

**Practice Guidelines for Perioperative Blood Management: An Updated Report**  
*American Society of Anesthesiologists*

**Bibliography by Section**

**I. Preoperative patient evaluation**

**Reviewing medical records (patient condition).**

*Observational studies, case reports, or comparisons without pertinent control groups*

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### **Laboratory tests.**

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***Coagulation profile (PT, aPTT, activated coagulation time [ACT], thromboelastogram [TEG]):***

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## ***II. Preadmission patient preparation***

### **Prevention/reduction of perioperative anemia.**

#### ***Erythropoietin:***

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*Randomized controlled trials; erythropoietin vs. no erythropoietin*

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*Nonrandomized comparative studies; erythropoietin vs. no erythropoietin*

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***Iron:***

*Randomized controlled trials*

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**Discontinuation of anticoagulants.**

**Warfarin:**

*Observational studies, case reports, or non-pertinent comparison groups*

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**Discontinuation of antithrombotics.**

**Clopidogrel, Ticagralor, Prasugrel or other thienopyridines:**

*Observational studies, case reports, or non-pertinent comparison groups*

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**Aspirin:**

*Observational studies, case reports, or non-pertinent comparison groups*

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### **Preadmission Autologous Blood Donation (PAD).**

*PAD versus allogeneic blood or blood products:*

Randomized controlled trials

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Nonrandomized comparative studies

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***PAD versus preprocedure acute normovolemic hemodilution (ANH):***

*Nonrandomized comparative studies*

1. Terada N, Arai Y, Matsuta Y, Maekawa S, Okubo K, Ogura K, Matsuda N, Yonei A: Acute normovolemic hemodilution for radical prostatectomy: can it replace preoperative autologous blood transfusion? *Int J Urol* 2001; 8:149-152

***PAD versus intraoperative or postoperative blood recovery:***

**Randomized controlled trials**

1. Waters JH, Lee JS, Klein E, O'Hara J, Zippe C, Potter PS: Preoperative autologous donation versus cell salvage in the avoidance of allogeneic transfusion in patients undergoing radical retropubic prostatectomy. Anesth Analg 2004; 98:537-542

**Nonrandomized comparative studies**

1. Gray CL, Amling CL, Polston GR, Powell CR, Kane CJ: Intraoperative cell salvage in radical retropubic prostatectomy. Urology 2001; 58:740-745
2. MacIvor D, Nelson J, Triulzi D: Impact of intraoperative red blood cell salvage on transfusion requirements and outcomes in radical prostatectomy. Transfusion 2009; 49:1431-1434
3. O'Hara PJ, Hertzer NR, Krajewski LP, Cox GS, Beven EG: Reduction in the homologous blood requirement for abdominal aortic aneurysm repair by the use of preadmission autologous blood donation. Surgery 1994; 115:69-76

***III. Preprocedure patient preparation***

**Reversal of anticoagulants.**

***Prothrombin complex concentrates (PCC): Bebulin, Profilin, Kcentra:***

**Observational studies, case reports, or non-pertinent comparison groups**

1. 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; 110:764-772
2. 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
3. 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

**Vitamin K:**

**Nonrandomized comparative studies**

1. 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; 41:78-83

**Antifibrinolytics for prophylaxis of excessive bleeding.**

***ε-Aminocaproic acid:***

**Randomized controlled trials; ε-aminocaproic acid vs placebo:**

1. 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; 98:337-342

2. 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; 96:576-582
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13. 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; 91:430-435

*Randomized controlled trials; ε-aminocaproic acid vs no antifibrinolytic therapy:*

1. 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; 22:231-236
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Nonrandomized comparative studies:

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2. Jordan D, Delphin E, Rose E: Prophylactic epsilon-aminocaproic acid (EACA) administration minimizes blood replacement therapy during cardiac surgery. Anesth Analg 1995; 80:827-829

Observational studies, case reports, or non-pertinent comparison groups:

