TABLE E-1 Evaluation of Latest Studies (Published after 2004) on Reducing Perioperative Blood Loss and Allogeneic Blood Transfusion in Patients Undergoing Major Spine Surgery

Authors	Blood-Sparing Technique	Study Methodology	Results	Authors' Conclusions	Level of Evidence*
Brookfield et al.[9], 2008	Autologous predonation	A retrospective review of 676 patients who underwent elective lumbar spine surgery with or without predonation	Patients who predonated blood had blood loss similar to that of patients who did not predonate. No major difference in allogeneic blood transfusion rates between the two groups	For patients with a normal coagulation profile, preoperative blood donation is not beneficial for short lumbar fusion procedures with instrumentation	III
Epstein et al.[15], 2006	Acute normovolemic hemodilution	68 patients had multilevel lumbar laminectomies (3-6 levels), predominantly with 1 or 2-level fusions and instrumentation, with or without normovolemic hemodilution	With use of normovolemic hemodilution, no homologous blood transfusions were required in 52 patients. 16 patients required transfusion of 31 units of homologous blood after surgery	With use of normovolemic hemodilution, 52 (76%) of 68 patients were able to avoid homologous transfusion	III
Epstein[16], 2008	Acute normovolemic hemodilution	A review article	For adolescents undergoing scoliosis/spine fusions, normovolemic hemodilution reduced allogeneic transfusion requirements from 79% to 37%. Without normovolemic hemodilution, 40% of patients undergoing lumbar spine fusions with instrumentation in one series required allogeneic blood transfusions. With use of normovolemic hemodilution in a comparable series, this frequency was reduced to 23.5%	Normovolemic hemodilution may be safely and effectively used by spine surgeons, particularly those who perform multilevel lumbar laminectomies with or without fusion	I
Gause et al.[24], 2008	Intraoperative red-blood-cell salvage	A retrospective study of 188 patients who underwent lumbar laminectomy and fusion with instrumentation: 141 had cell saver and 47 did not	A significant increase in the number of blood transfusions was found in the cell-saver group. The cell-saver group also had a significantly increased blood loss compared with the non-cell-saver group	Use of a cell saver for patients treated with lumbar fusion and instrumentation did not decrease the need for blood transfusion. Cell-saver use was associated with significantly greater blood loss	III
Schouten et al.[27], 2009	Antifibrinolytics	A systematic review of all randomized controlled trials of aprotinin, tranexamic acid, and aminocaproic acid involving children	In the scoliosis studies, aprotinin and tranexamic acid significantly reduced blood loss compared with that associated with a placebo	There is no evidence that suggests that alternative antifibrinolytics such as tranexamic acid were less effective than aprotinin in reducing	I

		undergoing cardiac or scoliosis surgery		blood loss in major pediatric surgery	
Tzortzopoulou et al.[28], 2008	Antifibrinolytics	A Cochrane review of 6 studies (254 patients) comparing abilities of aprotinin, tranexamic acid, and aminocaproic acid to reduce blood loss and transfusion requirements in children undergoing scoliosis surgery	Antifibrinolytic drugs decreased the amount of blood transfused by 327 mL and the amount of blood loss by 427 mL	Antifibrinolytic drugs reduced blood loss and transfusion requirements in children undergoing scoliosis surgery. Aprotinin, tranexamic acid, and aminocaproic acid seem to be similarly effective	I
Gill et al.[29], 2008	Antifibrinolytics	A systematic review investigating the efficacy of aprotinin, tranexamic acid, and epsilon-aminocaproic acid in terms of reducing blood loss and blood transfusions in patients undergoing spine surgery	Compared with control groups, all three antifibrinolytic agents were associated with decreased total blood loss and transfusion requirements in patients undergoing spine surgery	Aprotinin, tranexamic acid, and epsilon-aminocaproic acid are effective in reducing blood loss and transfusions in patients undergoing spine surgery. With the exception of aprotinin, these agents do not cause substantial morbidity or increase the risk of thromboembolic events	I
Tayyab et al.[35], 2008	Aprotinin	A retrospective study of 82 patients with adult scoliosis or kyphosis who underwent spine fusion surgery with instrumentation of ≥6 levels	The mean blood loss and amount of blood returned by a cell saver were significantly decreased in the aprotinin group. The aprotinin group received an average of 2.73 units of blood. This was significantly less than the average of 5.02 units that the controls received	Administration of aprotinin is a safe and effective method to reduce blood loss and decrease the need for transfusions without increasing the risk of complications in younger patients in relatively good general health who undergo spine deformity surgery requiring ≥6 levels of fusion	III
Kasimian et al.[36], 2008	Aprotinin	A study to evaluate the safety and efficacy of aprotinin in children with neuromuscular scoliosis undergoing spine fusion. Aprotinin: n = 14, control: n = 17	The total blood loss in the aprotinin group was significantly lower than that in the control group; intraoperative packed red-blood-cell transfusion requirements were also significantly lower in the aprotinin group	Use of aprotinin decreased blood loss and the rate of transfusions in children with neuromuscular scoliosis undergoing extensive spine fusion	III
Okubadejo et al.[41], 2007	Aprotinin	A matched-cohort comparison. 40 patients received high-dose aprotinin (Group A) intraoperatively, and 41 matched controls (Group NA) received no aprotinin	The average blood loss was 906 mL in Group A and 1.3 L in Group NA. Complications seen in Group A included 4 cases of acute renal failure requiring dialysis and 1 deep venous thrombosis. In Group	Aprotinin reduces intraoperative blood loss in long spine fusions for treatment of complex adult spine deformity but may increase the risk of acute renal failure, especially in women over the age of 60	III

