

# Practice Guidelines for Perioperative Blood Management

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

**P**RACTICE 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.†

### Methodology

#### 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, fresh-frozen plasma [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.

#### Purpose of the Guidelines

The purposes of these updated Guidelines are to improve the perioperative management of blood transfusion and

- What other guidelines are available on this topic?
  - These Practice Guidelines update “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 American Society of Anesthesiologists (ASA) in 2005 and published in 2006.<sup>1</sup>
  - Other guidelines on the topic for the management of blood transfusion have been published by the ASA, American College of Cardiology/American Heart Association,<sup>2</sup> Society of Thoracic Surgeons, Society of Cardiovascular Anesthesiologists,<sup>3</sup> and the American Association of Blood Banks.<sup>4</sup> The field of Blood Conservation has advanced considerably since the publication of the ASA Guidelines for Transfusion and Adjuvant Therapies in *ANESTHESIOLOGY* in 2006.
- Why was this guideline developed?
  - In October 2012, the Committee on Standards and Practice Parameters elected to search for new evidence to determine if recommendations in the existing practice guideline continue to be supported by current evidence. The resultant guideline, presented in this issue, includes an update of the scientific literature and findings from surveys of expert consultants and randomly selected ASA members.
- How does this statement differ from existing guidelines?
  - New evidence presented includes greater emphasis of the preoperative assessment of the patient, assessment of the risk for transfusion, and the use of adjunct medications to prevent and/or treat bleeding
  - The updated ASA practice guidelines differ from those published by other organizations in that:
    - They include greater use of pharmacologic therapies to minimize blood transfusions, such as erythropoietin for the anemic patient, prothrombin complex concentrates for urgent reversal of warfarin, and intraoperative antifibrinolytic therapy during selected cardiac and noncardiac procedures having a high risk for bleeding.
    - They advocate the use of transfusion algorithms, especially those based on thromboelastographic testing, blood ordering schedules, and restrictive transfusion strategies.
- Why does this statement differ from existing guidelines?
  - These ASA guidelines differ from the existing guidelines because they provide new evidence obtained from recent scientific literature along with findings from new surveys of expert consultants and randomly selected ASA members.

This article is featured in “This Month in Anesthesiology,” page 1A. Supplemental Digital Content is available for this article. Direct URL citations appear in the printed text and are available in both the HTML and PDF versions of this article. Links to the digital files are provided in the HTML text of this article on the Journal’s Web site ([www.anesthesiology.org](http://www.anesthesiology.org)). A complete bibliography used to develop these updated Guidelines, arranged alphabetically by author, is available as Supplemental Digital Content 1, <http://links.lww.com/ALN/B100>.

Submitted for publication October 15, 2014. Accepted for publication October 15, 2014. Approved by the ASA House of Delegates on October 15, 2014.

\* Revised by the American Society of Anesthesiologists Committee on Standards and Practice Parameters: Jeffrey L. Apfelbaum, M.D. (Committee Chair), Chicago, Illinois; Gregory A. Nuttall, M.D. (Task Force Chair), Rochester, Minnesota; Richard T. Connis, Ph.D., Woodinville, Washington; Chantal R. Harrison M.D., San Antonio, Texas; Ronald D. Miller, M.D., San Francisco, California; David G. Nickinovich, Ph.D., Bellevue, Washington; Nancy A. Nussmeier, M.D., Boston, Massachusetts; Andrew D. Rosenberg, M.D., Roslyn Heights, New York; Linda Shore-Lesserson M.D., New Hyde Park, New York; and John T. Sullivan M.D., M.B.A., Chicago, Illinois. These Guidelines have been endorsed by the Society of Cardiovascular Anesthesia, the Society for Obstetric Anesthesia and Perinatology, and the Society of Critical Care Anesthesiologists.

† American Society of Anesthesiologists: 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. *ANESTHESIOLOGY* 2006; 105:00–00

‡ FFP refers to plasma frozen within 8 h after phlebotomy, PF24 refers to plasma frozen within 24 h after phlebotomy, and Thawed Plasma refers to FFP stored up to 5 days at 1°–6°C after thawing. In the United States, 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.

Copyright © 2014, the American Society of Anesthesiologists, Inc. Wolters Kluwer Health, Inc. All Rights Reserved. *Anesthesiology* 2015; 122:241–00

adjuvant therapies and to reduce the risk of adverse outcomes associated with transfusions, bleeding, or anemia.

### 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 noncardiac surgery; (2) patients with pre-existing 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 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.

### 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.

### 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 revision 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 revision 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.

### Availability and Strength of Evidence

Preparation of these updated Guidelines followed a rigorous methodological process. Evidence was obtained from two principal sources such as 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 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 nonrandomized 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.

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

**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 nonsignificant findings are designated as equivocal (E).

Level 1: The literature contains a sufficient number of RCTs to conduct meta-analysis,<sup>||</sup> 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 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 noncomparative 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, as 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)

<sup>||</sup> All meta-analyses are conducted by the ASA Committee on Standards and Practice Parameters methodology group. Meta-analyses from other sources are reviewed but not included as evidence in this document.

<sup>#</sup> 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.

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.<sup>#</sup>

*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 these 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

### 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.

**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*)<sup>5-24</sup> 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*).<sup>25–45</sup>

**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 previous 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 of available laboratory test results including hemoglobin, hematocrit, and coagulation profiles and the ordering of 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:
  - Previous 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])
  - 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.

### Preadmission Patient Preparation

Preadmission patient preparation includes (1) treatment of anemia, (2) discontinuation of anticoagulants and antiplatelet agents, and (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 yr,\*\* 11.5 g/dl for children 5.0–11.99 yr, 12.0 g/dl for children 12.0–14.99 yr, and nonpregnant women  $\geq 15.0$  yr, 11.0 g/dl for pregnant women and 13.0 g/dl for men  $\geq 15.0$  yr.<sup>46,47</sup> Preadmission treatment of anemia includes the administration of erythropoietin and/or iron to improve preoperative hemoglobin levels.

**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*).<sup>48–62</sup> 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*).<sup>63–65</sup>

**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 (*Category B1-E evidence*).<sup>66</sup> Observational studies report blood loss volumes ranging from 265 to 756 ml, and blood transfusion requirements ranging from a mean of 0.08 to 0.5 units when clopidogrel is discontinued preoperatively (*Category B3 evidence*).<sup>67–69</sup> 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) (*Category A2-E evidence*).<sup>70,71</sup>

**Survey Findings:** Both the consultants and ASA members strongly agree regarding (1) discontinuing anticoagulation therapy (*e.g.*, warfarin, anti-Xa drugs, antithrombin agents) for elective surgery, in consultation with an appropriate specialist; (2) if clinically possible, discontinuing nonaspirin 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

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

patients requiring allogeneic transfusions and the volume of allogeneic blood transfused per patient (*Category A2-B evidence*).<sup>72-77††</sup>

**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 (*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 nonaspirin 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 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.

§§ The Task Force cautions that clopidogrel and aspirin should not be stopped before surgery in patients with coronary stents placed in the last 3 months for bare metal stents and 1 yr 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; 110:22-3. 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.<sup>2</sup>

||| 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.

- 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.|||

### Preprocedure Preparation

Preprocedure patient preparation includes the following strategies for reducing intraoperative allogeneic transfusion: (1) blood management protocols, (2) reversal of anticoagulants, (3) antifibrinolytics for prophylaxis of excessive blood loss,## and (4) acute normovolemic hemodilution (ANH).

**Blood Management Protocols.** Protocols for perioperative blood management include (1) multimodal protocols or algorithms, (2) restrictive *versus* liberal 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*).<sup>78-80</sup> RCTs demonstrate reduced blood transfusions and percentage of patients transfused when thromboelastography (TEG)-guided protocols or algorithms are compared with standard laboratory coagulation testing in cardiac surgery patients. (*Category A2-B evidence*).<sup>81-83</sup> An RCT reports reductions in allogeneic blood product requirements when comparing a rotational thromboelastometry (ROTEM)-guided algorithm with no algorithm for bleeding burn patients (*Category A1-B evidence*).<sup>84</sup> 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 usage 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 less than 8 g/dl and hematocrit values less than 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*).<sup>85–89</sup> RCT findings for mortality, cardiac, neurologic or pulmonary complications, and length of hospital stay were equivocal (*Category A2-E evidence*).<sup>85–93</sup>

**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*).<sup>94–99</sup>

**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 red blood cells (RBCs) is higher after the implementation of a massive transfusion protocol (*Category B3-E evidence*).<sup>100</sup>

**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*).<sup>101–110</sup> An RCT comparing a surgical blood order equation (SBOE) with a maximal surgical blood order schedule showed an improved crossmatch-to-transfusion ratio for SBOE (*Category A3 evidence*).<sup>111</sup>

**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) preprocedure administration of vitamin K.

**Literature Findings:** Observational studies and case reports indicate that four-factor PCCs administered preoperatively are followed by a reduction in International Normalized Ratio (INR) values (*Category B3/4-B evidence*), with thromboembolic events reported in 0.003% of patients following infusions (*Category B3 evidence*).<sup>112–114</sup> 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 (*Category B3-E evidence*).<sup>111</sup>

**Survey Findings:** Both the consultants and ASA members strongly agree that for urgent reversal of warfarin, administer 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 nonurgent reversal of warfarin, except when rapid restoration of anticoagulation after surgery is required.

#### **Antifibrinolytics for Prophylaxis of Excessive Blood Loss.**

##### **Literature Findings:**

**$\epsilon$ -Aminocaproic Acid.** Meta-analysis of placebo-controlled RCTs indicate that the use of  $\epsilon$ -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*).<sup>116–125</sup> An RCT comparing  $\epsilon$ -aminocaproic acid with placebo reports less blood loss and lower RBC transfusion requirements when  $\epsilon$ -aminocaproic acid is administered for prophylaxis of excessive bleeding after total knee replacement surgery and before tourniquet deflation (*Category A3-B evidence*).<sup>126</sup>

**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 (*Category A1-B evidence*).<sup>127–150</sup> 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*).<sup>151–157</sup>

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*).<sup>126,158–163</sup> One RCT did not show efficacy when tranexamic acid was administered after cardiac surgery and continued for 12 h (*Category A3-E evidence*).<sup>164</sup>

**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 (*Category A1-B evidence*).<sup>165–178</sup> 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 (*Category A1-B evidence*) and is equivocal regarding the number of patients transfused with allogeneic blood (*Category A1-E evidence*).<sup>179–188</sup>

**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 usage 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.<sup>\*\*\*</sup>
  - 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.

\*\*\* 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).

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

- 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 PCCs in consultation with the appropriate specialist, or administer FFP.
- Administer vitamin K for selected patients for nonurgent 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.‡‡‡

### Intraoperative and Postoperative Management of Blood Loss

Intraoperative and postoperative interventions include (1) allogeneic red blood cell transfusion, (2) reinfusion of recovered red blood cells, (3) intraoperative and postoperative patient monitoring, and (4) treatment of 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 mortality, infectious complications, and length of stay in the intensive care unit or hospital (*Category B1-E evidence*).<sup>189–198</sup>

**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 nonleukocyte depletion (*Category A2-B evidence*).<sup>199–205</sup>

**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.*, nonblood cell recovery) is effective in reducing the volume of allogeneic blood transfused (*Category A1-B evidence*).<sup>206–217</sup>

#### 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.<sup>218–220</sup>

**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

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

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 [NIRS]), 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.

**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 examination features and (2) that additional monitoring may include echocardiography, renal monitoring (urine output), cerebral monitoring (*i.e.*, cerebral oximetry and NIRS), 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.*, 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.*, TEG, ROTEM).

**Literature Findings:** An observational study examining point-of-care measurement of aPTT and prothrombin time by a portable laser photometer reports shorter times for obtaining test results with point-of-care monitoring (*Category B2-B evidence*).<sup>221</sup> 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*).<sup>222</sup> An RCT reported equivocal findings for blood loss and transfusion requirements when TEG is compared with standard laboratory coagulation tests (*Category A3-E evidence*).<sup>223</sup> An RCT reported equivocal findings with ROTEM *versus* no fibrinolysis monitoring for RBC, FFP, and platelet transfusion requirements (*Category A3-E evidence*).<sup>224</sup> 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% to 80%, and a positive predictive value of 45% (*Category B2 evidence*).<sup>225,226</sup> Nonrandomized correlational studies reported significant correlations ( $P < 0.01$ ) with standard coagulation tests for fibrinogen level and platelet count, whereas correlations between ROTEM and prothrombin time (PT) and aPTT measures were not statistically significant (*Category B2 evidence*).<sup>227–232</sup>

**Survey Findings:** Both the consultants and ASA members agree that if coagulopathy is suspected, obtain viscoelastic assays (*e.g.*, TEG and 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.*, 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 or transfusion-associated circulatory overload such as hypoxemia, respiratory distress and increased 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*).<sup>233–236</sup> and case reports indicate that adverse outcomes including transfusion-related acute lung injury and delayed hemolytic transfusion reaction may occur after transfusion (*Category B4-H evidence*).<sup>237–239</sup> 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, increased 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*).<sup>240,241</sup>

**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.*,  $\epsilon$ -aminocaproic acid, tranexamic acid), (3) topical hemostatics (*i.e.*, fibrin glue, thrombin gel), (4) PCCs, (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*).<sup>242–248</sup>

**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  $\epsilon$ -aminocaproic acid is compared with placebo to treat postoperative blood loss in patients with chest drainage of 100 ml/h or more (*Category A3-E evidence*).<sup>249</sup> 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.*,  $\epsilon$ -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*).<sup>250–261</sup> RCTs indicate that thrombin gel is effective in reducing perioperative blood loss and time to hemostasis (*Category A2-B evidence*).<sup>262–264</sup>

**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.

**Prothrombin Complex Concentrates:**

**Literature Findings:** Observational studies and case reports indicate that intraoperative administration of four-factor PCCs are followed by a reduction in blood loss and normalization of INR values (*Category B3/4-B evidence*).<sup>265–268</sup>

**Survey Findings:** The consultants and ASA members both agree that, in patients with excessive bleeding and increased INR, consider the use of PCCs.