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2. Mangano DT, Tudor IC, Dietzel C: The risk associated with aprotinin in cardiac surgery. N Eng J Med 2006; 354:353-365

***Tranexamic acid:***

Randomized controlled trials; tranexamic acid vs placebo:

1. 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
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*Randomized controlled trials; tranexamic acid vs no antifibrinolytic therapy:*

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Nonrandomized comparative studies:

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Observational studies, case reports, or non-pertinent comparison groups:

1. Bokesch PM, Szabo G, Wojdyga R, Grocott HP, Smith PK, Mazer CD, Vetticaden S, Wheeler A, Levy JH: A phase 2 prospective, randomized, double-blind trial comparing the effects of tranexamic acid with ecallantide on blood loss from high-risk cardiac surgery with cardiopulmonary bypass (CONSERV-2 Trial). *J Thorac Cardiovasc Surg* 2012; 143:1022-1029
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## **Acute Normovolemic Hemodilution (ANH).**

### ***ANH versus no ANH:***

#### **Randomized controlled trials:**

1. Bennett J, Haynes S, Torella F, Grainger H, McCollum C: Acute normovolemic hemodilution in moderate blood loss surgery: a randomized controlled trial. *Transfusion* 2006; 46:1097-1103
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***ANH combined with intraoperative blood recovery (ICSB) versus either ANH or ISCB:***

**Randomized controlled trials:**

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Nonrandomized comparative studies

1. Copley LA, Richards BS, Safavi FZ, Newton PO: Hemodilution as a method to reduce transfusion requirements in adolescent spine fusion surgery. Spine 1999; 24:219-222
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**IV. Intraoperative and postoperative interventions**

**Blood management protocols.**

**Multimodal protocols or algorithms:**

Randomized controlled trials: general or point-of-care protocols or algorithms:

1. Capraro L, Kuitunen A, Salmenpera M, Kekomaki R: On-site coagulation monitoring does not affect hemostatic outcome after cardiac surgery. Acta Anaesthesiologica Scand 2001; 45:200-206
2. Nuttall GA, Oliver WC, Santrach PJ, Bryant S, Dearani JA, Schaff HV, Eret MH: Efficacy of a simple intraoperative transfusion algorithm for nonerythrocyte component utilization after cardiopulmonary bypass. Anesthesiology 2001; 94:773-781
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*Randomized controlled trials; thromboelastography (TEG) - guided protocols or algorithms:*

1. 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; 24:404-410
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*Randomized controlled trials; thromboelastography (TEG) - guided protocols or algorithms:*

1. 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; 109:376-381

*Nonrandomized comparative studies:*

1. Avidan MS, Alcock EL, Da Fonseca J, Ponte J, Despotis GJ, Hunt BJ: Comparison of structured use of routine laboratory tests or near-patient assessment with clinical judgement in the management of bleeding after cardiac surgery. *Br J Anaesth* 2004; 92:178-186
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*Observational studies, case reports, or non-pertinent comparison groups:*

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2. Cuenca J, Garcia-Erce JA, Martinez F, Perez-Serrano L, Herrera A, Munoz M: Perioperative intravenous iron, with or without erythropoietin, plus restrictive transfusion protocol reduce the need for allogeneic blood after knee replacement surgery. *Transfusion* 2006; 46:1112-1119
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Initiative: Blood product conservation is associated with improved outcomes and reduced costs after cardiac surgery. *J Thorac Cardiovasc Surg* 2013; 145:796-803

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***Liberal versus restrictive transfusion protocol:***

**Randomized controlled trials:**

1. Bracey AW, Radovancevic R, Riggs SA, Houston S, Cozart H, Vaughn WK, Radovancevic B, McAllister HA, Cooley DA: Lowering the hemoglobin threshold for transfusion in coronary artery bypass procedures: effect on patient outcome. *Transfusion* 1999; 39:1070-1077
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**Nonrandomized comparative studies:**

