SPINE Volume 33, Number 16, pp E543–E547

Effect of Fibrin Sealant on Drain Output and Duration of Hospitalization After Multilevel Anterior Cervical Fusion

A Retrospective Matched Pair Analysis

Jin S. Yeom, MD, Jacob M. Buchowski, MD, MS, Hong Xing Shen, MD, Gabriel Liu, MD, Torphong Bunmaprasert, MD, and K. Daniel Riew, MD

Study Design. Retrospective matched pair analysis.

Objective. To determine if fibrin sealant can decrease postoperative drain output and length of stay (LOS) after multilevel anterior cervical fusions.

Summary of Background Data. Despite careful hemostasis, bleeding after anterior cervical fusion can occur and may be life threatening. Although fibrin sealants are commonly used for hemostasis, no studies have been published on the efficacy of these products in achieving hemostasis after anterior cervical surgery.

Methods. A retrospective age-, gender-, and fusion level-matched pair analysis was performed on 30 pairs of patients who underwent anterior cervical fusion ≥ 3 levels. In the study group, after adequate hemostasis was obtained, before wound closure 2.0 mL of fibrin sealant was applied as a fine aerosolized spray over and around the plate/fusion sites and the soft tissues to seal the main operative field. A deep drain was used in all patients. Total drain output, time for the drainage to decrease to ≤20 mL per 8 hours shift, LOS, and number of readmissions were determined and analyzed by experienced and independent spine surgeons.

Results. Total drain output averaged 47 mL in the study group and 98 mL in the control group ($P < 0.0001$). Time for the drainage to decrease to ≤20 mL per shift averaged 17 hours (range, 8–29 hours) in the study group and 24 hours (range, 7–43 hours) in the control group ($P = 0.0054$). LOS averaged 1.2 days (range, 1–4 days) in the study group and 2.1 day (range, 1–5 days) in the control group ($P < 0.0001$). Two patients were readmitted within 4 days of discharge in each group because of swallowing difficulty, dyspnea, or pneumonia ($P = 1.000$). There were no adverse reactions attributable to the fibrin sealant.

Conclusion. Application of fibrin sealant at the end of multilevel anterior cervical fusion can significantly decrease postoperative drain output and LOS.

Key words: fibrin sealant, anterior cervical fusion, retropharyngeal hematoma. **Spine 2008;33:E543–E547**

From the Department of Orthopaedic Surgery, Washington University in St. Louis, St. Louis, MO.
Acknowledgment date: January 10, 2008. Revision date: February 20, 2008. Acceptance date: February 20, 2008.
The device(s)/drug(s) that is/are the subject of this manuscript is/are not FDA-approved for this indication and is/are not commercially available in the United States.
No funds were received in support of this work. No benefits in any form have been or will be received from a commercial party related directly or indirectly to the subject of this report.
Address correspondence and reprint requests to Jacob M. Buchowski, MD, MS, Department of Orthopaedic Surgery, Washington University in St. Louis, 660 S. Euclid Ave., Campus Box 8233, St. Louis, MO 63110; E-mail: buchowskij@wustl.edu

Postoperative bleeding after anterior cervical operations can lead to prolonged hospitalization and may at times result in life-threatening tracheal compression.[1] To minimize postoperative bleeding, we recently started applying a fibrin sealant in the wound before wound closure after all long-segment anterior cervical fusions (≥3 motion segments). Although fibrin sealants are commonly used for hemostasis,[2–4] no studies have been published on the efficacy of these products in achieving hemostasis after anterior cervical surgery. The purpose of this study was 2-fold: to determine whether the application of the fibrin sealant led to a decrease in postoperative drain output (a measure of postoperative bleeding) and, if observed, whether the decrease in postoperative drain output would lead to a decrease in the length of stay (LOS). To answer these questions, we carried out a retrospective age-, gender-, and fusion level-matched pair analysis comparing the surgical results in patients in whom a fibrin sealant was applied at the end of the operation immediately before wound closure (study group) *versus* those patients in whom a fibrin sealant was not applied (control group).