**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 (*Category A1-E evidence*).<sup>269–275</sup>

**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*).<sup>276,277</sup>

**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.

||||| 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 used.

\*\*\*\* Coagulation tests are not necessary when a massive transfusion protocol is used.

- 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 NIRS), 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.*, INR, aPTT, fibrinogen concentration) or viscoelastic assays (*e.g.*, TEG and 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, increased 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 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.
- PCCs may be used in patients with excessive bleeding and increased INR.
- Consider recombinant activated factor VII when traditional options for treating excessive bleeding due to coagulopathy have been exhausted.††††
- Fibrinogen concentrate may be used.

## Appendix 1. Summary of Recommendations

### I. Patient Evaluation

- Review previous medical records and interview the patient or family to identify:
  - Previous 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).

†††† 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.

‡‡‡‡ 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 before surgery in patients with coronary stents placed in the last 3 months for bare metal stents and 1 yr 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; 110:22–3.

- 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 nonaspirin 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

#### Blood Management Protocols

- Multimodal protocols or algorithms may be employed as strategies to reduce the usage 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 PCCs in consultation with the appropriate specialist, or administer FFP.
- Administer vitamin K for selected patients for nonurgent 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.‡‡‡

### 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 NIRS), 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.*, INR, aPTT, fibrinogen concentration) or viscoelastic assays (*e.g.*, thromboelastography [TEG] and 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, increased 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 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.

- PCCs may be used in patients with excessive bleeding and increased INR.
- Consider recombinant activated factor VII when traditional options for treating excessive bleeding due to coagulopathy have been exhausted. ††††
- Fibrinogen concentrate may be used.

## Appendix 2. Methods and Analyses

### State of the Literature

For these updated Guidelines, a review of studies used in the development of the 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 adjunct 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 antithrombotic agents
  - Clopidogrel or other thienopyridines
  - Aspirin
- Preadmission autologous blood donation (PAD)
  - PAD *versus* allogeneic blood or blood products
  - PAD *versus* preprocedure ANH
  - PAD *versus* intraoperative or postoperative blood recovery

#### Preprocedure Preparation

- Blood management protocol
  - Multimodality protocol or algorithm
  - Restrictive *versus* liberal transfusion protocol
  - Nontransfusion protocol (*i.e.*, bloodless surgery)

- Massive transfusion protocol
- Maximum surgical blood ordering schedule for elective procedures
- Reversal of anticoagulants
  - Vitamin K
  - PCCs
- Antifibrinolytics for prophylaxis of excessive blood loss
  - ε-Aminocaproic acid
  - Tranexamic acid
- ANH
  - ANH *versus* no ANH
  - ANH combined with intraoperative blood recovery *versus* either ANH or intraoperative blood recovery

#### 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
  - Postoperative blood recovery
    - Cell salvage
    - Whole blood
- 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
    - NIRS
    - Arterial blood gas measurement
    - Mixed venous oxygen saturation
  - Monitoring for non-RBC transfusion—coagulopathy
    - Platelet function monitoring
    - Viscoelastic hemostatic assays

- TEG
- ROTEM
  - Monitoring (periodic checking) for adverse effects of transfusions
    - Transfusion-related acute lung injury
    - Hemolytic (*ABO incompatibility*) transfusion reactions
    - Citrate toxicity (hypocalcemia)
    - Transfusion-associated circulatory overload
    - Bacterial contamination
    - Immunomodulation (*e.g.*, graft *versus* host disease infection)
- Treatment of excessive bleeding
  - Transfusion treatments:
    - Platelet transfusion
    - FFP transfusion
    - Cryoprecipitate
  - Pharmacologic treatments:
    - Desmopressin
    - Antifibrinolytics
    - $\epsilon$ -Aminocaproic acid
    - Tranexamic acid
    - Topical hemostatics
    - Fibrin glue
    - Thrombin gel
    - PCC
    - PCC *versus* FFP
    - Bebulin
    - Profilnin
    - Kcentra (Beriplex, Confidex)
    - Coagulation factor concentrates
    - Recombinant Factor VIIa
    - Treatments for hypofibrinogenemia:
      - Cryoprecipitate
      - Fibrinogen concentrate (Riastap)

For the literature review, potentially relevant clinical studies were identified *via* electronic and manual searches of the literature. The updated searches covered an 11-yr period from 2004 to 2014. Over 1800 new citations that addressed topics related to the evidence linkages were identified. These articles were reviewed and those meeting the appropriate criteria as outlined in the “Focus” section above were combined with pre-2005 articles used in the previous update, resulting in a total of 520 articles that contained direct linkage-related evidence. A complete bibliography used to develop these Guidelines, organized by section, is available as Supplemental Digital Content 2, <http://links.lww.com/ALN/B101>.

Initially, each pertinent study finding was classified and summarized to determine meta-analysis potential. Literature pertaining to 11 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)  $\epsilon$ -aminocaproic acid *versus* placebo; (3) tranexamic acid *versus* placebo administered before or during surgery, (4) ANH *versus* no ANH; (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 *versus* 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  $2 \times 2$  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 inter-rater reliability testing. Agreement levels using a kappa ( $\kappa$ ) statistic for two-rater agreement pairs were as follows: (1) type of study design,  $\kappa = 0.83$ – $0.94$ ; (2) type of analysis,  $\kappa = 0.87$ – $0.94$ ; (3) evidence linkage assignment,  $\kappa = 0.89$ – $0.96$ ; and (4) literature inclusion for database,  $\kappa = 0.44$ – $0.78$ . 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.

### 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,<sup>§</sup> (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 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 was 5 and 10 min.

### 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 disseminated intravascular coagulation 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* is now the leading cause of transfusion-associated fatalities. 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 (human leukocyte antigen or granulocyte specific) resulting in granulocytes aggregation and complement activation in the lung capillaries. The symptoms (fever, hypoxemia, acute respiratory distress, increased peak airway pressure) occur within 6 h after the transfusion. Except for the presence of fever, these symptoms are undistinguishable from those of *transfusion-associated circulatory overload*. 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 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 immunoglobulin E 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.



**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  $100 \times 10^9 /l$  and is usually indicated when the count is less than  $50 \times 10^9 /l$  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 70 ml/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 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 nonpregnant patients.
- Treat bleeding patients with von Willebrand disease types 1 and 2A with desmopressin and subsequently with specific VWF/FVIII concentrate, if available. Cryoprecipitate 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

\* This table displays some transfusion criteria that may suggest when to transfuse with the above blood products. The decision to apply some or all 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 h after phlebotomy, PF24 refers to plasma frozen within 24 h after phlebotomy, and Thawed Plasma refers to FFP stored up to 5 days at 1°–6°C after thawing. In the United States, it is a 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. || Cryoprecipitate may be indicated at a higher fibrinogen concentration in actively bleeding obstetric patients.

aPTT = activated partial thromboplastin time; INR = International Normalized Ratio; PCC = prothrombincomplex concentrates; PT = prothrombin time; RBC = red blood cell.

Table 2. Meta-analysis Summary

Linkages	N	Fisher Chi-Square	P Value	Weighted Stouffer Zc	P Value	Effect Size	Mantel- Haenszel OR	CI	Significance	Heterogeneity	
										Effect Size	Effect Size
<b>Preadmission patient preparation</b>											
<i>Prevent or reduction of perioperative anemia</i>											
Erythropoietin vs. placebo	8	67.93	0.001	-4.80	0.001	0.21	—	—	0.001	0.003	0.003
Blood volume transfused	15	—	—	—	—	—	0.38	0.27-0.53	—	0.039	0.039
Patients transfused	7	—	—	—	—	—	0.45	0.26-0.78	—	0.038	0.038
Pts. transfused (without iron)	8	—	—	—	—	—	0.34	0.23-0.52	—	0.179	0.179
Pts. transfused (with iron)	8	—	—	—	—	—	—	—	—	—	—
<b>Preadmission patient preparation</b>											
<i>Antifibrinolytics for Prophylaxis of Excessive Bleeding</i>											
<i>ε-Aminocaproic acid vs. placebo (administered before or during surgery)*</i>											
Total blood loss	7	58.34	0.001	-5.35	0.001	-0.28	—	—	0.490	0.597	0.597
Patients transfused	9	—	—	—	—	—	0.58	0.33-0.96	—	0.043	0.043
<i>Tranexamic acid vs. placebo (administered before or during surgery)*</i>											
Intraoperative blood loss	10	68.83	0.001	-4.41	0.001	-0.19	—	—	0.343	0.340	0.340
Postoperative blood loss	12	172.51	0.001	-10.20	0.001	-0.36	—	—	0.001	0.001	0.001
Total blood loss	13	180.64	0.001	-6.22	0.001	-0.30	—	—	0.051	0.002	0.002
Patients transfused†	13	—	—	—	—	—	0.29	0.13-0.86	—	0.005	0.005
<i>Tranexamic acid vs. placebo (administered after surgery)*</i>											
Total blood loss	5	91.77	0.001	-10.84	0.001	-0.59	—	—	0.043	0.001	0.001
Patients transfused†	6	—	—	—	—	—	0.33	0.49-2.38	—	0.001	0.001
<b>Acute Normovolemic Hemodilution (ANH)</b>											
<i>ANH vs. no ANH</i>											
Volume transfused with allogeneic blood	7	60.84	0.001	-2.79	0.003	-0.21	—	—	0.003	0.001	0.001
Patients transfused with allogeneic blood	11	—	—	—	—	—	0.59	0.38-0.90	—	0.308	0.308
<i>ANH + intraoperative bloodrecovery vs. intraoperative blood recovery</i>											
Volume transfused with allogeneic blood	7	64.52	0.001	-5.05	0.001	-0.21	—	—	0.011	0.017	0.017
Patients transfused with allogeneic blood	8	—	—	—	—	—	0.71	0.48-1.05	—	0.046	0.046
<b>Intraoperative and postoperative interventions</b>											
<i>Restrictive vs. liberal transfusion protocol</i>											
Volume transfused with allogeneic blood	5	49.88	0.001	-3.31	0.001	-0.13	—	—	0.022	0.001	0.001
<i>Intraoperative blood recovery vs. conventional transfusion</i>											
Volume transfused with allogeneic blood	7	66.07	0.001	-4.16	0.001	-0.26	—	—	0.036	0.001	0.001
Patients transfused with allogeneic blood†	9	—	—	—	—	—	0.29	0.10-1.22	—	0.001	0.001
<i>Drugs to treat excessive bleeding</i>											
<i>Desmopressin vs. placebo*</i>											
Postoperative blood loss	6	51.72	0.001	-2.34	0.010	-0.11	—	—	0.001	0.001	0.001
Patients transfused	5	—	—	—	—	—	0.92	0.51-1.66	—	0.125	0.125

(Continued)

Table 2. Continued

Linkages	Heterogeneity									
	N	Fisher Chi-Square	P Value	Weighted Stouffer Zc	P Value	Effect Size	Mantel-Haenszel OR	CI	Significance	Effect Size
<i>Topical hemostatics</i>										
Fibrin glue vs. no fibrin glue	11	145.03	0.001	-4.34	0.001	-0.29	—	—	0.001	0.001
Postop/total blood loss	7	—	—	—	—	—	0.58	0.34-0.97	—	0.012
Patients transfused										
Factor VII vs. no Factor VII*	5	44.55	0.001	-0.01	0.496	-0.21	—	—	0.075	0.001
Blood volume transfused	6	—	—	—	—	—	0.16	0.03-2.85	—	0.001
Patients transfused†										

\* Double-blind studies only. † DerSimonian-Laird random effects odds ratio. CI = 99% confidence interval; OR = odds ratio; pts = patients.

Table 3. Consultant Survey Responses\*

	N	Percent Responding to Each Item				
		Strongly Agree	Agree	Uncertain	Disagree	Strongly Disagree
<b>I. Patient Evaluation:</b>						
1. Review previous medical records and interview the patient or family to identify previous blood transfusion, history of drug-induced coagulopathy, presence of congenital coagulopathy, history of thrombotic events, and risk factors for organ ischemia	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

(Continued)

Table 3. Continued

	N	Percent Responding to Each Item				
		Strongly Agree	Agree	Uncertain	Disagree	Strongly Disagree
<b>II. Preadmission Patient Preparation:</b>						
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 transfusion)	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, antithrombin agents) for elective surgery	71	74.6†	14.1	11.3	0.0	0.0
8. If clinically possible, discontinue nonaspirin 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
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
<b>III. Preprocedure Preparation:</b>						
<i>Blood Management Protocols</i>						
12. Employ multimodal protocols or algorithms as strategies to reduce the usage 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
<i>Reversal of Anticoagulants</i>						
17. For urgent reversal of warafin, administer PCCs in consultation with the appropriate specialist, or administer FFP	71	53.5†	35.2	4.2	4.2	2.8

(Continued)

Table 3. Continued

	N	Percent Responding to Each Item				
		Strongly Agree	Agree	Uncertain	Disagree	Strongly Disagree
18. Administer vitamin K for nonurgent reversal of warafin, except when rapid restoration of anticoagulation after surgery is required <i>Antifibrinolytics for prophylaxis of excessive bleeding</i>	71	60.6†	28.2	5.6	1.4	4.2
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 <i>Acute Normovolemic Hemodilution</i>	69	30.4	49.3†	17.4	2.9	0.0
22. Use 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:						
<i>Allogeneic Red Blood Cell Transfusion</i>						
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 <i>Reinfusion of Recovered Red blood cells</i>	72	50.0†	33.3	11.1	5.6	0.0
25. Reinfuse recovered red blood cells as a blood-sparing intervention in the intraoperative and/or postoperative period <i>Intraoperative and Postoperative Patient Monitoring</i>	72	65.3†	23.6	9.7	1.4	0.0
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, electrocardiography) in addition to observing clinical symptoms and physical examination 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 NIRS), analysis of arterial blood gasses, and mixed venous oxygen saturation	72	69.4†	26.4	4.2	0.0	0.0

(Continued)

Table 3. Continued

	N	Percent Responding to Each Item				
		Strongly Agree	Agree	Uncertain	Disagree	Strongly Disagree
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 ROTEM, 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., 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, increased 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
<i>Treatment of Excessive Bleeding</i>						
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 anti-fibrinolytics (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 increased INR, consider the use of 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

\* N = the number of consultants who responded to each item. † Median.