1. Cuenca J, Garcia-Erce JA, Martinez F, Cardona R, Perez-Serrano L, Munoz M: Preoperative haematinics and transfusion protocol reduce the need for transfusion after total knee replacement. *Int J Surg* 2007; 5:89-94

***Non-transfusion protocol:***

**Nonrandomized comparative studies:**

1. 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
2. Whitson BA, Huddleston SJ, Savik K, Shumway SJ: Bloodless cardiac surgery is associated with decreased morbidity and mortality. *J Card Surg* 2007; 22:373-378

**Observational studies, case reports, or non-pertinent comparison groups**

1. Harwin SF, Pivec R, Johnson AJ, Naziri Q, Mont MA: Revision total hip arthroplasty in Jehovah's Witnesses. *Orthopedics* 2012; 35:e1145-e1151
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***Massive transfusion protocol:***

**Nonrandomized comparative studies:**

1. Simmons JW, White CE, Eastridge BJ, Mace JE, Wade CE, Blackbourne LH: Impact of policy change on US Army combat transfusion practices. *J Trauma* 2010; 69 (Suppl 1):S75-S80

**Observational studies, case reports, or non-pertinent comparison groups:**

1. Gutierrez MC, Goodnough LT, Druzin M, Butwick AJ: Postpartum hemorrhage treated with a massive transfusion protocol at a tertiary obstetric center: a retrospective study. *Int J Obstet Anesth* 2012; 21:230-235

***Maximum surgical blood ordering schedule for elective procedures:***

**Randomized controlled trials:**

1. Nuttall GA, Santrach PJ, Oliver WC Jr, Eretz MH, Horlocker TT, Cabanel ME, Trousdale RT, Bryant S, Currie TW: A prospective randomized trial of the surgical blood order equation for ordering red blood cells for total hip arthroplasty patients. *Transfusion* 1998; 38:828-833

**Observational studies, case reports, or non-pertinent comparison groups:**

1. 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 116:768-778
2. 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; 118:1286-1297
3. 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
4. Karger R, Bornmann A, Kretschmer V: Limited utility of algorithms predicting blood transfusions. *Blood Transfus* 2013; 11:426-432
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***Allogeneic red blood cell transfusion.***

***Age of stored RBCs:***

**Nonrandomized comparative studies:**

1. Andreasen JJ, Dethlefsen C, Modrau IS, Baech J, Schonheyder HC, Moeller JK, Johnsen SP: 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; 39:329-334

2. 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; 86:120-127
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4. 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; 50:1185-1195
5. 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; 358:1229-1239
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*Observational studies, case reports, or non-pertinent comparison groups*

1. Hebert PC, Chin-Yee I, Fergusson D, Blajchman M, Martineau R, Clinch J, Olberg B: A pilot trial evaluating the clinical effects of prolonged storage of red cells. Anesth Analg 2005; 100:1433-1438
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***Leukocyte reduction:***

*Randomized controlled trials:*

1. Bilgin YM, van de Watering LM, Eijsman L, Versteegh MI, Brand R, van Oers MH, Brand A: Double-blind, randomized controlled trial on the effect of leukoreduced erythrocyts transfusions in cardiac valve surgery. Circulation 2004; 109:2755-2760

2. Houbiers JG, Brand A, van de Watering LM, Hermans J, Verwey PJ, Bijnen AB, Pahlplatz P, Eeftinck Schattenkerk M, Wobbes T, de Vries JE: Randomised controlled trial comparing transfusion of leukocyte-depleted or buffy-coat-depleted blood in colorectal cancer. *Lancet* 1994; 344:573-578
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*Observational studies, case reports, or non-pertinent comparison groups*

1. Blumberg N, Heal JM, Gettings KF, Phipps RP, Masel D, Refaai MA, Kirkley SA, Fialkow LB: An association between decreased cardiopulmonary complications (TRALI and TACO) and implementation of universal leukoreduction of blood transfusions. *Transfusion* 2010; 50:2738-2744
2. Wallis JP, Chapman CE, Orr KE, Clark SC, Forty JR: Effect of WBC reduction of transfused RBCs on postoperative infection rates in cardiac surgery. *Transfusion* 2002; 42:1127-1134