■ Materials and Methods

Study Design

Beginning in May 2006, the senior author began to apply fibrin sealant (Tisseel, Baxter Healthcare Corp., Westlake Village, CA) immediately before closure in all patients who had multilevel anterior cervical fusion to improve hemostasis. Although we empirically noted an improvement in wound hemostasis employing this technique, we elected to conduct a study to determine if our observations were indeed true and to determine whether the application of the fibrin sealant led to a decrease in postoperative drain output (a measure of postoperative bleeding) and, if observed, whether the decrease in postoperative drain output would lead to a decrease in the LOS. To that end, we analyzed the results of 30 consecutive patients who had surgery from May 2006 to December 2006 by the senior author and in whom a fibrin sealant was used, and compared those results to a control group in whom a fibrin sealant was not used. The inclusion criteria for the study group included (1) cervical spondylosis with or without disc herniation causing radiculopathy and/or myelopathy, (2) anterior cervical fusion of 3 or more levels (*i.e.*, motion segments) between C3 and T1 using plate fixation (3) age 20 years or older. Exclusion criteria included (1) nondegenerative disorders including trauma, infection, or tumors, (2) 1 or 2 level fusions, (3) fusions extending proximally to C2 or distally to T2, (4) any

preplanned additional surgery during the same admission period, (5) bleeding diathesis or recent history of anticoagulation therapy, and (6) pregnancy. Thirty patients in the control group had surgery between January 2004 and May 2006 by the same surgeon without application of a fibrin sealant; they fulfilled the above inclusion and exclusion criteria. We designed the study to have 1:1 matching, and the matching criteria were age (within 5 years), gender, and number of fusion levels (3, 4, or 5 levels/motion segments). If 2 or more matching control patients could be found for one in the study group, the most recently operated patient was selected. Patient selection and all of the analyses were conducted by independent experienced spine surgeons who were not involved in the care of the patients. Approval from our Washington University in St. Louis institutional review board and written informed consent was obtained from all patients before commencing the study.

Application of Fibrin Sealant

All patients were operated on by a single surgeon in a single hospital. In both the study and control groups, after decompression, bone graft insertion, and plate fixation was completed, meticulous hemostasis was performed using bipolar electrocautery, hemostatic matrix (Surgiflow, Johnson & Johnson, Somerville, NJ), and demineralized bone matrix and thrombin paying particular attention to controlling bleeding from exposed bone or epidural vessels. After adequate hemostasis was obtained in the study group, 2.0 mL of fibrin sealant was applied as a fine aerosolized spray over and around the plate/fusion sites and the soft tissues to seal the main operative field. In both the study and control groups, a deep drain was placed and the wound was closed in layers.

Measurement of Postoperative Drain Output and Criteria for Discharge

All data including drain amount were obtained from the electronic medical record. In both the study and control groups, the drain output was measured and recorded 3 times a day in 8-hour increments (at 7 AM, 3 PM, and 11 PM) resulting in 3 eight-hour shifts. The drain was routinely removed when the drain output per 8-hour shift was ≤20 mL. Unless there were contraindications to discharge (*e.g.*, medical complications or factors), patients were discharged once the drain was removed.

Parameters for Comparison Between the Study and Control Groups

Four parameters were compared between the study and control groups (1) total drain output before the removal of the drain; (2) time for the drainage to decrease to ≤20 mL per 8-hour shift; (3) LOS (measured in days); and (4) number of patients requiring readmission within 1 month of the index procedure. Although the LOS was to a large extent based on the drain output, in some patients the LOS was determined by other factors (*e.g.*, medical complications). The LOS analysis was therefore performed twice: first, including all patients (even those whose discharge was delayed by factors other than drain output), and second, excluding the pairs of patients in one or both of whom discharge was affected by factors other than the drain output.

Statistical Analysis

Statistical analysis was conducted using the *t* test for continuous variables and χ^2 test or Fisher exact test to compare proportions, using SPSS statistical package (version 12.0; SPSS, Chicago, IL). The level of significance was set at $P < 0.05$.