			NA, there was 1 case of acute renal failure and 1 case of pulmonary embolus		
Shapiro et al.[42], 2007	Tranexamic acid	A retrospective review	Blood loss in the tranexamic acid group was decreased by 42%. Transfusion of homologous blood in the tranexamic acid group was decreased by 46% and autologous cell-saver blood, by 42%	Tranexamic acid significantly reduces both intraoperative blood loss and homologous transfusion in patients with Duchenne muscular dystrophy undergoing posterior spine fusion	IV
Elwatidy et al.[43], 2008	Tranexamic acid	A double-blind randomized placebo-controlled study. 64 patients were randomized equally into 2 groups (tranexamic acid and placebo). A loading dose of 2 g (for adults) or 30 mg/kg (for children), followed immediately by continuous infusion of 100 mg/hr (for adults) or 1 mg/kg/hr (for children) up to 5 hr postop	Patients who received tranexamic acid had a 49% reduction of blood loss and required 80% less blood transfusion than did patients who received a placebo	Prophylactic use of large doses of tranexamic acid provides an effective, safe, and inexpensive method for reducing blood loss during and after spine operations	II
Wong et al.[44], 2008	Tranexamic acid	151 adult patients undergoing spine fusion with instrumentation were randomized to receive 10 mg/kg intravenously after induction followed by a maintenance infusion of 1 mg/kg/hr of tranexamic acid, or an equivalent volume of placebo	The total estimated and calculated perioperative blood losses were approximately 25% and 30% lower in patients given tranexamic acid instead of the placebo	Tranexamic acid significantly reduced the total estimated and calculated perioperative blood losses in adult patients treated with elective posterior thoracic/lumbar spine fusion with instrumentation	II
Grant et al.[45], 2009	Tranexamic acid	A retrospective cohort including all patients with idiopathic scoliosis undergoing posterior spine instrumentation and fusion. Patients received either a low (10-mg/kg loading, 1-mg/kg/hr infusion) or high (20-mg/kg loading, 10-mg/kg/hr infusion) dose of tranexamic acid	High-dose tranexamic acid (n = 11) showed a trend toward a reduction in transfusion requirements compared with the low dose (n = 15), although this study was underpowered to show a significant difference	The use of the higher dose of tranexamic acid resulted in a 50% reduction in transfusion requirements for patients with idiopathic scoliosis. Given previous studies, there appears to be a dose-response effect	III
Thompson et	Epsilon-	A retrospective study	There were significant	Amicar was most	III

al.[47], 2008	aminocaproic acid (Amicar)	of 73 consecutive patients. Group 1 (n = 16) received no Amicar; Group 2 (n = 18) received Amicar for posterior spine fusion with segmental spine instrumentation only; and Group 3 (n = 39) received Amicar for both anterior spine fusion and posterior spine fusion with segmental spine instrumentation	decreases in the mean estimated intraoperative blood loss during posterior spine fusion with segmental spine instrumentation, total perioperative blood loss, and transfusion requirements in the 2 Amicar groups. However, Amicar had no significant effect on the estimated intraoperative blood loss during anterior spine fusion, chest tube drainage, or wound suction drainage for posterior spine fusion	effective in decreasing intraoperative estimated blood loss during posterior spine fusion with segmental spine instrumentation but had no significant effect during anterior spine fusion, postoperative chest tube drainage, or wound suction drainage for posterior spine fusion. The authors recommended that Amicar be used for posterior spine fusion with segmental spine instrumentation only	
Thompson et al.[48], 2008	Epsilon-aminocaproic acid	A retrospective case-control study of patients with neuromuscular scoliosis. Group 1 (n = 34) received no Amicar and Group 2 (n = 62) received Amicar (100 mg/kg over 15 min not to exceed 5 g after anesthesia induction followed by 10 mg/kg/hr until wound closure)	There was significantly less intraoperative blood loss, total perioperative blood loss, and transfusion requirements in Group 2. Postoperative suction drainage was also less, but not significantly so	Amicar was highly effective in decreasing perioperative blood loss and transfusion requirements in patients with neuromuscular scoliosis undergoing posterior spine fusion and segmental spine instrumentation	III
Kolban et al.[63], 2006	Recombinant factor VIIa	A retrospective review of 52 consecutive patients undergoing surgical correction of idiopathic scoliosis	Total intraoperative and combined intraoperative and postoperative blood losses, and requirements for packed red blood cells, were significantly less in patients treated with recombinant factor VIIa when compared with historical controls	Recombinant factor VIIa appears to be effective in reducing blood loss and transfusion in adolescent patients undergoing spine fusion surgery for the correction of idiopathic scoliosis	III
Sachs et al.[64], 2007	Recombinant factor VIIa	49 patients undergoing fusion of ≥3 vertebral segments were randomized and treated on losing 10% of their estimated blood volume and received 3 doses (at 2-hour intervals) of placebo or 30, 60, or 120 µg/kg of recombinant factor VIIa	The mean adjusted surgical blood loss was 2536 mL for the placebo group and 1120, 400, and 823 mL for the 3 × 30, 3 × 60, and 3 × 120-µg/kg recombinant factor VIIa groups, respectively. The mean surgical transfusion volume did not differ among the groups, but the adjusted transfusion volume was reduced by 81% to 95% with recombinant factor	No safety concerns were indicated for the use of recombinant factor VIIa, at all doses tested. Recombinant factor VIIa reduced adjusted blood loss and adjusted transfusion requirements during spine surgery	II