**Autologous red blood cell transfusion.**

***Intraoperative blood recovery:***

***Randomized controlled trials:***

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***Postoperative blood recovery:***

***Randomized controlled trials; cell salvage:***

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Randomized controlled trials; whole blood:

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Nonrandomized comparative studies; whole blood:

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*Observational studies, case reports, or non-pertinent comparison groups; cell salvage*

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*Observational studies, case reports, or non-pertinent comparison groups; whole blood:*

1. Jones HW, Savage L, White C, Goddard R, Lumley H, Kashif F, Gurusany K: Postoperative autologous blood salvage drains - are they useful in primary uncemented hip and knee arthroplasty? A prospective study of 186 cases. *Acta Orthop Belg* 2004; 70:466-473

**Intraoperative and postoperative patient monitoring.**

***Monitoring for inadequate perfusion and oxygenation of vital organs:***

**Randomized controlled trials:**

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*Observational studies, case reports, or non-pertinent comparison groups:*

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***Monitoring for non RBC transfusion coagulopathy:***

**Platelet function monitoring:**

**Observational studies, case reports, or non-pertinent comparison groups:**

1. 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. *Cardiothorac Vasc Anesth* 1993; 7:402-409
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3. 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

**Viscoelastic haemostatic assays (VHA):**

**Randomized controlled trials; Thromboelastography (TEG):**

1. 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; 42:2590-2593

**Nonrandomized comparative studies; Rotational thromboelastometry (ROTEM):**

1. Trzebicki J, Flakiewicz E, Kosieradzki M, Blaszczyk B, Kołacz M, Jureczko L, Pacholczyk M, Chmura A, Lagiewska B, Lisik W, Wasiak 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

**Observational studies, case reports, or non-pertinent comparison groups:**

2. Andreasen JB, Hvas AM, Christiansen K, Ravn HB: Can RoTEM® analysis be applied for haemostatic monitoring in paediatric congenital heart surgery? *Cardiol Young* 2011; 21:684-691
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- thromboelastogram, and conventional coagulation tests. *J Cardiothorac Vasc Anesth* 2006; 20:548-553
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  7. 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; 65:44-49
  8. Lee GC, Kicza AM, Liu KY, Nyman CB, Kaufman RM, Body SC: Does rotational thromboelastometry (ROTEM) improve prediction of bleeding after cardiac surgery? *Anesth Analg* 2012; 115:499-506
  9. Levrat A, Gros A, Rugeri L, Inaba K, Floccard B, Negrier C, David JS: Evaluation of rotation thrombelastography for the diagnosis of hyperfibrinolysis in trauma patients. *Br J Anaesth* 2008; 100: 792-797
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  12. 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; 19:212-219
  13. Stancheva A, Spassov L, Tzatchev K: Correlation between rotation thrombelastometry ROTEM analysis and standard haemostatic parameters during liver transplantation. *Clin Lab* 2011; 57:407-413
  14. Tirosh-Wagner T, Strauss T, Rubinstein M, Tamarin I, Mishaly D, Paret G, Kenet G: Point of care testing in children undergoing cardiopulmonary bypass. *Pediatr Blood Cancer* 2011; 56:794-798
  15. Weber CF, Gorlinger K, Meininger D, Herrmann E, Bingold T, Moritz A, Cohn LH, Zacharowski K: Point-of-care testing: a prospective, randomized clinical trial of efficacy in coagulopathic cardiac surgery patients. *Anesthesiology* 2012; 117:531-547

