

# What Is the Role of Autologous Blood Transfusion in Major Spine Surgery?

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## Abstract

Major spine surgery is associated with significant blood loss, which has numerous complications. Blood loss is therefore an important concern when undertaking any major spine surgery. Blood loss can be addressed by reducing intraoperative blood loss and replenishing perioperative blood loss. Reducing intraoperative blood loss helps maintain hemodynamic equilibrium and provides a clearer operative field during surgery.

Homologous blood transfusion is still the mainstay for replenishing blood loss in major spine surgery across the world, despite its known adverse effects. These significant adverse effects can be seen in up to 20% of patients. Autologous blood transfusion avoids the risks associated with homologous blood transfusion and has been shown to be cost-effective.

This article reviews the different methods of autologous transfusion and focuses on the use of intraoperative cell salvage in major spine surgery. Autologous blood transfusion is a proven alternative to homologous transfusion in major spine surgery, avoiding most, if not all of these adverse effects. However, autologous blood transfusion rates in major spine surgery remain low across the world. Autologous blood transfusion may obviate the need for homologous transfusion completely. We encourage spine surgeons to consider autologous blood transfusion wherever feasible.

Major spine surgery is associated with significant blood loss.<sup>1,2</sup> The expected blood loss in posterior spinal procedures may range from less than 1 L to in excess of 3 L. In anterior procedures with instrumentation, similar quantities of blood loss are expected. Blood loss in vertebral oste-

otomy may be as high as 4.7 L.<sup>3</sup> Blood loss may be substantial in major spine surgery for the majority of spinal disorders encountered in spine practice, including spinal stenosis, spondylolisthesis, adolescent idiopathic scoliosis, degenerative scoliosis, spine trauma, and spine tumors. In 2006, Berenholtz and colleagues<sup>4</sup> reported that at least 30% of 3,988 adult patients undergoing spinal fusion surgery in the United States received blood transfusion. Significant blood loss can be expected, especially during multi-level spinal decompression or fusion.<sup>5</sup> Children with neuromuscular scoliosis, adults with osteoporotic or degenerative spine disorders, and patients with spinal tumors are also more likely to experience increased bleeding during surgery.<sup>3</sup> Intraoperatively, up to 2 L of blood can be lost with an additional 500 to 1000 mL of blood collected postoperatively in the suction drains.<sup>6,7</sup> Significant blood loss results in fluid shifts, affecting cardiac, pulmonary, and renal functions, causing coagulopathy or even disseminated intravascular coagulation.<sup>3</sup>

Factors known to affect the amount of blood lost during major spine surgery include the duration of surgery, the number of vertebrae fused, the site of autologous bone graft harvest, and mean arterial pressure.<sup>8</sup> Attention should be paid to patient positioning to minimize pressure on the inferior vena cava. While measures have been employed by spine surgeons to address the above factors, a fair number of cases still require volume replacement with blood products. Presently, this replenishment is heavily reliant on homologous blood in most centers over the world.<sup>4,9</sup> Significant adverse effects associated with homologous transfusion are making different autologous transfusion techniques increasingly popular. Among them, intraoperative and postoperative cell salvage are attractive and viable options, which can be used in various types of spine surgeries, including emergency surgery.

Strategies devised to address blood loss in major spine surgery can be broadly classified into 2 categories: methods to reduce intraoperative blood loss, and methods to replenish perioperative blood loss (Figure 1).<sup>10</sup>

## METHODS TO REDUCE INTRAOPERATIVE BLOOD LOSS

Spine surgeons employ several measures to minimize intraoperative blood loss, including the assessment and correction of coagulopathy, preoperative tumor embolization, reduction of intra-abdominal pressure by