Table 1. Comparison of Demographic and Clinical Data in the Study and Control Groups

Case No.	Study Group (N = 30)	Control Group (N = 30)	*P*
Age* (yr)	54 ± 11 (32–82)	53 ± 10 (37–78)	0.9797
Gender			1.0000
Male	10 (33%)	10 (33%)	
Female	20 (67%)	20 (67%)	
No. fusion levels			1.0000
3	17 (57%)	17 (57%)	
4	11 (37%)	11 (37%)	
5	2 (7%)	2 (7%)	
Discectomy *vs.* corpectomy			0.9728
ACDF	45	43	
ACCF	30	31	
No. anterior revision cases	6 (20%)	2 (7%)	0.2542
Operation time* (min)	142 ± 36 (62–223)	141 ± 26 (97–190)	0.9118
Estimated blood loss* (mL)	92 ± 25 (50–150)	98 ± 34 (50–200)	0.3902

*The values are given as the mean ± SD, and range in parentheses.
ACDF indicates anterior cervical discectomy and fusion; ACCF, anterior cervical corpectomy and fusion.

■ Results

Participant Characteristics

Thirty-four patients in the study group met the inclusion/exclusion criteria; however, 4 patients had to be excluded because a matched control was not available. In total, 30 pairs of patients were included in this study (*i.e.*, 30 patients in each group). All patients had cervical spondylosis with or without disc herniation causing myelopathy and/or radiculopathy. The demographic and clinical features of the 30 pairs of enrolled patients are shown in Table 1. The mean age was 54 years (range, 32–82 years) in the study group and 53 years (range, 37–78 years) in the control group ($P = 0.9797$). As the patients were matched, the gender and levels of fusion were the same in both groups ($P = 1.0000$ each). All patients had combinations of corpectomies and discectomies. Corpectomies were performed to decompress retrovertebral compression or to minimize the number of fusion surfaces. When there was no retrovertebral compression, discectomies were performed. Among 105 fusion levels in each group, there were 30 corpectomies and 45 discectomies in the study group and 31 corpectomies and 43 discectomies in the control group ($P = 0.9728$). Six patients in the study group had a previous history of anterior cervical fusion, and two in the control group ($P = 0.2542$). In both groups, there were 17 patients who had 3-level arthrodeses, 4 patients who had 4-levels and 2 patients who had 5-levels. The average operation time was 142 minutes (range, 62–223 minutes) in the study group and 141 minutes (range, 97–190 minutes) in the control group ($P = 0.9118$). The estimated blood loss was 92 mL (range, 50–150 mL) in the study group and 98 mL (range, 50–200 mL) in the control group ($P = 0.3902$). These differences were not statistically significant.

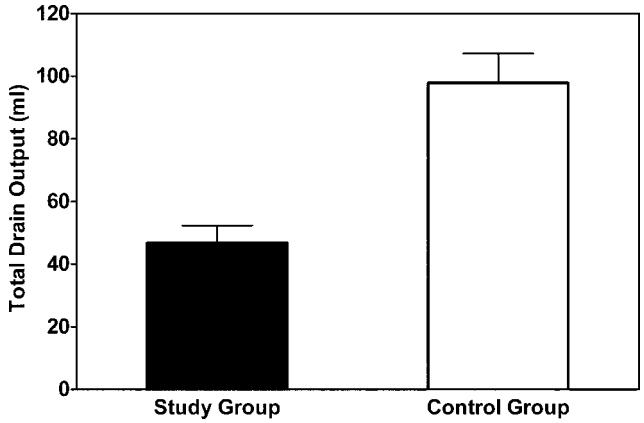

Figure 1. Graph illustrating the total drain output before drain removal in both the study and control groups ($P < 0.0001$).

Total Drain Output

The total drain output before drain removal averaged 47 mL (range, 7–145 hours) in the study group and 98 mL (range, 17–180 mL) in the control group (see Figure 1); this difference was statistically significant ($P < 0.0001$).