ANH = acute normovolemic hemodilution; aPTT = activated partial thromboplastin time; ASA = American Society of Anesthesiologists; FFP = fresh-frozen plasma; INR = International Normalized Ratio; NIRS = near infrared spectroscopy; PCC = prothrombin complex concentrates; PT = prothrombin time.

Table 4. ASA Membership Survey Responses\*

	N	Percent Responding to Each Item				
		Strongly Agree	Agree	Uncertain	Disagree	Strongly Disagree
I. Patient Evaluation:						
1. Review previous medical records and interview the patient or family to identify previous blood transfusion, history of drug-induced coagulopathy, presence of congenital coagulopathy, history of thrombotic events, and risk factors for organ ischemia	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 transfusion)	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, antithrombin agents) for elective surgery	350	70.9†	22.6	5.7	0.6	0.3
8. If clinically possible, discontinue nonaspirin 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
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:						
<i>Blood Management Protocols</i>						
12. Employ multimodal protocols or algorithms as strategies to reduce the usage of blood products	345	57.4†	29.3	9.6	3.8	0.0

(Continued)

Table 4. Continued

	N	Percent Responding to Each Item				
		Strongly Agree	Agree	Uncertain	Disagree	Strongly Disagree
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>i.e.</i> , 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
<i>Reversal of Anticoagulants</i>						
17. For urgent reversal of warfarin, administer PCCs in consultation with the appropriate specialist, or administer FFP	345	55.1†	36.2	7.5	0.9	0.3
18. Administer vitamin K for nonurgent reversal of warfarin, except when rapid restoration of anticoagulation after surgery is required	344	45.6	41.6†	9.6	2.6	0.6
<i>Antifibrinolytics for prophylaxis of excessive bleeding</i>						
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
<i>Acute Normovolemic Hemodilution</i>						
22. Use ANH to reduce allogeneic blood transfusion in patients at high risk for excessive bleeding ( <i>e.g.</i> , 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:						
<i>Allogeneic Red Blood Cell Transfusion</i>						
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
<i>Reinfusion of Recovered Red Blood Cell</i>						
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
<i>Intraoperative and Postoperative Patient Monitoring</i>						

(Continued)



Table 4. Continued

	N	Percent Responding to Each Item				
		Strongly Agree	Agree	Uncertain	Disagree	Strongly Disagree
26. Periodically conduct a visual assessment of the surgical field jointly with the surgeon to assess the presence of excessive microvascular ( <i>i.e.</i> , 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>i.e.</i> , blood pressure, heart rate, oxygen saturation, electrocardiography) in addition to observing clinical symptoms and physical examination 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>i.e.</i> , cerebral oximetry and NIRS), 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 ( <i>e.g.</i> , thromboelastography and ROTEM) 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 ( <i>e.g.</i> , 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, increased 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 <i>Treatment of Excessive Bleeding</i>	330	59.7†	24.5	8.5	5.8	1.5
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 ( <i>e.g.</i> , clopidogrel) platelet dysfunction	329	29.2	26.7†	21.0	16.4	6.7
36. In patients with excessive bleeding, obtain coagulation tests ( <i>i.e.</i> , 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

(Continued)

Table 4. Continued

	N	Percent Responding to Each Item				
		Strongly Agree	Agree	Uncertain	Disagree	Strongly Disagree
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 increased INR, consider the use of 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

\* N = the number of ASA members who responded to each item. † Median.

ANH = acute normovolemic hemodilution; aPTT = activated partial thromboplastin time; ASA = American Society of Anesthesiologists; FFP = fresh-frozen plasma, INR = International Normalized Ratio; NIRS = near infrared spectroscopy; PCC = prothrombin complex concentrates; PT = prothrombin time.

## Acknowledgments

Supported by the American Society of Anesthesiologists and developed under the direction of Jeffrey L. Apfelbaum, M.D., Chair, Committee on Standards and Practice Parameters.

## Competing Interests

The authors declare no competing interests.

## Correspondence

Address correspondence to the American Society of Anesthesiologists: 1061 American Lane, Schaumburg, Illinois 60173. These updated Practice Guidelines, and all ASA Practice Parameters, may be obtained at no cost through the Journal Web site, [www.anesthesiology.org](http://www.anesthesiology.org).

## References

- Practice guidelines for perioperative blood transfusion and adjuvant therapies: An updated report by the American Society of Anesthesiologists Task Force on blood transfusion and adjuvant therapies. *ANESTHESIOLOGY* 2006; 105:198–208
- Fleisher LA, Fleischmann KE, Auerbach AD, Barnason SA, Beckman JA, Bozkurt B, Davila-Roman VG, Gerhard-Herman MD, Holly TA, Kane GC, Marine JE, Nelson MT, Spencer CC, Thompson A, Ting HH, Uretsky BF, Wijeyesundera DN: 2014 ACC/AHA guideline on perioperative cardiovascular evaluation and management of patients undergoing noncardiac surgery: A report of the American College of Cardiology/American Heart Association Task Force on Practice Guidelines. *J Am Coll Cardiol* 2014; [Epub ahead of print]
- Ferraris VA, Ferraris SP, Saha SP, Hessel EA 2nd, Haan CK, Royston BD, Bridges CR, Higgins RS, Despotis G, Brown JR, Spiess BD, Shore-Lesserson L, Stafford-Smith M, Mazer CD, Bennett-Guerrero E, Hill SE, Body S: Perioperative blood transfusion and blood conservation in cardiac surgery: The Society of Thoracic Surgeons and the Society of Cardiovascular Anesthesiologists clinical practice guideline. *Ann Thorac Surg* 2007; 83:S27–86
- Carson JL, Carless PS, Hebert PC: Transfusion thresholds and other strategies for guiding allogeneic red blood transfusion. *Cochrane Database Syst Rev* 2012; 4:CD002042
- Benoist S, Panis Y, Pannegon V, Alves A, Valleur P: Predictive factors for perioperative blood transfusions in rectal resection for cancer: A multivariate analysis of a group of 212 patients. *Surgery* 2001; 129:433–9
- Bjessmo S, Ivert T: Blood loss after coronary artery bypass surgery: Relations to patient variables and antithrombotic treatment. *Scand Cardiovasc J* 2000; 34:438–45
- Bocchieri KA, Scheinerman SJ, Graver LM: Exchange transfusion before cardiopulmonary bypass in sickle cell disease. *Ann Thorac Surg* 2010; 90:323–4
- Cash KL, Brown T, Sausais L, Uehlinger J, Reed LJ: Severe delayed hemolytic transfusion reaction secondary to anti-At(a). *Transfusion* 1999; 39:834–7
- De Santo LS, Amarelli C, Della Corte A, Scardone M, Bancone C, Carozza A, Grassia MG, Romano G: Blood transfusion after on-pump coronary artery bypass grafting: Focus on modifiable risk factors. *Eur J Cardiothorac Surg* 2013; 43:359–66
- Engström KG, Appelblad M, Brorsson B: Mechanisms behind operating room blood transfusions in coronary artery bypass graft surgery patients with insignificant bleeding. *J Cardiothorac Vasc Anesth* 2002; 16:539–44
- Fox JS, Amaranath L, Hoeltge GA, Andrich JT: Autologous blood transfusion and intraoperative cell salvage in a patient with homozygous sickle cell disease. *Cleve Clin J Med* 1994; 61:137–40
- Gaudino M, Luciani N, Piancone FL, Bruno P, Rossi M, Schiavello R, Possati G: Perioperative management of a

- patient with Werlhof disease undergoing myocardial revascularization. *J Cardiovasc Surg (Torino)* 1999; 40:227-8
13. Gerrah R, Shargal Y, Elami A: Impaired oxygenation and increased hemolysis after cardiopulmonary bypass in patients with glucose-6-phosphate dehydrogenase deficiency. *Ann Thorac Surg* 2003; 76:523-7
  14. Hendriks HG, van der Meer J, Klompmaaker IJ, Choudhury N, Hagens JA, Porte RJ, de Kam PJ, Slooff MJ, de Wolf JT: Blood loss in orthotopic liver transplantation: A retrospective analysis of transfusion requirements and the effects of auto-transfusion of cell saver blood in 164 consecutive patients. *Blood Coagul Fibrinolysis* 2000; 11(suppl 1):S87-93
  15. Katz K, Tamary H, Lahav J, Soudry M, Cohen IJ: Increased operative bleeding during orthopaedic surgery in patients with type I Gaucher disease and bone involvement. *Bull Hosp Jt Dis* 1999; 58:188-90
  16. Lindgren L, Yli-Hankala A, Halme L, Koskimies S, Orko R: Transfusion-related acute lung injury (TRALI) after fresh frozen plasma in a patient with coagulopathy. *Acta Anaesthesiol Scand* 1996; 40:641-4
  17. Lison S, Spannagl M, Dietrich W; Working Group of Perioperative Hemostasis: Hemophilia A in cardiac operations: A model of reduced thrombin generation. *Ann Thorac Surg* 2011; 91:1606-8
  18. Netzer G, Shah CV, Iwashyna TJ, Lanken PN, Finkel B, Fuchs B, Guo W, Christie JD: Association of RBC transfusion with mortality in patients with acute lung injury. *Chest* 2007; 132:1116-23
  19. Pagani FD, Polito RJ, Bolling SF: Mitral valve reconstruction in sickle cell disease. *Ann Thorac Surg* 1996; 61:1841-3
  20. Potter PS, Waters JH, Burger GA, Mraović B: Application of cell-salvage during cesarean section. *ANESTHESIOLOGY* 1999; 90:619-21
  21. Sutton SW, Hunley EK, Duncan MA, Rodriguez R, Meyers TP: Sickle cell disease and aortic valve replacement: Use of cardiopulmonary bypass, partial exchange transfusion, platelet sequestration, and continuous hemofiltration. *Tex Heart Inst J* 1999; 26:283-8
  22. Uen WC, Chou YH, Liu CC, Lin SM, Chen TJ: Successful resection of sigmoid colon cancer in a patient with factor XI deficiency. *J Formos Med Assoc* 1998; 97:283-5
  23. Vichinsky EP, Haberkern CM, Neumayr L, Earles AN, Black D, Koshy M, Pegelow C, Abboud M, Ohene-Frempong K, Iyer RV: A comparison of conservative and aggressive transfusion regimens in the perioperative management of sickle cell disease. The Preoperative Transfusion in Sickle Cell Disease Study Group. *N Engl J Med* 1995; 333:206-13
  24. Walsh TS, Palmer J, Watson D, Biggin K, Seretny M, Davidson H, Harkness M, Hay A: Multicentre cohort study of red blood cell use for revision hip arthroplasty and factors associated with greater risk of allogeneic blood transfusion. *Br J Anaesth* 2012; 108:63-71
  25. Karkouti K, Wijeyesundera DN, Beattie WS; Reducing Bleeding in Cardiac Surgery (RBC) Investigators: Risk associated with preoperative anemia in cardiac surgery: A multicenter cohort study. *Circulation* 2008; 117:478-84
  26. Karkouti K, Wijeyesundera DN, Yau TM, McCluskey SA, Chan CT, Wong PY, Beattie WS: Influence of erythrocyte transfusion on the risk of acute kidney injury after cardiac surgery differs in anemic and nonanemic patients. *ANESTHESIOLOGY* 2011; 115:523-30
  27. Kohli N, Mallipeddi PK, Neff JM, Sze EH, Roat TW: Routine hematocrit after elective gynecologic surgery. *Obstet Gynecol* 2000; 95(6 pt 1):847-50
  28. Kulier A, Levin J, Moser R, Rumpold-Seitlinger G, Tudor IC, Snyder-Ramos SA, Moehle P, Mangano DT; Investigators of the Multicenter Study of Perioperative Ischemia Research Group; Ischemia Research and Education Foundation: Impact of preoperative anemia on outcome in patients undergoing coronary artery bypass graft surgery. *Circulation* 2007; 116:471-9
  29. Le Roux PD, Elliott JP, Winn HR: Blood transfusion during aneurysm surgery. *Neurosurgery* 2001; 49:1068-74
  30. Musallam KM, Tamim HM, Richards T, Spahn DR, Rosendaal FR, Habbal A, Khreiss M, Dahdaleh FS, Khavandi K, Sfeir PM, Soweid A, Hoballah JJ, Taher AT, Jamali FR: Preoperative anaemia and postoperative outcomes in non-cardiac surgery: A retrospective cohort study. *Lancet* 2011; 378:1396-407
  31. Pirat A, Sargin D, Torgay A, Arslan G: Identification of pre-operative predictors of intraoperative blood transfusion requirement in orthotopic liver transplantation. *Transplant Proc* 2002; 34:2153-5
  32. Williams GD, Bratton SL, Riley EC, Ramamoorthy C: Coagulation tests during cardiopulmonary bypass correlate with blood loss in children undergoing cardiac surgery. *J Cardiothorac Vasc Anesth* 1999; 13:398-404
  33. Brener SJ, Bhatt DL, Moliterno DJ, Schneider JP, Ellis SG, Topol EJ: Revisiting optimal anticoagulation with unfractionated heparin during coronary stent implantation. *Am J Cardiol* 2003; 92:1468-71
  34. Despotis GJ, Levine V, Filos KS, Santoro SA, Joist JH, Spitznagel E, Goodnough LT: Evaluation of a new point-of-care test that measures PAF-mediated acceleration of coagulation in cardiac surgical patients. *ANESTHESIOLOGY* 1996; 85:1311-23
  35. Ereth MH, Nuttall GA, Klindworth JT, MacVeigh I, Santrach PJ, Orszulak TA, Harmsen WS, Oliver WC Jr: Does the platelet-activated clotting test (HemoSTATUS) predict blood loss and platelet dysfunction associated with cardiopulmonary bypass? *Anesth Analg* 1997; 85:259-64
  36. Ereth MH, Nuttall GA, Santrach PJ, Klindworth JT, Oliver WC Jr, Schaff HV: The relation between the platelet-activated clotting test (HemoSTATUS) and blood loss after cardiopulmonary bypass. *ANESTHESIOLOGY* 1998; 88:962-9
  37. Gelb AB, Roth RI, Levin J, London MJ, Noall RA, Hauck WW, Cloutier M, Verrier E, Mangano DT: Changes in blood coagulation during and following cardiopulmonary bypass: Lack of correlation with clinical bleeding. *Am J Clin Pathol* 1996; 106:87-99
  38. Gravlee GP, Arora S, Lavender SW, Mills SA, Hudspeth AS, Cordell AR, James RL, Brockschmidt JK, Stuart JJ: Predictive value of blood clotting tests in cardiac surgical patients. *Ann Thorac Surg* 1994; 58:216-21
  39. Horlocker TT, Nuttall GA, Dekutoski MB, Bryant SC: The accuracy of coagulation tests during spinal fusion and instrumentation. *Anesth Analg* 2001; 93:33-8
  40. Karkouti K, McCluskey SA, Syed S, Pazaratz C, Poonawala H, Crowther MA: The influence of perioperative coagulation status on postoperative blood loss in complex cardiac surgery: A prospective observational study. *Anesth Analg* 2010; 110:1533-40
  41. Murray D, Pennell B, Olson J: Variability of prothrombin time and activated partial thromboplastin time in the diagnosis of increased surgical bleeding. *Transfusion* 1999; 39:56-62
  42. Myers ER, Clarke-Pearson DL, Olt GJ, Soper JT, Berchuck A: Preoperative coagulation testing on a gynecologic oncology service. *Obstet Gynecol* 1994; 83:438-44
  43. Nuttall GA, Oliver WC, Beynen FM, Santrach PJ, Strickland RA, Murray MJ: Determination of normal *versus* abnormal activated partial thromboplastin time and prothrombin time after cardiopulmonary bypass. *J Cardiothorac Vasc Anesth* 1995; 9:355-61
  44. Nuttall GA, Oliver WC, Ereth MH, Santrach PJ: Coagulation tests predict bleeding after cardiopulmonary bypass. *J Cardiothorac Vasc Anesth* 1997; 11:815-23
  45. Reich DL, Yanakakis MJ, Vela-Cantos FP, DePerio M, Jacobs E: Comparison of bedside coagulation monitoring tests with standard laboratory tests in patients after cardiac surgery. *Anesth Analg* 1999; 88:312-9
  46. World Health Organization. Iron deficiency anaemia: Assessment, prevention, and control. A guide for programme managers. World Health Organization 2001