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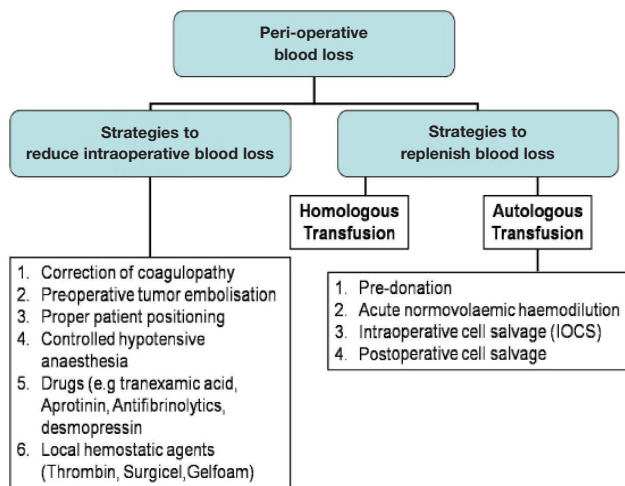
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**Figure 1.** Strategies to reduce and replenish blood loss in major spinal surgery.

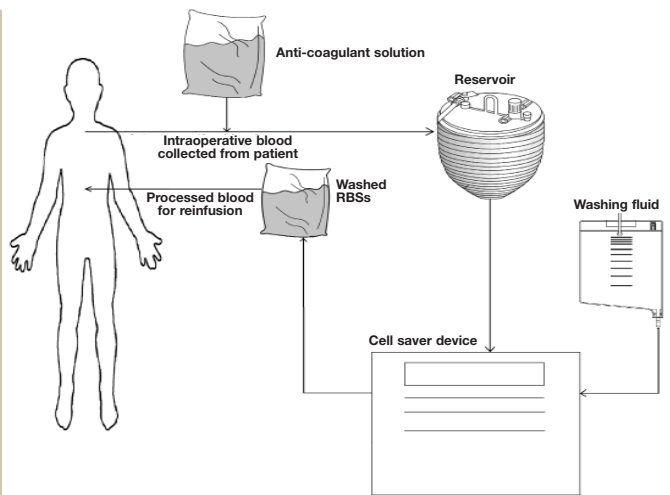
proper positioning of the patient, and controlled hypotensive anesthesia to lower mean arterial pressure.<sup>3,9-11</sup> In addition, pharmacological agents can also help reduce intraoperative blood loss and provide a clearer operative field for the surgeon. These agents may be local or systemic. Examples of systemic agents include anti-fibrinolytics like Tranexamic acid, Aprotinin, and Epsilon Amino Caproic Acid.<sup>2,8,12-14</sup> Local hemostatic agents include Thrombin, Surgicel, and Gelfoam.<sup>9</sup> A detailed discussion on the above techniques falls outside the scope of this review.

### METHODS TO REPLENISH PERIOPERATIVE BLOOD LOSS

Perioperative blood loss can be replenished by the following 2 methods: homologous blood transfusion and autologous blood transfusion.

#### Homologous Blood Transfusion

Homologous blood transfusion remains the mainstay for replacing perioperative blood loss in major spine surgery in many centers all over the world.<sup>4,9</sup> This is in spite of the fact that homologous blood transfusion is associated with several well-documented adverse effects. These adverse effects may be broadly classified as infective or immunological. Infective complications include transmission of viral (ie, principally Hepatitis, cytomegalovirus, and human immunodeficiency virus), bacterial, parasitic, and even prion disease. Immunological complications include allergic reactions, acute and delayed hemolytic reactions, graft versus host disease (GVHD), alloimmunization, and autoimmunization.<sup>6</sup> In extreme cases, homologous blood transfusion has also been known to cause transfusion-related acute lung injury. There is also a risk of immunosuppression, which may predispose the patient to postoperative infections,<sup>3,15,16</sup> prolonging hospital stay, and increasing treatment costs.<sup>16</sup> In addition, homologous blood



**Figure 2.** Schematic diagram showing the intraoperative set-up of a standard red blood cell washing device, one of the main devices used in intraoperative cell salvage.

transfusions have been associated with increased risk of tumor recurrence, acute lung injury, perioperative myocardial infarction, postoperative low-output cardiac failure, and increased 5-year mortality. The risks of postoperative infections and tumor recurrence associated with homologous blood transfusion are also dose-dependent.<sup>17</sup>

#### Autologous Blood Transfusion

Autologous blood transfusion involves the reinfusion of the patient's own blood by 1 or more of the following methods:<sup>18</sup>