Time for Drainage to Decrease to ≤20 mL per Shift

The time for the drainage to decrease to ≤20 mL per shift averaged 17 hours (range, 8–29 hours) in the study group and 24 hours (range, 7–43 hours) in the control group (see Figure 2); this difference was statistically significant ($P = 0.0054$).

Length of Stay

As a whole, the LOS was 1.2 days (range, 1–4 days for a cumulative total of 37 days) in the study group and 2.1 day (range, 1–5 days for a cumulative total of 64 days) in the control group (see Figure 3A); the difference between the groups was statistically significant ($P < 0.0001$). The LOS was not always determined by the drain output: discharge was delayed in 16 patients because of factors such as cardiac history, old age, unsatisfactory overall medical condition, fever, swallowing difficulty, exacerbation of Crohn disease, and other unspecified reasons. In addition, 4 patients, who wanted to leave the hospital early were discharged even though the drain output was >20 mL per shift. Given these shortcomings, we analyzed the LOS excluding the 12 pairs of patients in one or both of whom discharge was affected by factors other than drain output. As is shown in Figure 3B, the LOS was 1.1 day (range, 1–2 days for a cumulative total of 19 days) in the study group and 1.6 days (range, 1–2 days for a cumulative total of 29 days) in the control group; the difference between the groups was statistically significant ($P = 0.0009$). In the study group, 17 patients stayed for 1 night and only 1 patient stayed for 2 nights; unlike in the study group where almost all patients (17 of 18 patients) could be discharged on the first postoperative day, in the control group, 7 patients stayed for 1 night and 11 patients for 2 nights.

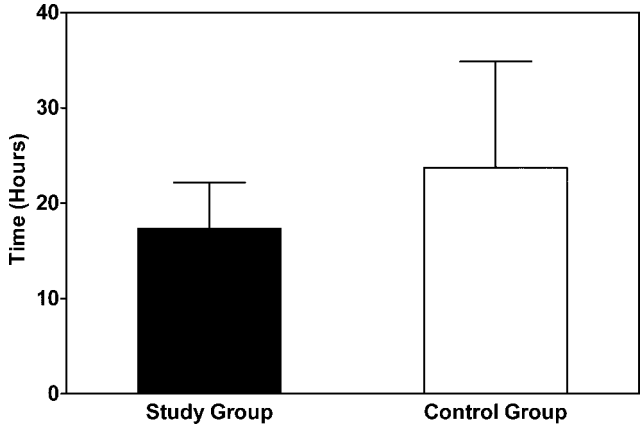

Figure 2. Graph illustrating the time for the drainage to decrease to ≤20 mL in both the study and control groups ($P = 0.0054$).