47. Worldwide prevalence of anaemia 1993–2005: WHO global database on anaemia. Edited by de Benoist B, McLean E, Egli I, and Cogswell M. [http://whqlibdoc.who.int/publications/2008/9789241596657\\_eng.pdf](http://whqlibdoc.who.int/publications/2008/9789241596657_eng.pdf)
48. de Andrade JR, Jove M, Landon G, Frei D, Guilfoyle M, Young DC: Baseline hemoglobin as a predictor of risk of transfusion and response to Epoetin alfa in orthopedic surgery patients. *Am J Orthop (Belle Mead NJ)* 1996; 25:533–42
49. de Pree C, Mermillod B, Hoffmeyer P, Beris P: Recombinant human erythropoietin as adjuvant treatment for autologous blood donation in elective surgery with large blood needs (> or = 5 units): A randomized study. *Transfusion* 1997; 37:708–14
50. Faris PM, Ritter MA, Abels RI: The effects of recombinant human erythropoietin on perioperative transfusion requirements in patients having a major orthopaedic operation. The American Erythropoietin Study Group. *J Bone Joint Surg Am* 1996; 78:62–72
51. Feagan BG, Wong CJ, Kirkley A, Johnston DW, Smith FC, Whitsitt P, Wheeler SL, Lau CY: Erythropoietin with iron supplementation to prevent allogeneic blood transfusion in total hip joint arthroplasty. A randomized, controlled trial. *Ann Intern Med* 2000; 133:845–54
52. Goodnough LT, Price TH, Friedman KD, Johnston M, Ciavarella D, Khan N, Sacher R, Vogler WR, Wissel M, Abels RI: A phase III trial of recombinant human erythropoietin therapy in non-anemic orthopedic patients subjected to aggressive removal of blood for autologous use: Dose, response, toxicity, and efficacy. *Transfusion* 1994; 34:66–71
53. Hayashi J, Kumon K, Takanashi S, Kawashima Y, Eguchi S, Takaku F, Yamamura H: Subcutaneous administration of recombinant human erythropoietin before cardiac surgery: A double-blind, multicenter trial in Japan. *Transfusion* 1994; 34:142–6
54. Kettelhack C, Hones C, Messinger D, Schlag PM: Randomized multicentre trial of the influence of recombinant human erythropoietin on intraoperative and postoperative transfusion need in anaemic patients undergoing right hemicolectomy for carcinoma. *Br J Surg* 1998; 85:63–67
55. Kosmadakis N, Messaris E, Maris A, Katsaragakis S, Leandros E, Konstadoulakis MM, Androulakis G: Perioperative erythropoietin administration in patients with gastrointestinal tract cancer: Prospective randomized double-blind study. *Ann Surg* 2003; 237:417–21
56. Mercuriali F, Inghilleri G, Biffi E, Colotti MT, Vinci A, Oriani G: Epoetin alfa in low hematocrit patients to facilitate autologous blood donation in total hip replacement: A randomized, double-blind, placebo-controlled, dose-ranging study. *Acta Haematol* 1998; 100:69–76
57. Price TH, Goodnough LT, Vogler W, Sacher RA, Hellman RM, Johnston MF, Bolgiano DC, Abels RI: The effect of recombinant human erythropoietin on the efficacy of autologous blood donation in patients with low hematocrits: A multicenter, randomized, double-blind, controlled trial. *Transfusion* 1996; 36:29–36
58. Qvist N, Boesby S, Wolff B, Hansen CP: Recombinant human erythropoietin and hemoglobin concentration at operation and during the postoperative period: Reduced need for blood transfusions in patients undergoing colorectal surgery—prospective double-blind placebo-controlled study. *1999; 23:30–5*
59. Scott SN, Boeve TJ, McCulloch TM, Fitzpatrick KA, Karnell LH: The effects of epoetin alfa on transfusion requirements in head and neck cancer patients: A prospective, randomized, placebo-controlled study. *Laryngoscope* 2002; 112(7 pt 1):1221–9
60. Shapiro GS, Boachie-Adjei O, Dhawlikar SH, Maier LS: The use of Epoetin alfa in complex spine deformity surgery. *Spine (Phila Pa 1976)* 2002; 27:2067–71
61. Sowade O, Warnke H, Scigalla P, Sowade B, Franke W, Messinger D, Gross J: Avoidance of allogeneic blood transfusions by treatment with epoetin beta (recombinant human erythropoietin) in patients undergoing open-heart surgery. *Blood* 1997; 89:411–8
62. Walpoth B, Galliker B, Spirig P, Haeberli A, Rosenmund A, Althaus U, Nydegger UE: Use of epoetin alfa in autologous blood donation programs for patients scheduled for elective cardiac surgery. *Semin Hematol* 1996; 33(2 suppl 2):75–6
63. Andrews CM, Lane DW, Bradley JG: Iron pre-load for major joint replacement. *Transfus Med* 1997; 7:281–6
64. Garrido-Martín P, Nassar-Mansur MI, de la Llana-Ducros R, Virgos-Aller TM, Rodríguez Fortunez PM, Ávalos-Pinto R, Jimenez-Sosa A, Martínez-Sanz R: The effect of intravenous and oral iron administration on perioperative anaemia and transfusion requirements in patients undergoing elective cardiac surgery: A randomized clinical trial. *Interact Cardiovasc Thorac Surg* 2012; 15:1013–8
65. Weisbach V, Skoda P, Rippel R, Lauer G, Glaser A, Zingsem J, Zimmermann R, Eckstein R: Oral or intravenous iron as an adjuvant to autologous blood donation in elective surgery: A randomized, controlled study. *Transfusion* 1999; 39:465–72
66. Dotan ZA, Mor Y, Leibovitch I, Varon D, Golomb J, Duvdevani M, Ramon J: The efficacy and safety of perioperative low molecular weight heparin substitution in patients on chronic oral anticoagulant therapy undergoing transurethral prostatectomy for bladder outlet obstruction. *J Urol* 2002; 168:610–3
67. Firanesco CE, Martens EJ, Schönberger JP, Soliman Hamad MA, van Straten AH: Postoperative blood loss in patients undergoing coronary artery bypass surgery after preoperative treatment with clopidogrel. A prospective randomised controlled study. *Eur J Cardiothorac Surg* 2009; 36:856–62
68. Firanesco CE, Martens EJ, Schönberger JP, Soliman Hamad MA, van Straten AH: Postoperative blood loss in patients undergoing coronary artery bypass surgery after preoperative treatment with clopidogrel. A prospective randomised controlled study. *Eur J Cardiothorac Surg* 2009; 36:856–62
69. Shim JK, Choi YS, Oh YJ, Bang SO, Yoo KJ, Kwak YL: Effects of preoperative aspirin and clopidogrel therapy on perioperative blood loss and blood transfusion requirements in patients undergoing off-pump coronary artery bypass graft surgery. *J Thorac Cardiovasc Surg* 2007; 134:59–64
70. Devereaux PJ, Mrkobrada M, Sessler DI, Leslie K, Alonso-Coello P, Kurz A, Villar JC, Sigamani A, Biccard BM, Meyhoff CS, Parlow JL, Guyatt G, Robinson A, Garg AX, Rodseth RN, Botto F, Lurati Buse G, Xavier D, Chan MT, Tiboni M, Cook D, Kumar PA, Forget P, Malaga G, Fleischmann E, Amir M, Eikelboom J, Mizera R, Torres D, Wang CY, VanHelder T, Paniagua P, Berwanger O, Srinathan S, Graham M, Pasin L, Le Manach Y, Gao P, Pogue J, Whitlock R, Lamy A, Kearon C, Baigent C, Chow C, Pettit S, Chrolavicius S, Yusuf S; POISE-2 Investigators: Aspirin in patients undergoing noncardiac surgery. *N Engl J Med* 2014; 370:1494–503
71. Oscarsson A, Gupta A, Fredrikson M, Järhult J, Nyström M, Pettersson E, Darvish B, Krook H, Swahn E, Eintrei C: To continue or discontinue aspirin in the perioperative period: A randomized, controlled clinical trial. *Br J Anaesth* 2010; 104:305–12
72. Avall A, Hyllner M, Bengtson JP, Carlsson L, Bengtsson A: Postoperative inflammatory response after autologous and allogeneic blood transfusion. *ANESTHESIOLOGY* 1997; 87:511–6
73. Bouchard D, Marcheix B, Al-Shamary S, Vanden Eynden F, Demers P, Robitaille D, Pellerin M, Perrault LP, Carrier M: Preoperative autologous blood donation reduces the need for allogeneic blood products: a prospective randomized study. *Can J Surg* 2008; 51:422–7
74. Chen G, Zhang FJ, Gong M, Yan M: Effect of perioperative autologous *versus* allogeneic blood transfusion on the immune system in gastric cancer patients. *J Zhejiang Univ Sci B* 2007; 8:560–5