- reinfusing pre-donated blood
- acute normovolemic hemodilution
- intraoperative cell salvage (IOCS)
- postoperative cell salvage (POCS) from the blood collected in surgical drains

Autologous blood transfusion is becoming increasingly popular because it offers several benefits over homologous transfusion. The main benefit is that it markedly reduces the risks associated with homologous blood transfusion. It is also suitable in patients with religious prohibitions against homologous blood transfusion, like Jehovah's Witnesses.<sup>18,19</sup> Autologous blood transfusion has also been reported to reduce the risk of GVHD associated with homologous blood transfusion during subsequent pregnancies in girls undergoing scoliosis surgery.<sup>18</sup>

#### PRE-DONATED AUTOLOGOUS TRANSFUSION

Pre-donated autologous transfusion is a viable alternative to homologous transfusion. Its main drawback is that the patient who pre-donates blood before major spine surgery has a lower preoperative hemoglobin level.<sup>20</sup> This is a major concern in many patients with degenerative spine

disorders requiring major spine surgery as these patients tend to be elderly and have concomitant cardiovascular comorbidities. This renders them susceptible to adverse cardiac events due to anemia.

There is often a mismatch between the quantity of pre-donated blood and the actual intraoperative requirement. It has been reported that there is a tendency towards wastage of pre-donated blood, which is half a unit on average.<sup>20</sup> On the other hand, there is also a risk of over-transfusion in patients who may not bleed as much as expected during surgery.<sup>21</sup> Autologous pre-donation cannot completely obviate the need for homologous blood in about 40% of cases.<sup>6</sup> This apparent mismatch between supply and demand stems from the fact that it is often difficult to accurately predict the actual quantity of blood loss until the time of surgery itself.<sup>20</sup>

It has been shown that patients who pre-donate blood are more likely to be transfused earlier and more frequently than patients who have not done so.<sup>22</sup> This may paradoxically increase their risk of tissue ischemia as a result of decreased postoperative hematocrit level.<sup>22</sup> In addition, autologous pre-donation is not possible in emergency situations such as spinal trauma surgery and urgent decompression surgery for metastatic spinal disorders where the demand for blood transfusion is usually quite high. Autologous pre-donation also requires a guarantee that surgery will be done at a specified time. Finally, it demands remarkable communication and coordination between surgeons, anesthetists, specialist personnel at the blood bank, and staff in the intensive care unit.

Brookfield and colleagues<sup>20</sup> made a few pertinent observations about autologous pre-donation. The first key finding was that pre-donation did not appear to decrease the homologous blood transfusion requirement as compared to the non-donating patients. They further pointed out that waste of blood was a significant problem. To illustrate this, they reported that 45-55% of all pre-donated units in the blood transfusion department at the University of Miami over a period of 5 years were unused and discarded. They also suggested that cell salvage alone appeared sufficient to meet the transfusion requirement in the non-donating group without having to introduce pre-donation. In addition, they reported that since pre-donation tended to lower the pre-operative hemoglobin levels, patients who pre-donated blood in fact tended to require more blood replacement than patients who were replaced with cell salvage alone. This paradoxically increases the autologous transfusion rates in pre-donating patients, in turn, driving up transfusion costs.

In summary, the application of autologous pre-donation in major spinal surgery has several limitations, including medical contraindications, supply-demand mismatch, the high potential for wastage, the risk of complications, and its unsuitability in emergency spinal surgery. Furthermore, when used singly, it may be associated with higher autologous transfusion rates, thereby increasing costs.

## ACUTE NORMOVOLLEMIC HEMODILUTION

Acute normovolemic hemodilution is the controlled withdrawal of the whole blood from the patient during induction of anesthesia and restoring the volume with crystalloid or colloid, thus reducing the red cell concentration during surgery. The volume of blood withdrawn is titrated according to the hematocrit and usually varies between 1 to 3 units. Each 1 mL of whole blood removed is replaced with 3 to 4 mL of crystalloid or colloid.<sup>23</sup> This results in hemodilution and the intraoperative hematocrit falls to about 28%. As a result of hemodilution, the quantity of red blood cells lost during surgery is reduced. The saved blood is returned to the patient at the end of the procedure or within 6 hours of its collection.