***Monitoring (periodic checking) for adverse effects of transfusions:***

**Transfusion-related acute lung injury (TRALI):**

**Observational studies, case reports, or non-pertinent comparison groups:**

1. 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; 93:707-713
2. Chung YT, Wu YC, Chen YH: Postoperative pulmonary edema, transfusion-related?--a case report. *Acta Anaesthesiol Sin* 2003; 41:43-46
3. Toy P, Gajic O, Bacchetti P, Looney MR, Gropper MA, Hubmayr R, Lowell CA, Norris PJ, Murphy EL, Weiskopf RB, Wilson G, Koenigsberg M, Lee D, Schuller R, Wu P,

Grimes B, Gandhi MJ, Winters JL, Mair D, Hirschler N, Rosen RS, Matthat MA: Transfusion-related acute lung injury: incidence and risk factors. *Blood* 2012; 119:1757-1767

Hemolytic transfusion reactions (ABO incompatibility):

Observational studies, case reports, or non-pertinent comparison groups:

- 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; 23:107-112

Bacterial contamination:

Nonrandomized comparative studies:

- 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; 73:138-142
- 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; 34:1608-1616
- Murphy GJ, Reeves BC, Rogers CA, Rizve SI, Culliford L, Angelini GD: Increased mortality, postoperative morbidity and cost after red blood cell transfusion in patients having cardiac surgery. *Circulation* 2007; 116:2544-2552
- Sreeram GM, Welsby IJ, Sharma AD, Philips-Bute B, Smith PK, Slaughter TF: Infectious complications after cardiac surgery: lack of association with FFP or platelet transfusions. *J Cardiothorac Vasc Anesth* 2005; 19:430-434

Observational studies, case reports, or non-pertinent comparison groups

- Banbury MK, Brizzio ME, Rajeswaran J, Lytle BW, Blackstone EH: Transfusion increases the risk of postoperative infection after cardiac surgery. *J Am Coll Surg* 2006; 202:131-138
- Dzik WH, Andersen JK, O'Neill EM, Assmann SF, Kalish LA, Stowell CP: A prospective, randomized clinical trial of universal WBC reduction. *Transfusion* 2002; 42:1114-1122

**Treatment of excessive bleeding.**

**Platelet transfusion (PLT or A-PLT):**

Nonrandomized comparative studies:

- Pereboom ITA, de Boer MT, Haagsma EB, Hendriks HGD, Lisman T, Porte RJ: Platelet transfusion during liver transplantation is associated with increased postoperative mortality due to acute lung injury. *Anesth Analg* 2009; 108:1083-1091

Observational studies, case reports, or non-pertinent comparison groups

- Lemmer JH Jr, Metzdorff MT, Krause AH Jr, Martin MA, Okies JE, Hill JG: Emergency coronary artery bypass graft surgery in abciximab-treated patients. *Ann Thorac Surg* 2000; 69:90-95

***Fresh frozen plasma transfusion (FFP or A-FFP):***

**Randomized controlled trials:**

1. Consten ECJ, Henny CP, Eijsman L, Dongelmans DA, van Oers MHJ: The routine use of fresh frozen plasma in operations with cardiopulmonary bypass is not justified. *J Thorac Cardiovasc Surg* 1996; 112:162-167
2. Wilhelm M, Franke U, Cohnert T, Weber P, Kaukemuller 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; 19:657-661

**Observational studies, case reports, or non-pertinent comparison groups**

1. 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; 40:641-644
2. Murray DJ, Pennell BJ, Weinstein SL, Olson JD: Packed red cells in acute blood loss: Dilutional coagulopathy as a cause of surgical bleeding. *Anesth Analg* 1995; 80:336-342

***Pharmacologic treatments:***

**Desmopressin (DDAVP):**

**Randomized controlled trials; Desmopressin vs. placebo:**

1. Alanay A, Acaroglu E, Ozdemir O, Ercegen O, Bulutcu E, Surat A: Effects of deamino-8-D-arginine vasopressin on blood loss and coagulation factors in scoliosis surgery. A double-blind randomized clinical trial. *Spine* 1999; 24:877-882
2. 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; 110:1107-1117
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Randomized controlled trials; Desmopressin vs. no Desmopressin:

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Antifibrinolytics (for treatment of excessive bleeding)

Randomized controlled trials;  $\epsilon$ -Aminocaproic acid:

1. 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; 72:521-526

Topical hemostatics; Fibrin glue:

Randomized controlled trials

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Observational studies, case reports, or non-pertinent comparison groups

Yu L, Gu T, Song L, Shi E, Fang Q, Wang C, Zhao J: Fibrin sealant provides superior hemostasis for sternotomy compared with bone wax. *Ann Thorac Surg* 2012; 93:641-644

Topical hemostatics; Thrombin gel:

Randomized controlled trials

1. 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; 135:1200-1204
2. Mathiasen RA, Cruz RM: Prospective, randomized, controlled clinical trial of a novel matrix hemostatic sealant in children undergoing adenoidectomy. *Otolaryngol Head Neck Surg* 2004; 131:601-605
3. 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; 3:245-250

Prothrombin complex concentrates (PCC):

Observational studies, case reports, or non-pertinent comparison groups

1. Bhardwaj M, Bunsell R: Beriplex P/N: an alternative to fresh frozen plasma in severe haemorrhage. *Anaesthesia* 2007; 62:832-834
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4. Stuklis RG, O'Shaughnessy DF, Ohri SK: Novel approach to bleeding in patients undergoing cardiac surgery with liver dysfunction. *Eur J Cardiothorac Surg* 2001; 19:219-220

Coagulation factor concentrates; Recombinant human activated Factor VII, Factor VIIa:

Randomized controlled trials

1. 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
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9. Shao YF, Yang JM, Chau GY, Sirivatanaucksorn Y, Zhong SX, Erhardtzen E, Nivatvongs S, Lee PH: Safety and hemostatic effects of recombinant activated factor VII in cirrhotic patients undergoing partial hepatectomy; a multicenter, randomized, double-blind, placebo-controlled trial. *Am J Surg* 2006; 191:245-249

Nonrandomized comparative studies

1. Andersen ND, Bhattacharya SD, Williams JB, Fosbol EL, Lockhart EL, Patel MB, Gaca JG, Welsby IJ, Hughes GC: Intraoperative use of low-dose recombinant activated factor VII during thoracic aortic operations. *Ann Thorac Surg* 2012; 93:1921-1928
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3. Hendriks HG, Meijer K, de Wolf JT, Klompmaker IJ, Porte RJ, de Kam PJ, Hagenaars AJ, Melsen T, Slooff MJ, van der Meer J: Reduced transfusion requirements by recombinant factor VIIa in orthotopic liver transplantation: a pilot study. *Transplantation* 2001; 71:402-405
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*Observational studies, case reports, or non-pertinent comparison groups*

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6. Moscardo F, Perez F, de la Rubia J, Balerdi B, Lorenzo JI, Senent ML, Aznar I, Carceller S, Sanz MA: Successful treatment of severe intra-abdominal bleeding associated with disseminated intravascular coagulation using recombinant activated factor VII. Br J Haematol 2001; 114:174-176
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8. Phillips LE, McLintock C, Pollock W, Gatt S, Popham P, Jankelowitz G, Ogle R, Cameron PA: Recombinant activated Factor VII in obstetric hemorrhage: experiences from the Australian and New Zealand haemostasis registry. Anesth Analg 2009; 109:1908-1915
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Treatments for hypofibrinogenemia; Fibrinogen concentrate (Riastap™ or Haemocomplettan™):

Randomized controlled trials

1. 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
2. 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

Observational studies, case reports, or non-pertinent comparison groups

1. Karlsson M, Ternström L, Hyllner M, Baghaei F, Flinck A, Skrtic S, Jeppsson A: Prophylactic fibrinogen infusion reduces bleeding after coronary artery bypass surgery. A prospective randomised pilot study. *Thromb Haemost* 2009; 102:137-144
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