75. Hedström M, Flordal PA, Ahl T, Svensson J, Dalén N: Autologous blood transfusion in hip replacement. No effect on blood loss but less increase of plasminogen activator inhibitor in a randomized series of 80 patients. *Acta Orthop Scand* 1996; 67:317–20
76. Heiss MM, Mempel W, Delanoff C, Jauch KW, Gabka C, Mempel M, Dieterich HJ, Eissner HJ, Schildberg FW: Blood transfusion-modulated tumor recurrence: First results of a randomized study of autologous *versus* allogeneic blood transfusion in colorectal cancer surgery. *J Clin Oncol* 1994; 12:1859–67
77. Kajikawa M, Nonami T, Kurokawa T, Hashimoto S, Harada A, Nakao A, Takagi H: Autologous blood transfusion for hepatectomy in patients with cirrhosis and hepatocellular carcinoma: Use of recombinant human erythropoietin. *Surgery* 1994; 115:727–34
78. Capraro L, Kuitunen A, Salmenperä M, Kekomäki R: On-site coagulation monitoring does not affect hemostatic outcome after cardiac surgery. *Acta Anaesthesiol Scand* 2001; 45:200–6
79. Nuttall GA, Oliver WC, Santrach PJ, Bryant S, Dearani JA, Schaff HV, Ereth MH: Efficacy of a simple intraoperative transfusion algorithm for nonerythrocyte component utilization after cardiopulmonary bypass. *ANESTHESIOLOGY* 2001; 94:773–81
80. Wong CJ, Vandervoort MK, Vandervoort SL, Donner A, Zou G, MacDonald JK, Freedman J, Karkouti K, MacDonald SJ, Feagan BG: A cluster-randomized controlled trial of a blood conservation algorithm in patients undergoing total hip joint arthroplasty. *Transfusion* 2007; 47:832–41
81. Ak K, Isbir CS, Tetik S, Atalan N, Tekeli A, Aljodi M, Civelek A, Arsan S: Thromboelastography-based transfusion algorithm reduces blood product use after elective CABG: A prospective randomized study. *J Card Surg* 2009; 24:404–10
82. Royston D, von Kier S: Reduced haemostatic factor transfusion using heparinase-modified thrombelastography during cardiopulmonary bypass. *Br J Anaesth* 2001; 86:575–8
83. Shore-Lesserson L, Manspeizer HE, DePerio M, Francis S, Vela-Cantos F, Ergin MA: Thromboelastography-guided transfusion algorithm reduces transfusions in complex cardiac surgery. *Anesth Analg* 1999; 88:312–9
84. Schaden E, Kimberger O, Kraincuk P, Baron DM, Metnitz PG, Kozek-Langenecker S: Perioperative treatment algorithm for bleeding burn patients reduces allogeneic blood product requirements. *Br J Anaesth* 2012; 109:376–81
85. Bracey AW, Radovancevic R, Riggs SA, Houston S, Cozart H, Vaughn WK, Radovancevic B, McAllister HA Jr, Cooley DA: Lowering the hemoglobin threshold for transfusion in coronary artery bypass procedures: Effect on patient outcome. *Transfusion* 1999; 39:1070–7
86. Bush RL, Pevco WC, Holcroft JW: A prospective, randomized trial limiting perioperative red blood cell transfusions in vascular patients. *Am J Surg* 1997; 174:143–8
87. Carson JL, Brooks MM, Abbott JD, Chaitman B, Kelsey SF, Triulzi DJ, Srinivas V, Menegus MA, Marroquin OC, Rao SV, Noveck H, Passano E, Hardison RM, Smitherman T, Vagoonescu T, Wimmer NJ, Williams DO: Liberal *versus* restrictive transfusion thresholds for patients with symptomatic coronary artery disease. *Am Heart J* 2013; 165: 964–71.e1
88. Johnson RG, Thurer RL, Kruskal MS, Sirois C, Gervino EV, Critchlow J, Weintraub RM: Comparison of two transfusion strategies after elective operations for myocardial revascularization. *J Thorac Cardiovasc Surg* 1992; 104:307–14
89. So-Osman C, Nelissen R, Te Slaa R, Coene L, Brand R, Brand A: A randomized comparison of transfusion triggers in elective orthopaedic surgery using leucocyte-depleted red blood cells. *Vox Sang* 2010; 98:56–64
90. Carson JL, Terrin ML, Barton FB, Aaron R, Greenburg AG, Heck DA, Magaziner J, Merlino FE, Bunce G, McClelland B, Duff A, Noveck H: A pilot randomized trial comparing symptomatic *vs.* hemoglobin-level-driven red blood cell transfusions following hip fracture. *Transfusion* 1998; 38:522–9
91. Carson JL, Terrin ML, Noveck H, Sanders DW, Chaitman BR, Rhoads GG, Nemo G, Dragert K, Beaupre L, Hildebrand K, Macaulay W, Lewis C, Cook DR, Dobbin G, Zakriya KJ, Apple FS, Horney RA, Magaziner J; FOCUS Investigators: Liberal or restrictive transfusion in high-risk patients after hip surgery. *N Engl J Med* 2011; 365:2453–62
92. Grover M, Talwalkar S, Casbard A, Boralessa H, Contreras M, Boralessa H, Brett S, Goldhill DR, Soni N: Silent myocardial ischaemia and haemoglobin concentration: A randomized controlled trial of transfusion strategy in lower limb arthroplasty. *Vox Sang* 2006; 90:105–12
93. Hajjar LA, Vincent JL, Galas FR, Nakamura RE, Silva CM, Santos MH, Fukushima J, Kalil Filho R, Sierra DB, Lopes NH, Mauad T, Roquim AC, Sundin MR, Leão WC, Almeida JP, Pomerantzeff PM, Dallan LO, Jatene FB, Stolf NA, Auler JO Jr: Transfusion requirements after cardiac surgery: the TRACS randomized controlled trial. *JAMA* 2010; 304:1559–67
94. Harwin SF, Issa K, Naziri Q, Johnson AJ, Mont MA: Results of primary total knee arthroplasty in Jehovah's Witness patients. *J Arthroplasty* 2013; 28:49–55
95. Magner D, Ouellette JR, Lee JR, Colquhoun S, Lo S, Nissen NN: Pancreaticoduodenectomy after neoadjuvant therapy in a Jehovah's witness with locally advanced pancreatic cancer: Case report and approach to avoid transfusion. *Am Surg* 2006; 72:435–7
96. Pasic M, D'Ancona G, Unbehaun A, Hetzer R: Bloodless third complex heart operation in a Jehovah's Witness patient with extremely low preoperative haemoglobin level. *Interact Cardiovasc Thorac Surg* 2012; 14:692–3
97. Podestà A, Parodi E, Dottori V, Crivellari R, Passerone GC: Epoetin alpha in elective coronary and valve surgery in Jehovah's Witnesses patients. Experience in 45 patients. *Minerva Cardioangiolog* 2002; 50:125–31
98. Stoye A, Chapin JW, Botha J, Grant W: Bloodless liver transplantation in a Jehovah's Witness. *Int Anesthesiol Clin* 2011; 49:108–15
99. Vaislic CD, Dalibon N, Ponzio O, Ba M, Jugan E, Lagneau F, Abbas P, Olliver Y, Gaillard D, Baget F, Sportiche M, Chedid A, Chaoul G, Maribas P, Dupuy C, Robine B, Kasanin N, Michon H, Ruat JM, Habis M, Bouharaoua T: Outcomes in cardiac surgery in 500 consecutive Jehovah's Witness patients: 21 year experience. *J Cardiothorac Surg* 2012; 7:95
100. Simmons JW, White CE, Eastridge BJ, Mace JE, Wade CE, Blackburne LH: Impact of policy change on US Army combat transfusion practices. *J Trauma* 2010; 69(suppl 1):S75–80
101. Dexter F, Ledolter J, Davis E, Witkowski TA, Herman JH, Epstein RH: Systematic criteria for type and screen based on procedure's probability of erythrocyte transfusion. *ANESTHESIOLOGY* 2012; 116:768–78
102. Frank SM, Rothschild JA, Masear CG, Rivers RJ, Merritt WT, Savage WJ, Ness PM: Optimizing preoperative blood ordering with data acquired from an anesthesia information management system. *ANESTHESIOLOGY* 2013; 118:1286–97
103. Kajja I, Bimenya GS, Eindhoven GB, ten Duis HJ, Sibinga CT: Surgical blood order equation in femoral fracture surgery. *Transfus Med* 2011; 21:7–12
104. Karger R, Bornmann A, Kretschmer V: Limited utility of algorithms predicting blood transfusions. *Blood Transfus* 2013; 11:426–32
105. Krupp NL, Weinstein G, Chalian A, Berlin JA, Wolf P, Weber RS: Validation of a transfusion prediction model in head and neck cancer surgery. *Arch Otolaryngol Head Neck Surg* 2003; 129:1297–302
106. Mahadevan D, Challand C, Clarke A, Keenan J: Maximum surgical blood ordering schedules for revision lower limb arthroplasty. *Arch Orthop Trauma Surg* 2011; 131:663–7

107. Nuttall GA, Horlocker TT, Santrach PJ, Oliver WC Jr, Dekutoski MB, Bryant S: Use of the surgical blood order equation in spinal instrumentation and fusion surgery. *Spine (Phila Pa 1976)* 2000; 25:602–5
108. Palmer T, Wahr JA, O'Reilly M, Greenfield ML: Reducing unnecessary cross-matching: A patient-specific blood ordering system is more accurate in predicting who will receive a blood transfusion than the maximum blood ordering system. *Anesth Analg* 2003; 96:369–75
109. Subramanian A, Sagar S, Kumar S, Agrawal D, Albert V, Misra MC: Maximum surgical blood ordering schedule in a tertiary trauma center in northern India: A proposal. *J Emerg Trauma Shock* 2012; 5:321–7
110. van Klei WA, Moons KG, Leyssius AT, Knape JT, Rutten CL, Grobbee DE: A reduction in type and screen: Preoperative prediction of RBC transfusions in surgery procedures with intermediate transfusion risks. *Br J Anaesth* 2001; 87:250–7
111. Nuttall GA, Santrach PJ, Oliver WC Jr, Ereth MH, Horlocker TT, Cabanela ME, Trousdale RT, Bryant S, Currie TW: A prospective randomized trial of the surgical blood order equation for ordering red cells for total hip arthroplasty patients. *Transfusion* 1998; 38:828–33
112. Hanke AA, Joch C, Görlinger K: Long-term safety and efficacy of a pasteurized nanofiltrated prothrombin complex concentrate (Beriplex P/N): A pharmacovigilance study. *Br J Anaesth* 2013; 110:764–72
113. Schick KS, Fertmann JM, Jauch KW, Hoffmann JN: Prothrombin complex concentrate in surgical patients: Retrospective evaluation of vitamin K antagonist reversal and treatment of severe bleeding. *Crit Care* 2009; 13:R191
114. Wong Y: Use of prothrombin complex concentrate for vitamin K antagonist reversal before surgical treatment of intracranial hemorrhage. *Clin Med Insights Case Rep* 2011; 4:1–6
115. Barnette RE, Wendling WW, Schweiger JW, Brister NW, Schartel SA, Chen D, Shuman CA, McClurken JB, Jeevanandam V: Intravenous vitamin K1 prior to orthotopic heart transplantation: Effects *in vivo* and *in vitro*. *Acta Anaesthesiol Scand* 1997; 41(1 pt 1):78–83
116. Amar D, Grant FM, Zhang H, Boland PJ, Leung DH, Healey JA: Antifibrinolytic therapy and perioperative blood loss in cancer patients undergoing major orthopedic surgery. *ANESTHESIOLOGY* 2003; 98:337–42
117. Daily PO, Lamphere JA, Dembitsky WP, Adamson RM, Dans NF: Effect of prophylactic epsilon-aminocaproic acid on blood loss and transfusion requirements in patients undergoing first-time coronary artery bypass grafting. A randomized, prospective, double-blind study. *J Thorac Cardiovasc Surg* 1994; 108:99–106
118. Dalmau A, Sabaté A, Acosta F, Garcia-Huete L, Koo M, Sansano T, Rafecas A, Figueras J, Jaurrieta E, Parrilla P: Tranexamic acid reduces red cell transfusion better than epsilon-aminocaproic acid or placebo in liver transplantation. *Anesth Analg* 2000; 91:29–34
119. Florentino-Pineda I, Thompson GH, Poe-Kochert C, Huang RP, Haber LL, Blakemore LC: The effect of amicar on perioperative blood loss in idiopathic scoliosis: The results of a prospective, randomized double-blind study. *Spine (Phila Pa 1976)* 2004; 29:233–8
120. Harley BJ, Beaupré LA, Jones CA, Cinats JG, Guenther CR: The effect of epsilon aminocaproic acid on blood loss in patients who undergo primary total hip replacement: A pilot study. *Can J Surg* 2002; 45:185–90
121. Kikura M, Levy JH, Tanaka KA, Ramsay JG: A double-blind, placebo-controlled trial of epsilon-aminocaproic acid for reducing blood loss in coronary artery bypass grafting surgery. *J Am Coll Surg* 2006; 202:216–22
122. Kluger R, Olive DJ, Stewart AB, Blyth CM: Epsilon-aminocaproic acid in coronary artery bypass graft surgery: Preincision or postheparin? *ANESTHESIOLOGY* 2003; 99:1263–9
123. Menichetti A, Tritapepe L, Ruvolo G, Speziale G, Cogliati A, Di Giovanni C, Pacilli M, Criniti A: Changes in coagulation patterns, blood loss and blood use after cardiopulmonary bypass: Aprotinin *vs* tranexamic acid *vs* epsilon aminocaproic acid. *J Cardiovasc Surg (Torino)* 1996; 37:401–7
124. Ray M, Hatcher S, Whitehouse SL, Crawford S, Crawford R: Aprotinin and epsilon aminocaproic acid are effective in reducing blood loss after primary total hip arthroplasty—a prospective randomized double-blind placebo-controlled study. *J Thromb Haemost* 2005; 3:1421–7
125. Troianos CA, Sypula RW, Lucas DM, D'Amico F, Mathie TB, Desai M, Pasqual RT, Pellegrini RV, Newfeld ML: The effect of prophylactic epsilon-aminocaproic acid on bleeding, transfusions, platelet function, and fibrinolysis during coronary artery bypass grafting. *ANESTHESIOLOGY* 1999; 91:430–5
126. Camarasa MA, Ollé G, Serra-Prat M, Martín A, Sánchez M, Ricós P, Pérez A, Opisso L: Efficacy of aminocaproic, tranexamic acids in the control of bleeding during total knee replacement: A randomized clinical trial. *Br J Anaesth* 2006; 96:576–82
127. Ahn SW, Shim JK, Youn YN, Song JW, Yang SY, Chung SC, Kwak YL: Effect of tranexamic acid on transfusion requirement in dual antiplatelet-treated anemic patients undergoing off-pump coronary artery bypass graft surgery. *Circ J* 2012; 76:96–101
128. Caglar GS, Tasci Y, Kaykicioglu F, Haberal A: Intravenous tranexamic acid use in myomectomy: A prospective randomized double-blind placebo controlled study. *Eur J Obstet Gynecol Reprod Biol* 2008; 137:227–31
129. Choi WS, Irwin MG, Samman N: The effect of tranexamic acid on blood loss during orthognathic surgery: A randomized controlled trial. *J Oral Maxillofac Surg* 2009; 67:125–33
130. Claeys MA, Vermeersch N, Haentjens P: Reduction of blood loss with tranexamic acid in primary total hip replacement surgery. *Acta Chir Belg* 2007; 107:397–401
131. Coffey A, Pittman J, Halbrook H, Fehrenbacher J, Beckman D, Hormuth D: The use of tranexamic acid to reduce post-operative bleeding following cardiac surgery: A double-blind randomized trial. *Am Surg* 1995; 61:566–8
132. Crescenti A, Borghi G, Bignami E, Bertarelli G, Landoni G, Casiraghi GM, Briganti A, Montorsi F, Rigatti P, Zangrillo A: Intraoperative use of tranexamic acid to reduce transfusion rate in patients undergoing radical retropubic prostatectomy: Double blind, randomised, placebo controlled trial. *BMJ* 2011; 343:d5701
133. Dadure C, Sauter M, Bringuier S, Bigorre M, Raux O, Rochette A, Canaud N, Capdevila X: Intraoperative tranexamic acid reduces blood transfusion in children undergoing craniostylosis surgery: A randomized double-blind study. *ANESTHESIOLOGY* 2011; 114:856–61
134. Ekbäck G, Axelsson K, Rytberg L, Edlund B, Kjellberg J, Weckström J, Carlsson O, Schött U: Tranexamic acid reduces blood loss in total hip replacement surgery. *Anesth Analg* 2000; 91:1124–30
135. Goobie SM, Meier PM, Pereira LM, McGowan FX, Prescilla RP, Scharp LA, Rogers GF, Proctor MR, Meara JG, Soriano SG, Zurakowski D, Sethna NF: Efficacy of tranexamic acid in pediatric craniostylosis surgery: A double-blind, placebo-controlled trial. *ANESTHESIOLOGY* 2011; 114:862–71
136. Jansen AJ, Andreica S, Claeys M, D'Haese J, Camu F, Jochmans K: Use of tranexamic acid for an effective blood conservation strategy after total knee arthroplasty. *Br J Anaesth* 1999; 83:596–601
137. Katsaros D, Petricevic M, Snow NJ, Woodhall DD, Van Bergen R: Tranexamic acid reduces postbypass blood use:

- A double-blinded, prospective, randomized study of 210 patients. *Ann Thorac Surg* 1996; 61:1131–5
138. Lemay E, Guay J, Côté C, Roy A: Tranexamic acid reduces the need for allogenic red blood cell transfusions in patients undergoing total hip replacement. *Can J Anaesth* 2004; 51:31–7
  139. Menichetti A, Tritapepe L, Ruvolo G, Speziale G, Cogliati A, Di Giovanni C, Pacilli M, Criniti A: Changes in coagulation patterns, blood loss and blood use after cardiopulmonary bypass: Aprotinin *vs* tranexamic acid *vs* epsilon aminocaproic acid. *J Cardiovasc Surg (Torino)* 1996; 37:401–7
  140. Neilipovitz DT, Murto K, Hall L, Barrowman NJ, Splinter WM: A randomized trial of tranexamic acid to reduce blood transfusion for scoliosis surgery. *Anesth Analg* 2001; 93:82–7
  141. Orpen NM, Little C, Walker G, Crawford EJ: Tranexamic acid reduces early post-operative blood loss after total knee arthroplasty: A prospective randomised controlled trial of 29 patients. *Knee* 2006; 13:106–10
  142. Pleym H, Stenseth R, Wahba A, Bjella L, Karevold A, Dale O: Single-dose tranexamic acid reduces postoperative bleeding after coronary surgery in patients treated with aspirin until surgery. *Anesth Analg* 2003; 96:923–8
  143. Taghaddomi RJ, Mirzaee A, Attar AS, Shirdel A: Tranexamic acid reduces blood loss in off-pump coronary artery bypass surgery. *J Cardiothorac Vasc Anesth* 2009; 23:312–5
  144. Vanek T, Jares M, Fajt R, Straka Z, Jirasek K, Kolesar M, Brucek P, Maly M: Fibrinolytic inhibitors in off-pump coronary surgery: A prospective, randomized, double-blind TAP study (tranexamic acid, aprotinin, placebo). *Eur J Cardiothorac Surg* 2005; 28:563–8
  145. Wei M, Jian K, Guo Z, Wang L, Jiang D, Zhang L, Tarkka M: Tranexamic acid reduces postoperative bleeding in off-pump coronary artery bypass grafting. *Scand Cardiovasc J* 2006; 40:105–9
  146. Wong J, Abrishami A, El Beheiry H, Mahomed NN, Roderick Davey J, Gandhi R, Syed KA, Muhammad Ovais Hasan S, De Silva Y, Chung F: Topical application of tranexamic acid reduces postoperative blood loss in total knee arthroplasty: A randomized, controlled trial. *J Bone Joint Surg Am* 2010; 92:2503–13
  147. Wu CC, Ho WM, Cheng SB, Yeh DC, Wen MC, Liu TJ, P'eng FK: Perioperative parenteral tranexamic acid in liver tumor resection: A prospective randomized trial toward a “blood transfusion”-free hepatectomy. *Ann Surg* 2006; 243:173–80
  148. Yamasaki S, Masuhara K, Fuji T: Tranexamic acid reduces blood loss after cementless total hip arthroplasty-prospective randomized study in 40 cases. *Int Orthop* 2004; 28:69–73
  149. Zabeeda D, Medalion B, Sverdlov M, Ezra S, Schachner A, Ezri T, Cohen AJ: Tranexamic acid reduces bleeding and the need for blood transfusion in primary myocardial revascularization. *Ann Thorac Surg* 2002; 74:733–8
  150. Zufferey PJ, Miquet M, Quenet S, Martin P, Adam P, Albaladejo P, Mismetti P, Molliex S: tranexamic acid in hip-fracture surgery (THIF) study: Tranexamic acid in hip fracture surgery: A randomized controlled trial. *Br J Anaesth* 2010; 104:23–30
  151. Andreasen JJ, Nielsen C: Prophylactic tranexamic acid in elective, primary coronary artery bypass surgery using cardiopulmonary bypass. *Eur J Cardiothorac Surg* 2004; 26:311–7
  152. Casati V, Sandrelli L, Speziali G, Calori G, Grasso MA, Spagnolo S: Hemostatic effects of tranexamic acid in elective thoracic aortic surgery: A prospective, randomized, double-blind, placebo-controlled study. *J Thorac Cardiovasc Surg* 2002; 123:1084–91
  153. Dryden PJ, O'Connor JP, Jamieson WR, Reid I, Ansley D, Sadeghi H, Burr LH, Munro AI, Merrick PM: Tranexamic acid reduces blood loss and transfusion in reoperative cardiac surgery. *Can J Anaesth* 1997; 44:934–41
  154. Hardy JF, Bélisle S, Dupont C, Harel F, Robitaille D, Roy M, Gagnon L: Prophylactic tranexamic acid and epsilon-aminocaproic acid for primary myocardial revascularization. *Ann Thorac Surg* 1998; 65:371–6
  155. Jares M, Vanek T, Straka Z, Brucek P: Tranexamic acid reduces bleeding after off-pump coronary artery bypass grafting. *J Cardiovasc Surg (Torino)* 2003; 44:205–8
  156. Karski JM, Teasdale SJ, Norman P, Carroll J, VanKessel K, Wong P, Glynn MF: Prevention of bleeding after cardiopulmonary bypass with high-dose tranexamic acid. Double-blind, randomized clinical trial. *J Thorac Cardiovasc Surg* 1995; 110:835–42
  157. Penta de Peppo A, Pierri MD, Scafuri A, De Paulis R, Colantuono G, Caprara E, Tomai F, Chiariello L: Intraoperative antifibrinolysis and blood-saving techniques in cardiac surgery. Prospective trial of 3 antifibrinolytic drugs. *Tex Heart Inst J* 1995; 22:231–6
  158. Benoni G, Fredin H: Fibrinolytic inhibition with tranexamic acid reduces blood loss and blood transfusion after knee arthroplasty: A prospective, randomised, double-blind study of 86 patients. *J Bone Joint Surg Br* 1996; 78:434–40
  159. Benoni G, Lethagen S, Nilsson P, Fredin H: Tranexamic acid, given at the end of the operation, does not reduce postoperative blood loss in hip arthroplasty. *Acta Orthop Scand* 2000; 71:250–4
  160. Good L, Peterson E, Lisander B: Tranexamic acid decreases external blood loss but not hidden blood loss in total knee replacement. *Br J Anaesth* 2003; 90:596–9
  161. Hiiippala ST, Strid IJ, Wennerstrand MI, Arvela JV, Niemelä HM, Mäntylä SK, Kuisma RP, Ylinen JE: Tranexamic acid radically decreases blood loss and transfusions associated with total knee arthroplasty. *Anesth Analg* 1997; 84:839–44
  162. Hiiippala S, Strid L, Wennerstrand M, Arvela V, Mäntylä S, Ylinen J, Niemelä H: Tranexamic acid (Cyklokapron) reduces perioperative blood loss associated with total knee arthroplasty. *Br J Anaesth* 1995; 74:534–7
  163. Lin PC, Hsu CH, Huang CC, Chen WS, Wang JW: The blood-saving effect of tranexamic acid in minimally invasive total knee replacement: Is an additional pre-operative injection effective? *J Bone Joint Surg Br* 2012; 94:932–6
  164. Casati V, Bellotti F, Gerli C, Franco A, Oppizzi M, Cossolini M, Calori G, Benussi S, Alfieri O, Torri G: Tranexamic acid administration after cardiac surgery: A prospective, randomized, double-blind, placebo-controlled study. *ANESTHESIOLOGY* 2001; 94:8–14
  165. Bennett SR: Perioperative autologous blood transfusion in elective total hip prosthesis operations. *Ann R Coll Surg Engl* 1994; 76:95–8
  166. Bennett J, Haynes S, Torella F, Grainger H, McCollum C: Acute normovolemic hemodilution in moderate blood loss surgery: A randomized controlled trial. *Transfusion* 2006; 46:1097–103
  167. Boldt J, Weber A, Mailer K, Papsdorf M, Schuster P: Acute normovolaemic haemodilution *vs* controlled hypotension for reducing the use of allogeneic blood in patients undergoing radical prostatectomy. *Br J Anaesth* 1999; 82:170–4
  168. Fischer M, Matsuo K, Gonen M, Grant F, Dematteo RP, D'Angelica MI, Mascarenhas J, Brennan MF, Allen PJ, Blumgart LH, Jarnagin WR: Relationship between intraoperative fluid administration and perioperative outcome after pancreaticoduodenectomy: Results of a prospective randomized trial of acute normovolemic hemodilution compared with standard intraoperative management. *Ann Surg* 2010; 252:952–8
  169. Ford SM, Unsworth-White MJ, Aziz T, Tooze JA, van Besouw JP, Bevan DH, Treasure T: Platelet pheresis is not a useful adjunct to blood-sparing strategies in cardiac surgery. *J Cardiothorac Vasc Anesth* 2002; 16:321–9