There is convincing evidence that acute normovolemic hemodilution is effective in reducing homologous transfusion in patients undergoing spinal surgery. Its efficacy is further increased when used in combination with other modalities such as controlled hypotensive anesthesia, pre-operative autologous blood donation, and cell salvage.<sup>24,25</sup> Epstein and colleagues<sup>23</sup> evaluated the use of normovolemic hemodilution alone in 68 patients who underwent multilevel lumbar laminectomy and fusion and found that only 23.5% of patients required homologous transfusion.

In a study evaluating the efficacy of hemodilution in children with adolescent idiopathic scoliosis undergoing posterior spinal fusion, Copley and colleagues<sup>24</sup> compared the transfusion requirements in 2 groups of patients. In one group, a combination of hemodilution, hypotensive anesthesia, and cell salvage was used (ie, the hemodilution group), and in the other group, a combination of hypotensive anesthesia and cell salvage without hemodilution was used (ie, the non-hemodilution group). They found that transfusion was required in 34 out of 43 (79%) patients in the non-hemodilution group, compared with 16 out of 43 patients (37%) in the hemodilution group. The non-hemodilution group received a total of 61 units of packed cells, 57 of which were autologous, 2 were donor directed, and only 2 were homologous, compared with 16 units of packed cells, of which 15 were autologous and 1 homologous, in the hemodilution group. It was shown that hemodilution, when used in combination with hypotensive anesthesia and cell salvage, brought about reductions in overall transfusion requirements and homologous blood transfusion rates in the study population. They observed that although cell saver was not shown to be effective in the study, its selective use was still recommended.

In a separate study, Hur and colleagues<sup>25</sup> compared a cohort of 119 patients undergoing spinal surgery with a historical matched cohort of patients as control. All the patients in the study cohort were subjected to a protocol which involved a combination of acute normovolemic hemodilution, controlled hypotensive anesthesia, preoperative autologous blood donation, and intraoperative

cell salvage, whereas the control cohort received none of the above. They reported that the homologous transfusion requirement was 86% (25 out of 29 patients) in the control group, compared to 3.4% (4 out of 119 patients) in the study group.

As shown above, normovolemic hemodilution is a useful adjunct to other modalities as part of the blood conserving strategy. Despite its apparent efficacy, acute normovolemic hemodilution is not suitable for all patients. Its application is limited by premorbid conditions affecting the pulmonary, cardiac, and renal functions of the patient. Normovolemic hemodilution is also contraindicated in patients with significant cardiovascular disease, significant anemia, severe sepsis, respiratory failure, congestive cardiac failure, end stage renal disease, hemorrhagic shock, and in patients with a history of stroke.<sup>23</sup>

### CELL SALVAGE

Cell salvage is an elegant way of preserving operative blood loss that would otherwise have been discarded. It was designed with the idea of combating the consequences of significant blood loss during surgery. Cell salvage may be performed intraoperatively from blood salvaged from the operative field or postoperatively from blood in the suction drains. IOCS is by far more widely employed than POCS.

IOCS—also known as intraoperative automatic transfusion—was first attempted by Blundell<sup>26</sup> in 1818, a gynecologist who used the technique to treat patients with postpartum hemorrhage. Blood is collected from the operative field and anticoagulant (ie, heparinized-saline) is added. The mixture is processed through different filters and centrifuged.<sup>27</sup> The red blood cells (RBCs) collected are then washed and filtered through a semi-membrane which removes free hemoglobin, plasma, platelets, white blood cells, and heparin.<sup>17</sup> IOCS can retrieve 60-80% of red cells lost due to intraoperative blood loss.<sup>21</sup> In IOCS, the salvaged blood that returns to the patient does not contain platelets or coagulation factors.<sup>10</sup>

The majority of IOCS systems in the market may be broadly classified into 2 groups: RBC washing devices or hemofiltration-only devices.

RBC washing devices collect the shed blood, wash, and centrifugally separate out the RBCs before returning the processed RBCs to the patient, whereas hemofiltration-only devices collect the shed blood, pass this through a filter, and reinfuse the processed blood without washing.

