often associated with platelet transfusion as platelets are stored a 20-24 C which facilitates the growth of bacteria. There has been a significant decrease in the fatalities associated with bacterial contamination since 2001, as processes to detect bacterial contamination in platelets have been put into place. Bacterial contamination is manifested by hyperthermia and hypotension. Treatment consists of stopping the transfusion, starting antibiotics, and supportive measures.

Allergic reactions are caused by IgE antibodies in the patient against proteins in the plasma of the blood component transfused. As very small amounts of allergenic protein is needed to cause a reaction, any blood components can be associated with such a reaction except for washed blood. Symptoms usually are restricted to urticaria and other erythematous skin manifestations and subside spontaneously or with diphenhydramine administration. Occasionally allergic reactions are more severe and result in anaphylaxis.

Citrate is the anticoagulant used to collect blood components and it is present in significant amounts in all blood components. It readily binds calcium and magnesium. When large numbers of blood components are transfused over a short period of time, the metabolism of citrate is overwhelmed and the patient develops *citrate toxicity* (hypocalcemia and hypomagnesemia) which may result in adverse cardiac manifestations.