			VIIa		
Guay[73], 2006	Intrathecal morphine	A meta-analysis of 24 studies on regional anesthesia and blood loss associated with different surgical procedures	Regional anesthesia reduced the number of patients receiving transfusion for total hip replacement (p = 0.0009) and spine fusion (p = 0.04)	Neuraxial blocks have a clear and definite effect on surgical blood loss, but they do not reduce the number of patients receiving transfusion except for those undergoing total hip replacement and spine fusion	I
Eschertzhuber et al.[76], 2008	Intrathecal morphine	46 children were randomized to receive 5 mg/kg of morphine + 1 mg/kg of sufentanil (low-dose intrathecal opioid) or 15 mg/kg of morphine + 1 mg/kg of sufentanil (high-dose intrathecal opioid), or no intrathecal opioid	Intraoperative blood loss was significantly reduced by low and high-dose intrathecal opioids, with no difference between the two intrathecal opioid groups	Intrathecal administration of opioids significantly reduces blood loss and postoperative opioid demand. These effects were seen with the low-dose regimen, and the high dose did not improve efficacy	II
Rajagopalan et al.[85], 2008	Temperature regulation	A systematic search of published randomized trials that compared blood loss and/or transfusion requirements between normothermic and mildly hypothermic (34-36°C) surgical patients. 14 studies were included in the analysis of blood loss, and 10, in the transfusion analysis	The median (quartiles) temperature difference between the normothermic and hypothermic patients was 0.85°C (0.60°C versus 1.1°C). The ratio of geometric means of total blood loss in the normothermic and hypothermic patients was 0.84 (0.74 versus 0.96). Normothermia also reduced transfusion requirements, with an overall estimated relative risk of 0.78	Even mild hypothermia (<1°C) significantly increases blood loss by approximately 16% (4%-26%) and increases the relative risk for transfusion by approximately 22% (3%-37%). Maintaining normothermia reduces blood loss and transfusion requirements by clinically important amounts	I
Rodríguez-Vela et al.[96], 2009	Minimally invasive surgery	30 patients undergoing 1-level posterior lumbar spine fusion were prospectively randomized to undergo surgery via a mini-open (n = 15) or classic (n = 15) approach	The mean intraoperative blood loss was 318 mL in the mini-open group and 757 mL in the classic group	Mini-open surgery for lumbar spine fusion minimizes muscular lumbar damage and reduces intraoperative blood loss. Additional investigations are necessary to verify the achievement of a stable lumbar spine fusion in the long term	II
Park and Ha[97], 2007	Minimally invasive surgery	A cohort of 61 patients undergoing 1-level posterior lumbar interbody fusion by a single surgeon at a single center via a minimally invasive (n = 32) or traditional (n = 29) approach	On average, the intraoperative blood loss was 433 mL, postoperative drainage was 175 mL, and transfusion requirement was 0.2 unit in the minimally invasive group and 738 mL, 483 mL, and 1 unit,	Minimally invasive surgery for posterior lumbar interbody fusion reduces blood loss and transfusion requirements. However, the minimally invasive technique needs a longer surgical time and prudent attention to	III

			respectively, in the traditional group	lower the risk of technical complications	
Anand et al.[98], 2008	Minimally invasive surgery	A case series of 12 patients undergoing minimally invasive percutaneous fusion for lumbar degenerative scoliosis	The mean intraoperative blood loss was 260 mL (160 mL for the anterior part and 100 mL for the posterior part)	A combination of minimally invasive surgical techniques is feasible for lumbar degenerative scoliosis surgery and reduces blood loss	IV

*See JBJS Instructions to Authors for a complete description of the levels of evidence.