In an RBC washing device (Figure 2), blood aspirated from the operative field is mixed with anticoagulant solution and drawn into a reservoir by vacuum suction. The filter removes the tissue fragments and tiny air bubbles from blood. The filtered blood is then transferred to a centrifuge, which separates the blood components according to their density. Packed cells are kept in the

bowl, while the waste products are removed. Red cells are then washed by a wash pump with washing solution to remove the remaining unwanted components like damaged cells, anticoagulants, activated serum, cell enzymes, and FDP. The final product is a concentrated suspension of RBC ready for reinfusion. It can also be stored at room temperature for 6 hours, and at 1°C to 6°C for 24 hours, if it is not reinfused immediately.<sup>28,29</sup>

In IOCS, the possibility of an ABO-incompatibility or isoimmunization to red blood cells, leukocytes, platelets, and other antigens is completely obviated. Systemic anticoagulation is unnecessary because heparin is added at the suction tip. All anticoagulant is then removed by the cell washing procedure so that only minimal heparin is introduced to the patient. There is still, however, a small increase in the risk of dilutional coagulopathy because no coagulation factors are reinfused to the patient. This risk increases in proportion to the amount of salvaged blood that is returned.

In major spine surgery where very significant blood loss is anticipated, IOCS offers an attractive alternative to homologous blood transfusion.<sup>3</sup> The expected blood loss in posterior spinal procedures may range from less than 1 L to in excess of 3 L. In anterior procedures with instrumentation, similar quantities of blood loss are expected. Blood loss in vertebral osteotomy may be as high as 4.7 L.<sup>3</sup> A vast majority of spinal disorders encountered in spine practice, including spinal stenosis, spondylolisthesis, adolescent idiopathic scoliosis, degenerative scoliosis, and spine trauma, are all amenable to IOCS.<sup>27</sup> In particular, in emergency situations where the risk of perioperative blood loss is high, such as spinal trauma surgery (eg, thoracolumbar fractures), IOCS is the only viable alternative to homologous transfusion.<sup>30</sup>

The efficacy of IOCS and POCS in avoiding homologous blood use has been shown in different types of spine surgery including spinal trauma surgery<sup>30</sup> and adult degenerative spinal disorders requiring single or multilevel fusion.<sup>3,31</sup> Behrman and Keim<sup>1</sup> found that the requirements for homologous and pre-donated autologous transfusion were reduced by 37% with IOCS alone and by 68% when IOCS was supplemented by postoperative cell salvage from surgical drains in the immediate postoperative period. Blanchette and colleagues<sup>16</sup> also reported that patients who received cell salvage were at lower risk of receiving homologous blood transfusion. In an elegant study evaluating the efficacy of perioperative cell salvage in reducing homologous blood requirements and its cost-effectiveness in adult posterior lumbar spine fusion, Savvidou and colleagues<sup>27</sup> conducted a randomized prospective study in 50 consecutive patients who were randomly allocated to 2 groups. Group A (n = 25) received perioperative cell salvage while Group B (n = 25) did not. Their homologous blood transfusion requirements and total incurred costs were then compared. The mean homologous transfusion volume in Group A was 175 mL, compared with 980 mL in



Group B; this difference was statistically significant. In addition, the mean cost of transfusion in Group A was also found to be significantly lower than Group B (approximately \$123 vs \$1508, respectively). They also showed that there was no statistical difference in the surgery time and postoperative hemoglobin and hematocrit levels in these 2 groups.