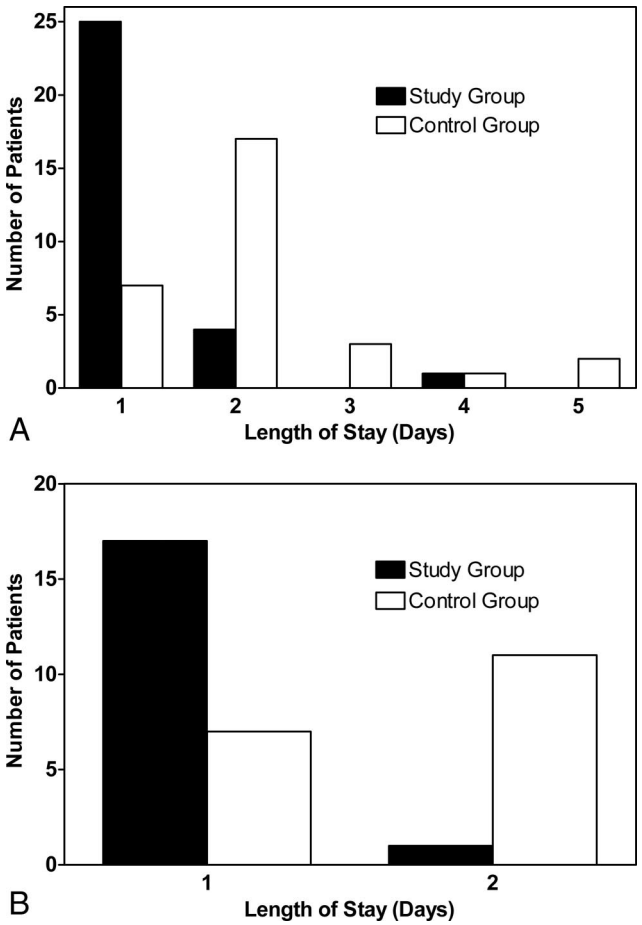

Figure 3. **A**, Length of stay (LOS) for the entire patient population (30 patient pairs) in the study and the control groups ($P < 0.0001$). **B**, LOS in patients (18 patient pairs) in whom discharge was determined solely by the drain output rather than other factors (*e.g.*, medical complications) ($P = 0.0009$).

Readmission Because of Postoperative Complications

After discharge, 2 patients in each group were readmitted within 4 days of the index procedure because of postoperative complications. There were no other readmissions related to the initial surgery within the first month of the index procedure. One patient in each group was readmitted because of swallowing difficulty, and in both

cases this was successfully treated with administration of corticosteroids. The second patient in the study group was readmitted because of pneumonia, which was treated successfully with antibiotics. The second patient in the control group was readmitted because of retropharyngeal swelling and associated dyspnea, which was successfully treated with administration of corticosteroids. None of the patients required reoperations for hematoma or dysphagia. There were no adverse reactions attributable to the fibrin sealant.

■ Discussion

Postoperative bleeding after anterior cervical fusions may prolong hospitalization and may at times cause symptomatic retropharyngeal hematoma formation leading to airway obstruction and in some cases even death.[1] Meticulous hemostasis and reduction in postoperative bleeding, therefore, is crucial and plays an important role in the success of anterior cervical fusions. Despite the importance of postoperative bleeding on the development of potentially life-threatening complications, no studies designed to specifically evaluate a method to reduce postoperative bleeding after anterior cervical fusions have been performed. For this reason, we elected to develop an easy, safe, and cost-effective method to decrease postoperative bleeding through the use of existing and easily available hemostatic agents.

Various systemic and topical hemostatic agents are available. Systemic agents include: ε-aminocaproic acid, aprotinin, desmopressin, and tranexamic acid, all of which have been used successfully in spinal operations that carry a risk of significant bleeding (such as thoracolumbar reconstructive surgery).[4–11] These agents may result in complications (including deep venous thrombosis, pulmonary embolism, renal failure, and severe bradycardia)[4] are expensive, and typically inappropriate for anterior cervical fusions where the probability of major bleeding is extremely low. On the other hand, topical hemostatic agents that reduce postoperative bleeding can be useful for cervical procedures. A wide variety of topical hemostatic agents exist and most can be used to control intraoperative bleeding during spinal surgery.[2,3] The most common topical hemostatic agents used in spine surgery include bone wax (Ethicon, Norderstedt, Germany), hemostatic sponges, gelatin matrix products (mixed with thrombin), and fibrin sealants.[4,12] Hemostatic sponges may be either gelatin-based [*e.g.*, Gelfoam (Pharmacia and Upjohn, Kalamazoo, MI)], collagen-based [*e.g.*, Instat (Johnson & Johnson)], or oxidized cellulose-based [*e.g.*, Surgicel (Johnson & Johnson)]. Gelatin matrix products include Surgiflow (Johnson & Johnson). Fibrin sealants, also known as fibrin glues, such as Tisseel (Baxter Healthcare Corp.) consist of fibrinogen and thrombin that form a fibrin clot. Although the use of fibrin sealants has been described in spinal surgery, these products do not adhere strongly on wet surfaces, have little impact on actively bleeding wounds, and require 15 to 45 minutes to prepare.[2–4] Nevertheless, they are commonly and effectively used for treatment of cerebrospinal fluid leakage by "sealing" the site of dural tear.[13–15]