170. Guo JR, Yu J, Jin XJ, Du JM, Guo W, Yuan XH: Effects of acute normovolemic hemodilution on perioperative coagulation and fibrinolysis in elderly patients undergoing hepatic carcinectomy. *Chin Med Sci J* 2010; 25:146–50
171. Jarnagin WR, Gonen M, Maithel SK, Fong Y, D'Angelica MI, Dematteo RP, Grant F, Wuest D, Kundu K, Blumgart LH, Fischer M: A prospective randomized trial of acute normovolemic hemodilution compared to standard intraoperative management in patients undergoing major hepatic resection. *Ann Surg* 2008; 248:360–9
172. Kahraman S, Altunkaya H, Celebioğlu B, Kanbak M, Paşaoğlu I, Erdem K: The effect of acute normovolemic hemodilution on homologous blood requirements and total estimated red blood cell volume lost. *Acta Anaesthesiol Scand* 1997; 41:614–7
173. Matot I, Scheinin O, Jurim O, Eid A: Effectiveness of acute normovolemic hemodilution to minimize allogeneic blood transfusion in major liver resections. *ANESTHESIOLOGY* 2002; 97:794–800
174. Menges T, Wagner RM, Welters I, Ruwoldt R, Boldt J, Hempelmann G: The role of the protein C-thrombomodulin system and fibrinolysis during cardiovascular surgery: Influence of acute preoperative plasmapheresis. *J Cardiothorac Vasc Anesth* 1996; 10:482–9
175. Olsfanger D, Fredman B, Goldstein B, Shapiro A, Jedeikin R: Acute normovolaemic haemodilution decreases postoperative allogeneic blood transfusion after total knee replacement. *Br J Anaesth* 1997; 79:317–21
176. Ramnath AN, Naber HR, de Boer A, Leusink JA: No benefit of intraoperative whole blood sequestration and autotransfusion during coronary artery bypass grafting: Results of a randomized clinical trial. *J Thorac Cardiovasc Surg* 2003; 125:1432–7
177. Triulzi DJ, Gilmor GD, Ness PM, Baumgartner WA, Schultheis LW: Efficacy of autologous fresh whole blood or platelet-rich plasma in adult cardiac surgery. *Transfusion* 1995; 35:627–34
178. Wajon P, Gibson J, Calcroft R, Hughes C, Thrift B: Intraoperative plateletpheresis and autologous platelet gel do not reduce chest tube drainage or allogeneic blood transfusion after reoperative coronary artery bypass graft. *Anesth Analg* 2001; 93:536–42
179. Blais RE, Hadjipavlou AG, Shulman G: Efficacy of autotransfusion in spine surgery: Comparison of autotransfusion alone and with hemodilution and apheresis. *Spine (Phila Pa 1976)* 1996; 21:2795–800
180. Casati V, Speziali G, D'Alessandro C, Cianchi C, Antonietta Grasso M, Spagnolo S, Sandrelli L: Intraoperative low-volume acute normovolemic hemodilution in adult open-heart surgery. *ANESTHESIOLOGY* 2002; 97:367–73
181. Helm RE, Klemperer JD, Rosengart TK, Gold JP, Peterson P, DeBois W, Altorki NK, Lang S, Thomas S, Isom OW, Krieger KH: Intraoperative autologous blood donation preserves red cell mass but does not decrease postoperative bleeding. *Ann Thorac Surg* 1996; 62:1431–41
182. Höhn L, Schweizer A, Licker M, Morel DR: Absence of beneficial effect of acute normovolemic hemodilution combined with aprotinin on allogeneic blood transfusion requirements in cardiac surgery. *ANESTHESIOLOGY* 2002; 96:276–82
183. Kochamba GS, Pfeffer TA, Sintek CF, Khonsari S: Intraoperative autotransfusion reduces blood loss after cardiopulmonary bypass. *Ann Thorac Surg* 1996; 61:900–3
184. Licker M, Sierra J, Kalangos A, Panos A, Diaper J, Ellenberger C: Cardioprotective effects of acute normovolemic hemodilution in patients with severe aortic stenosis undergoing valve replacement. *Transfusion* 2007; 47:341–50
185. Lisander B, Jonsson R, Nordwall A: Combination of blood-saving methods decreases homologous blood requirements in scoliosis surgery. *Anaesth Intensive Care* 1996; 24:555–8
186. McGill N, O'Shaughnessy D, Pickering R, Herbertson M, Gill R: Mechanical methods of reducing blood transfusion in cardiac surgery: Randomised controlled trial. *BMJ* 2002; 324:1299
187. Shulman G, Solanki DR, Hadjipavlou A: Augmented autologous transfusions in major reconstructive spine surgery. *J Clin Apher* 1998; 13:62–8
188. Wolowczyk L, Nevin M, Smith FC, Baird RN, Lamont PM: Haemodilutional effect of standard fluid management limits the effectiveness of acute normovolaemic haemodilution in AAA surgery—results of a pilot trial. *Eur J Vasc Endovasc Surg* 2003; 26:405–11
189. Andreasen JJ, Dethlefsen C, Modrau IS, Baech J, Schonheyder HC, Moeller JK, Johnsen SP; North-West Denmark Transfusion Study Group: Storage time of allogeneic red blood cells is associated with risk of severe postoperative infection after coronary artery bypass grafting. *Eur J Cardiothorac Surg* 2011; 39:329–34
190. Cata JP, Klein EA, Hoeltge GA, Dalton JE, Mascha E, O'Hara J, Russell A, Kurz A, Ben-Elihayhu S, Sessler DI: Blood storage duration and biochemical recurrence of cancer after radical prostatectomy. *Mayo Clin Proc* 2011; 86:120–7
191. Chen J, Singhapricha T, Memarzadeh M, Ziman A, Yuan S, Hu KQ, Steadman RH, Busuttill RW, Xia VW: Storage age of transfused red blood cells during liver transplantation and its intraoperative and postoperative effects. *World J Surg* 2012; 36:2436–42
192. Edgren G, Kamper-Jørgensen M, Eloranta S, Rostgaard K, Custer B, Ullum H, Murphy EL, Busch MP, Reilly M, Melbye M, Hjalgrim H, Nyrén O: Duration of red blood cell storage and survival of transfused patients (CME). *Transfusion* 2010; 50:1185–95
193. Koch CG, Li L, Sessler DI, Figueroa P, Hoeltge GA, Mihaljevic T, Blackstone EH: Duration of red-cell storage and complications after cardiac surgery. *N Engl J Med* 2008; 358:1229–39
194. McKenny M, Ryan T, Tate H, Graham B, Young VK, Dowd N: Age of transfused blood is not associated with increased postoperative adverse outcome after cardiac surgery. *Br J Anaesth* 2011; 106:643–9
195. Mynster T, Nielsen HJ: The impact of storage time of transfused blood on postoperative infectious complications in rectal cancer surgery. *Danish RANX05 Colorectal Cancer Study Group. Scand J Gastroenterol* 2000; 35:212–7
196. Vamvakas EC, Carven JH: Length of storage of transfused red cells and postoperative morbidity in patients undergoing coronary artery bypass graft surgery. *Transfusion* 2000; 40:101–9
197. van de Watering L, Lorinser J, Versteegh M, Westendorp R, Brand A: Effects of storage time of red blood cell transfusions on the prognosis of coronary artery bypass graft patients. *Transfusion* 2006; 46:1712–8
198. van Straten AH, Soliman Hamad MA, van Zundert AA, Martens EJ, ter Woorst JF, de Wolf AM, Scharnhorst V: Effect of duration of red blood cell storage on early and late mortality after coronary artery bypass grafting. *J Thorac Cardiovasc Surg* 2011; 141:231–7
199. Bilgin YM, van de Watering LM, Eijssman L, Versteegh MI, Brand R, van Oers MH, Brand A: Double-blind, randomized controlled trial on the effect of leukocyte-depleted erythrocyte transfusions in cardiac valve surgery. *Circulation* 2004; 109:2755–60
200. Houbiers JG, Brand A, van de Watering LM, Hermans J, Verwey PJ, Bijnen AB, Pahlplatz P, Eeftink Schattenkerk M, Wobbes T, de Vries JE: Randomised controlled trial comparing transfusion of leucocyte-depleted or buffy-coat-depleted blood in surgery for colorectal cancer. *Lancet* 1994; 344:573–8
201. Jensen LS, Andersen AJ, Christiansen PM, Hokland P, Juhl CO, Madsen G, Mortensen J, Møller-Nielsen C, Hanberg-Sørensen F, Hokland M: Postoperative infection and natural killer cell function following blood transfusion in patients



- undergoing elective colorectal surgery. *Br J Surg* 1992; 79:513–6
202. Jensen LS, Kissmeyer-Nielsen P, Wolff B, Qvist N: Randomised comparison of leucocyte-depleted *versus* buffy-coat-poor blood transfusion and complications after colorectal surgery. *Lancet* 1996; 348:841–5
  203. Tartter PI, Mohandas K, Azar P, Endres J, Kaplan J, Spivack M: Randomized trial comparing packed red cell blood transfusion with and without leukocyte depletion for gastrointestinal surgery. *Am J Surg* 1998; 176:462–6
  204. Titlestad IL, Ebbesen LS, Ainsworth AP, Lillevang ST, Qvist N, Georgsen J: Leukocyte-depletion of blood components does not significantly reduce the risk of infectious complications. Results of a double-blinded, randomized study. *Int J Colorectal Dis* 2001; 16:147–53
  205. van de Watering LM, Hermans J, Houbiers JG, van den Broek PJ, Bouter H, Boer H, Harvey MS, Huysmans HA, Brand A: Beneficial effects of leukocyte depletion of transfused blood on postoperative complications in patients undergoing cardiac surgery: A randomized clinical trial. *Circulation* 1998; 97:562–8
  206. Clagett GP, Valentine RJ, Jackson MR, Mathison C, Kakish HB, Bengtson TD: A randomized trial of intraoperative autotransfusion during aortic surgery. *J Vasc Surg* 1999; 29:22–30
  207. Daane CR, Golab HD, Meeder JH, Wijers MJ, Bogers AJ: Processing and transfusion of residual cardiopulmonary bypass volume: Effects on haemostasis, complement activation, postoperative blood loss and transfusion volume. *Perfusion* 2003; 18:115–21
  208. Damgaard S, Steinbrüchel DA: Autotransfusion with cell saver for off-pump coronary artery bypass surgery: A randomized trial. *Scand Cardiovasc J* 2006; 40:194–8
  209. Ekbäck G, Schött U, Axelsson K, Carlberg M: Perioperative autotransfusion and functional coagulation analysis in total hip replacement. *Acta Anaesthesiol Scand* 1995; 39:390–5
  210. Goel P, Pannu H, Mohan D, Arora R: Efficacy of cell saver in reducing homologous blood transfusions during OPCAB surgery: A prospective randomized trial. *Transfus Med* 2007; 17:285–9
  211. Laub GW, Dharan M, Riebman JB, Chen C, Moore R, Bailey BM, Fernandez J, Adkins MS, Anderson W, McGrath LB: The impact of intraoperative autotransfusion on cardiac surgery. A prospective randomized double-blind study. *Chest* 1993; 104:686–9
  212. McGill N, O'Shaughnessy D, Pickering R, Herbertson M, Gill R: Mechanical methods of reducing blood transfusion in cardiac surgery: Randomised controlled trial. *BMJ* 2002; 324:1299
  213. Mercer KG, Spark JI, Berridge DC, Kent PJ, Scott DJ: Randomized clinical trial of intraoperative autotransfusion in surgery for abdominal aortic aneurysm. *Br J Surg* 2004; 91:1443–8
  214. Murphy GJ, Rogers CS, Lansdowne WB, Channon I, Alwair H, Cohen A, Caputo M, Angelini GD: Safety, efficacy, and cost of intraoperative cell salvage and autotransfusion after off-pump coronary artery bypass surgery: A randomized trial. *J Thorac Cardiovasc Surg* 2005; 130:20–8
  215. Niranjana G, Asimakopoulos G, Karagounis A, Cockerill G, Thompson M, Chandrasekaran V: Effects of cell saver autologous blood transfusion on blood loss and homologous blood transfusion requirements in patients undergoing cardiac surgery on- *versus* off-cardiopulmonary bypass: A randomised trial. *Eur J Cardiothorac Surg* 2006; 30:271–7
  216. Rainaldi MP, Tazzari PL, Scagliarini G, Borghi B, Conte R: Blood salvage during caesarean section. *Br J Anaesth* 1998; 80:195–8
  217. Spark JI, Chetter IC, Kester RC, Scott DJ: Allogeneic *versus* autologous blood during abdominal aortic aneurysm surgery. *Eur J Vasc Endovasc Surg* 1997; 14:482–6
  218. Sarkanović ML, Gvozdenović L, Savić D, Ilić MP, Jovanović G: Autologous blood transfusion in total knee replacement surgery. *Vojnosanit Pregl* 2013; 70:274–8
  219. Shenolikar A, Wareham K, Newington D, Thomas D, Hughes J, Downes M: Cell salvage auto transfusion in total knee replacement surgery. *Transfus Med* 1997; 7:277–80
  220. Thomas D, Wareham K, Cohen D, Hutchings H: Autologous blood transfusion in total knee replacement surgery. *Br J Anaesth* 2001; 86:669–73
  221. Nuttall GA, Oliver WC Jr, Beynen FM, Dull JJ, Murray MJ, Nichols WL: Intraoperative measurement of activated partial thromboplastin time and prothrombin time by a portable laser photometer in patients following cardiopulmonary bypass. *J Cardiothorac Vasc Anesth* 1993; 7:402–9
  222. Williams GD, Bratton SL, Riley EC, Ramamoorthy C: Coagulation tests during cardiopulmonary bypass correlate with blood loss in children undergoing cardiac surgery. *J Cardiothorac Vasc Anesth* 1999; 13:398–404
  223. Wang SC, Shieh JF, Chang KY, Chu YC, Liu CS, Loong CC, Chan KH, Mandell S, Tsou MY: Thromboelastography-guided transfusion decreases intraoperative blood transfusion during orthotopic liver transplantation: Randomized clinical trial. *Transplant Proc* 2010; 42:2590–3
  224. Trzebicki J, Flakiewicz E, Kosieradzki M, Blaszczyk B, Kofacz M, Jureczko L, Pacholczyk M, Chmura A, Lagiewska B, Lisik W, Wasiaik D, Kosson D, Kwiatkowski A, Lazowski T: The use of thromboelastometry in the assessment of hemostasis during orthotopic liver transplantation reduces the demand for blood products. *Ann Transplant* 2010; 15:19–24
  225. Davidson SJ, McGrowder D, Roughton M, Kelleher AA: Can ROTEM thromboelastometry predict postoperative bleeding after cardiac surgery? *J Cardiothorac Vasc Anesth* 2008; 22:655–61
  226. Reinhöfer M, Brauer M, Franke U, Barz D, Marx G, Lösche W: The value of rotation thromboelastometry to monitor disturbed perioperative haemostasis and bleeding risk in patients with cardiopulmonary bypass. *Blood Coagul Fibrinolysis* 2008; 19:212–9
  227. Andreasen JB, Hvas AM, Christiansen K, Ravn HB: Can RoTEM® analysis be applied for haemostatic monitoring in paediatric congenital heart surgery? *Cardiol Young* 2011; 21:684–91
  228. Haas T, Spielmann N, Mauch J, Madjdpour C, Speer O, Schmutz M, Weiss M: Comparison of thromboelastometry (ROTEM®) with standard plasmatic coagulation testing in paediatric surgery. *Br J Anaesth* 2012; 108:36–41
  229. Herbstreit F, Winter EM, Peters J, Hartmann M: Monitoring of haemostasis in liver transplantation: Comparison of laboratory based and point of care tests. *Anaesthesia* 2010; 65:44–9
  230. Ogawa S, Szlam F, Chen EP, Nishimura T, Kim H, Roback JD, Levy JH, Tanaka KA: A comparative evaluation of rotation thromboelastometry and standard coagulation tests in hemodilution-induced coagulation changes after cardiac surgery. *Transfusion* 2012; 52:14–22
  231. Oswald E, Stalzer B, Heitz E, Weiss M, Schmutz M, Strasak A, Innerhofer P, Haas T: Thromboelastometry (ROTEM) in children: Age-related reference ranges and correlations with standard coagulation tests. *Br J Anaesth* 2010; 105:827–35
  232. Stancheva A, Spassov L, Tzatchev K: Correlation between rotation thromboelastometry ROTEM analysis and standard haemostatic parameters during liver transplantation. *Clin Lab* 2011; 57:407–13
  233. Chelemer SB, Prato BS, Cox PM Jr, O'Connor GT, Morton JR: Association of bacterial infection and red blood cell transfusion after coronary artery bypass surgery. *Ann Thorac Surg* 2002; 73:138–42