Given the sealing effect of fibrin sealants, we recently began to use this modality to reduce postoperative bleeding. Because no studies have been published on the efficacy of these products in achieving hemostasis following anterior cervical surgery, we conducted a retrospective age-, gender-, and fusion level-matched pair analysis comparing the results in patients in whom a fibrin sealant was applied *versus* those patients in whom a fibrin sealant was not applied to determine whether the application of the fibrin sealant led to a decrease in postoperative drain output and LOS. This study demonstrates that fibrin sealants can effectively diminish drain output. Furthermore, the use of fibrin sealants leads to a significantly shorter LOS with the vast majority of patients being discharged on the first postoperative day, even after 3- to 5-level anterior procedures.

The fibrin sealant costs approximately $192 for 2.0 mL and $440 for 5.0 mL, whereas one hospital day costs approximately $1000. Among the 18 patient pairs whose discharge was purely determined by the drain output, patients in the study group had a cumulative LOS of 19 days compared with 29 days for patients in the control group, equaling a reduction in the LOS of 10 days. Among the remaining 12 patient pairs who discharge was affected by factors other than drain output, patients in the study group had a cumulative LOS of 18 days compared with 35 days for patients in the control group. As the LOS in these 12 patient pairs was determined by factors other than drain output, it is difficult to draw any conclusions regarding the efficacy of fibrin sealants to reduce the LOS in these 12 patient pairs. Nevertheless, assuming the worst case scenario, the use of a fibrin sealant led to significant cost savings: as a result of using 2.0 mL of fibrin sealant ($192) in each of 30 patients (with a total expense of $5760), the LOS was reduced by 10 days (with a reduction in costs of approximately $10,000) equaling a net savings of >$4000 in just 30 patients. Obviously, multiplied by the number of long anterior cervical cases done in 1 year, this would represent even greater savings.

With increasing cost of medical care, a lot of attention has been paid to decreasing the LOS with the associated potential cost savings. Perhaps, an even greater value of using fibrin sealant is to reduce postoperative bleeding with the theoretical reduction in potentially life-threatening complications such as airway obstruction due to hematoma formation. Although the current study demonstrated the efficacy of fibrin sealants in reducing postoperative bleeding and LOS, our study population was not large enough to determine whether the use of a fibrin sealant would decrease the frequency of these severe complications. Because these complications are relatively rare, a large-scale (and perhaps an even multicenter study) will be required to assess the efficacy of fibrin sealants at reducing the likelihood of these complications.

A potential weakness of this study is that it is not a prospective randomized trial. However, this study is an

age-, gender- and level-matched pair analysis in which the study and control group patients underwent essentially the same operative procedure with comparable operative time and estimated blood loss. Additionally, one surgeon performed all of the procedures using identical techniques. Another potential weakness is that the senior author used a drain output of <20 mL in an 8-hour period as the criteria for pulling the drain and discharging the patient, so long as there were no other mitigating medical factors. It is possible that patients might have done fine with pulling the drain with much higher outputs, thus decreasing the hospital stay for all patients. The 20-mL figure was derived from the senior author's experience that amounts greater than this resulted in unacceptable reoperation rates.

Although this study demonstrates that the use of a fibrin sealant results in a reduction in postoperative bleeding, we must stress that the use of a fibrin sealant does not obviate the need for meticulous hemostasis before application of the fibrin sealant and closure for 2 main reasons. First, as stated above, fibrin sealants are known to be less effective on actively bleeding surfaces because of the poor capability of the sealants to adhere to wet surfaces. Second, by sealing the anterior aspect of the spine, the use of these products in the setting of continued active bleeding (especially bleeding from the decorticated endplates or epidural vessels) could potentially result in catastrophic epidural hematoma formation. In our experience, hemostasis using bipolar electrocautery, hemostatic gelatin matrix, and demineralized bone matrix, and thrombin before application of the fibrin sealant provides adequate hemostasis, and we only apply a fibrin sealant after confirming effective hemostasis within the disc space and epidural space.

■ Conclusion

In summary, based on this retrospective age-, gender- and fusion level-matched pair analysis, it would appear that the application of a fibrin sealant at the end of multilevel anterior cervical fusion can significantly decrease postoperative drain output and LOS. The use of a fibrin sealant, however, does not obviate the need for careful and meticulous hemostasis before application of the sealant.

■ Key Points

- Although fibrin sealants are commonly used for hemostasis, no studies have been published on the efficacy of these products in achieving hemostasis after anterior cervical surgery.
- A retrospective age-, gender- and fusion level-matched pair analysis was performed to determine if the use of a fibrin sealant can decrease postoperative drain output and LOS after multilevel anterior cervical fusions (≥3 motion segments).
- Total drain output, time for the drainage to decrease to ≤20 mL per shift, and LOS were all significantly lower in patients in whom a fibrin sealant was used at the end of the procedure compared with the patients in the control group.
- Given the results of our study, we recommend that the use of a fibrin sealant be considered at the end of a multilevel anterior cervical fusion; however, we must emphasize, that the use of a fibrin sealant does not obviate the need for careful and meticulous hemostasis.

References

1. Epstein NE, Hollingsworth R, Nardi D, et al. Can airway complications following multilevel anterior cervical surgery be avoided? *J Neurosurg* 2001; 94:185–8.
2. Block JE. Severe blood loss during spinal reconstructive procedures: the potential usefulness of topical hemostatic agents. *Med Hypotheses* 2005;65: 617–21.
3. Renkens KL Jr, Payner TD, Leipzig TJ, et al. A multicenter, prospective, randomized trial evaluating a new hemostatic agent for spinal surgery. *Spine* 2001;26:1645–50.
4. Szpalski M, Gunzburg R, Sztern B. An overview of blood-sparing techniques used in spine surgery during the perioperative period. *Eur Spine J* 2004; 13(suppl 1):18–27.
5. Bednar DA, Bednar VA, Chaudhary A, et al. Tranexamic acid for hemostasis in the surgical treatment of metastatic tumors of the spine. *Spine* 2006;31: 954–7.
6. Bitan FD. Aprotinin in spine surgery: review of the literature. *Orthopedics* 2004;27(suppl 6):681–3.
7. Cole JW, Murray DJ, Snider RJ, et al. Aprotinin reduces blood loss during spinal surgery in children. *Spine* 2003;28:2482–5.
8. Hu SS. Blood loss in adult spinal surgery. *Eur Spine J* 2004;13(suppl 1): 3–5.
9. Lentschener C, Cottin P, Bouaziz H, et al. Reduction of blood loss and transfusion requirement by aprotinin in posterior lumbar spine fusion. *Anesth Analg* 1999;89:590–7.
10. Neilipovitz DT. Tranexamic acid for major spinal surgery. *Eur Spine J* 2004; 13(suppl 1):62–5.
11. Urban MK, Beckman J, Gordon M, et al. The efficacy of antifibrinolytics in the reduction of blood loss during complex adult reconstructive spine surgery. *Spine* 2001;26:1152–6.
12. Schonauer C, Tessitore E, Barbagallo G, et al. The use of local agents: bone wax, gelatin, collagen, oxidized cellulose. *Eur Spine J* 2004; 13(suppl 1):89–96.
13. Hida K, Yamaguchi S, Seki T, et al. Nonsuture dural repair using polyglycolic acid mesh and fibrin glue: clinical application to spinal surgery. *Surg Neurol* 2006;65:136–42.
14. Patel MR, Caruso PA, Yousuf N, et al. CT-guided percutaneous fibrin glue therapy of cerebrospinal fluid leaks in the spine after surgery. *AJR Am J Roentgenol* 2000;175:443–6.
15. Patel MR, Louie W, Rachlin J. Postoperative cerebrospinal fluid leaks of the lumbosacral spine: management with percutaneous fibrin glue. *AJNR Am J Neuroradiol* 1996;17:495–500.