234. Koch CG, Li L, Duncan AI, Mihaljevic T, Cosgrove DM, Loop FD, Starr NJ, Blackstone EH: Morbidity and mortality risk associated with red blood cell and blood-component transfusion in isolated coronary artery bypass grafting. *Crit Care Med* 2006; 34:1608–16
235. Murphy GJ, Reeves BC, Rogers CA, Rizvi SI, Culliford L, Angelini GD: Increased mortality, postoperative morbidity, and cost after red blood cell transfusion in patients having cardiac surgery. *Circulation* 2007; 116:2544–52
236. Sreeram GM, Welsby IJ, Sharma AD, Phillips-Bute B, Smith PK, Slaughter TF: Infectious complications after cardiac surgery: Lack of association with fresh frozen plasma or platelet transfusions. *J Cardiothorac Vasc Anesth* 2005; 19:430–4
237. Bux J, Becker F, Seeger W, Kilpatrick D, Chapman J, Waters A: Transfusion-related acute lung injury due to HLA-A2-specific antibodies in recipient and NB1-specific antibodies in donor blood. *Br J Haematol* 1996; 93:707–13
238. Chung YT, Wu YC, Chen YH: Postoperative pulmonary edema, transfusion-related?—a case report. *Acta Anaesthesiol Sin* 2003; 41:43–6
239. Yasuda H, Ohto H, Yamaguchi O, Sakuma S, Suzuki T, Mita M, Tsuneyama H, Uchikawa M: Three episodes of delayed hemolytic transfusion reactions due to multiple red cell antibodies, anti-Di, anti-Jk and anti-E. *Transfus Sci* 2000; 23:107–12
240. Consten EC, Henny CP, Eijssman L, Dongelmans DA, van Oers MH: The routine use of fresh frozen plasma in operations with cardiopulmonary bypass is not justified. *J Thorac Cardiovasc Surg* 1996; 112:162–7
241. Wilhelmi M, Franke U, Cohnert T, Weber P, Kaukemüller J, Fischer S, Wahlers T, Haverich A: Coronary artery bypass grafting surgery without the routine application of blood products: Is it feasible? *Eur J Cardiothorac Surg* 2001; 19:657–61
242. Casas JI, Zuazu-Jausoro I, Mateo J, Oliver A, Litvan H, Muniz-Diaz E, Aris A, Caralps JM, Fontcuberta J: Aprotinin *versus* desmopressin for patients undergoing operations with cardiopulmonary bypass. A double-blind placebo-controlled study. *J Thorac Cardiovasc Surg* 1995; 110:1107–17
243. Despotis GJ, Levine V, Saleem R, Spitznagel E, Joist JH: Use of point-of-care test in identification of patients who can benefit from desmopressin during cardiac surgery: A randomized controlled trial. *Lancet* 1999; 354:106–10
244. Karnezis TA, Stulberg SD, Wixson RL, Reilly P: The hemostatic effects of desmopressin on patients who had total joint arthroplasty. A double-blind randomized trial. *J Bone Joint Surg Am* 1994; 76:1545–50
245. Pleym H, Stenseth R, Wähba A, Bjella L, Tromsdal A, Karevold A, Dale O: Prophylactic treatment with desmopressin does not reduce postoperative bleeding after coronary surgery in patients treated with aspirin before surgery. *Anesth Analg* 2004; 98:578–84
246. Sheridan DP, Card RT, Pinilla JC, Harding SM, Thomson DJ, Gauthier L, Drotar D: Use of desmopressin acetate to reduce blood transfusion requirements during cardiac surgery in patients with acetylsalicylic-acid-induced platelet dysfunction. *Can J Surg* 1994; 37:33–6
247. Temeck BK, Bachenheimer LC, Katz NM, Coughlin SS, Wallace RB: Desmopressin acetate in cardiac surgery: A double-blind, randomized study. *South Med J* 1994; 87:611–5
248. Wong AY, Irwin MG, Hui TW, Fung SK, Fan ST, Ma ES: Desmopressin does not decrease blood loss and transfusion requirements in patients undergoing hepatectomy. *Can J Anaesth* 2003; 50:14–20
249. Ray MJ, Hales MM, Brown L, O'Brien MF, Stafford EG: Postoperatively administered aprotinin or epsilon aminocaproic acid after cardiopulmonary bypass has limited benefit. *Ann Thorac Surg* 2001; 72:521–6
250. Codispoti M, Mankad PS: Significant merits of a fibrin sealant in the presence of coagulopathy following paediatric cardiac surgery: Randomised controlled trial. *Eur J Cardiothorac Surg* 2002; 22:200–5
251. Figueras J, Llado L, Miro M, Ramos E, Torras J, Fabregat J, Serrano T: Application of fibrin glue sealant after hepatectomy does not seem justified: Results of a randomized study in 300 patients. *Ann Surg* 2007; 245:536–42
252. Jackson MR, Gillespie DL, Longenecker EG, Goff JM, Fiala LA, O'Donnell SD, Gomperts ED, Navalta LA, Hestlow T, Alving BM: Hemostatic efficacy of fibrin sealant (human) on expanded poly-tetrafluoroethylene carotid patch angioplasty: A randomized clinical trial. *J Vasc Surg* 1999; 30:461–6
253. Kjaergard HK, Trumbull HR: Vivostat system autologous fibrin sealant: Preliminary study in elective coronary bypass grafting. *Ann Thorac Surg* 1998; 66:482–6
254. Kluba T, Fiedler K, Kunze B, Ipach I, Suckel A: Fibrin sealants in orthopaedic surgery: Practical experiences derived from use of QUIXIL® in total knee arthroplasty. *Arch Orthop Trauma Surg* 2012; 132:1147–52
255. Levy O, Martinowitz U, Oran A, Tauber C, Horoszowski H: The use of fibrin tissue adhesive to reduce blood loss and the need for blood transfusion after total knee arthroplasty. A prospective, randomized, multicenter study. *J Bone Joint Surg Am* 1999; 81:1580–8
256. Mawatari M, Higo T, Tsutsumi Y, Shigematsu M, Hotokebuchi T: Effectiveness of autologous fibrin tissue adhesive in reducing postoperative blood loss during total hip arthroplasty: A prospective randomised study of 100 cases. *J Orthop Surg (Hong Kong)* 2006; 14:117–21
257. Notarnicola A, Moretti L, Martucci A, Spinarelli A, Tafuri S, Pesce V, Moretti B: Comparative efficacy of different doses of fibrin sealant to reduce bleeding after total knee arthroplasty. *Blood Coagul Fibrinolysis* 2012; 23:278–84
258. Rousou J, Levitsky S, Gonzalez-Lavin L, Cosgrove D, Magilligan D, Weldon C, Hiebert C, Hess P, Joyce L, Bergsland J: Randomized clinical trial of fibrin sealant in patients undergoing re sternotomy or reoperation after cardiac operations. A multicenter study. *J Thorac Cardiovasc Surg* 1989; 97:194–203
259. Sabatini L, Trecci A, Imarisio D, Uslenghi MD, Bianco G, Scagnelli R: Fibrin tissue adhesive reduces postoperative blood loss in total knee arthroplasty. *J Orthop Traumatol* 2012; 13:145–51
260. Wang GJ, Goldthwaite CA Jr, Burks S, Crawford R, Spotnitz WD; Orthopaedic Investigators Group: Fibrin sealant reduces perioperative blood loss in total hip replacement. *J Long Term Eff Med Implants* 2003; 13:399–411
261. Wang GJ, Hungerford DS, Savory CG, Rosenberg AG, Mont MA, Burks SG, Mayers SL, Spotnitz WD: Use of fibrin sealant to reduce bloody drainage and hemoglobin loss after total knee arthroplasty: A brief note on a randomized prospective trial. *J Bone Joint Surg Am* 2001; 83-A:1503–5
262. Chapman WC, Clavien PA, Fung J, Khanna A, Bonham A: Effective control of hepatic bleeding with a novel collagen-based composite combined with autologous plasma: Results of a randomized controlled trial. *Arch Surg* 2000; 135:1200–4
263. Mathiasen RA, Cruz RM: Prospective, randomized, controlled clinical trial of a novel matrix hemostatic sealant in children undergoing adenoidectomy. *Otolaryngol Head Neck Surg* 2004; 131:601–5
264. Powell DM, Chang E, Farrior EH: Recovery from deep-plane rhytidectomy following unilateral wound treatment with autologous platelet gel: A pilot study. *Arch Facial Plast Surg* 2001; 3:245–50
265. Bhardwaj M, Bunsell R: Beriplex P/N: An alternative to fresh frozen plasma in severe haemorrhage. *Anaesthesia* 2007; 62:832–4

266. Bruce D, Nokes TJ: Prothrombin complex concentrate (Beriplex P/N) in severe bleeding: Experience in a large tertiary hospital. *Crit Care* 2008; 12:R105
267. Lorenz R, Kienast J, Otto U, Kiehl M, Schreiter D, Haertel S, Barthels M: Successful emergency reversal of phenprocoumon anticoagulation with prothrombin complex concentrate: A prospective clinical study. *Blood Coagul Fibrinolysis* 2007; 18:565–70
268. Stuklis RG, O'Shaughnessy DF, Ohri SK: Novel approach to bleeding in patients undergoing cardiac surgery with liver dysfunction. *Eur J Cardiothorac Surg* 2001; 19:219–20
269. Diprose P, Herbertson MJ, O'Shaughnessy D, Gill RS: Activated recombinant factor VII after cardiopulmonary bypass reduces allogeneic transfusion in complex non-coronary cardiac surgery: Randomized double-blind placebo-controlled pilot study. *Br J Anaesth* 2005; 95:596–602
270. Friederich PW, Henny CP, Messelink EJ, Geerdink MG, Keller T, Kurth KH, Büller HR, Levi M: Effect of recombinant activated factor VII on perioperative blood loss in patients undergoing retropubic prostatectomy: A double-blind placebo-controlled randomised trial. *Lancet* 2003; 361:201–5
271. Johansson PI, Eriksen K, Nielsen SL, Rojkjaer R, Alsbjorn B: Recombinant FVIIa decreases perioperative blood transfusion requirement in burn patients undergoing excision and skin grafting—results of a single centre pilot study. *Burns* 2007; 33:435–40
272. Lodge JP, Jonas S, Jones RM, Olausson M, Mir-Pallardo J, Soefelt S, Garcia-Valdecasas JC, McAlister V, Mirza DF; rFVIIa OLT Study Group: Efficacy and safety of repeated perioperative doses of recombinant factor VIIa in liver transplantation. *Liver Transpl* 2005; 11:973–9
273. Lodge JP, Jonas S, Oussoultzoglou E, Malagó M, Jayr C, Cherqui D, Anthuber M, Mirza DF, Kuhlman L, Bechstein WO, Díaz JC, Tartiere J, Eyraud D, Fridberg M, Erhardtsen E, Mimoz O: Recombinant coagulation factor VIIa in major liver resection: A randomized, placebo-controlled, double-blind clinical trial. *ANESTHESIOLOGY* 2005; 102:269–75
274. Raobaikady R, Redman J, Ball JA, Maloney G, Grounds RM: Use of activated recombinant coagulation factor VII in patients undergoing reconstruction surgery for traumatic fracture of pelvis or pelvis and acetabulum: A double-blind, randomized, placebo-controlled trial. *Br J Anaesth* 2005; 94:586–91
275. Shao YF, Yang JM, Chau GY, Sirivatanauksorn Y, Zhong SX, Erhardtsen E, Nivatvongs S, Lee PH: Safety and hemostatic effect of recombinant activated factor VII in cirrhotic patients undergoing partial hepatectomy: A multicenter, randomized, double-blind, placebo-controlled trial. *Am J Surg* 2006; 191:245–9
276. Fenger-Eriksen C, Jensen TM, Kristensen BS, Jensen KM, Tønnesen E, Ingerslev J, Sørensen B: Fibrinogen substitution improves whole blood clot firmness after dilution with hydroxyethyl starch in bleeding patients undergoing radical cystectomy: A randomized, placebo-controlled clinical trial. *J Thromb Haemost* 2009; 7:795–802
277. Rahe-Meyer N, Solomon C, Hanke A, Schmidt DS, Knoerzer D, Hochleitner G, Sørensen B, Hagl C, Pichlmaier M: Effects of fibrinogen concentrate as first-line therapy during major aortic replacement surgery: A randomized, placebo-controlled trial. *ANESTHESIOLOGY* 2013; 118:40–50