One important factor to take into account when evaluating the cost-effectiveness of IOCS is that the cost of cell salvage does not increase proportionately with the quantity of blood that is transfused, because the cell salvage device is usually a fixed cost for the entire surgery, except for the recurrent cost of some consumables. Therefore, Chanda and colleagues<sup>5</sup> suggest that IOCS is more cost-effective in cases where larger volumes of blood are transfused. In smaller volume salvage, they showed that it was probably cheaper to use homologous blood. However, even in such cases where the volume of blood salvage is small, they reasoned that it is still beneficial to use IOCS because it avoids the hidden cost of treating bacterial sepsis and other infections, and immune-mediated adverse events which are associated with homologous blood transfusion. Ray and colleagues<sup>31</sup> performed an RBC survival study of IOCS blood using Chromium isotope labeling technique and showed that the long term survival of salvaged red blood cells was not affected by the salvaging process.<sup>31</sup>

Existing literature suggests that intraoperative cell salvage is a reliable method of autologous blood transfusion, which is effective in reducing homologous blood transfusion demand in a cost-effective manner.<sup>5</sup> In 2010, a Cochrane meta-analysis of studies published until 2009 showed cell salvage to be effective in reducing homologous blood transfusion in adult elective surgery. There was a 38% reduction in exposure to homologous red blood cell transfusion, giving an average saving of 0.68 units of homologous blood per patient. Cell salvage was found to be the most effective in orthopedic surgery, with no negative impact on morbidity or mortality. The study also observed that patients who had received cell salvaged blood had a reduced incidence of postoperative infections.<sup>32</sup> In 1998, Domen,<sup>33</sup> at the Cleveland Clinic, released a 5-year review of transfusion-related adverse events which reported that the rate of adverse events was substantially less in cell salvage, compared with homologous transfusion (0.027% vs 0.14%, respectively). IOCS may be used singly or in combination with other modalities like normovolemic hemodilution, preoperative autologous blood donation, and hypotensive anesthesia.<sup>5,34</sup>

### PROSPECT OF IOCS IN SPINAL TUMOR SURGERY

Intraoperative blood loss is one of the feared problems associated with spine tumor surgery, which can result from tumor hypervascularity, dilated epidural venous

plexus, soft tissues, paraspinal blood vessels, and even uninvolved bone.<sup>9</sup> The use of autologous transfusion in spinal tumor surgery is controversial. Many would even consider it contraindicated in any form of tumor surgery. Bilsky and Fraser<sup>9</sup> reported that a typical patient undergoing tumor decompression and instrumentation in the thoracic and lumbar spine may lose 1500 mL of blood despite preoperative tumor embolization, and requires an average of 3 units of packed red blood cells. This blood loss is presently replenished by homologous blood transfusion at most centers all over the world. This reliance on homologous blood places a significant burden on limited blood bank resources worldwide.

For a long time, intraoperative cell salvage was thought to be contraindicated in tumor surgery because of the theoretical concern of promoting tumor dissemination by reintroducing malignant cells into the circulation. Over 24 years have passed since the Council Report from the American Medical Association in 1986 stated that IOCS was contraindicated in tumor surgery.<sup>35</sup> Yet, there has been no concrete evidence to support such a statement to date. On the contrary, developments in transfusion technology are making it increasingly possible to use IOCS in tumor surgery for various malignant conditions.

Cell salvage has already been successfully applied in urological<sup>36,37</sup> and gynecological tumor surgery,<sup>38,39</sup> as well as in hepatocellular carcinoma-associated orthotopic liver transplantation.<sup>40</sup> However, there remains much reservation amongst the spine surgery community about the use of cell salvage in spine tumor surgery. In a review by Bilsky and Fraser,<sup>9</sup> the authors commented that “although some spine tumor surgeons use cell saver, there is at least a theoretical risk of tumor dissemination; the authors do not routinely use cell saver.” In our review of the literature, there has not been a single published report of the use of IOCS in spine tumor surgery to date.

In an early study in 1995 on patients undergoing radical hysterectomy by Connor and colleagues,<sup>39</sup> it was shown that cell saver use did not appear to cotransfuse tumor cells. In that study, 31 patients who received cell-salvaged blood were compared to 40 patients who did not receive cell-salvaged blood. The salvaged samples were subjected to cytological analysis and no tumor cells were found.

There is abundant literature documenting the finding that the simultaneous use of a leucocyte depletion filter (LDF) reduces the risk of cotransfusion of tumor cells even further.<sup>41,42</sup> Edelman and colleagues,<sup>36</sup> in a study on renal cell carcinoma, transitional cell carcinoma, and prostate carcinoma cells, found that LDF was able to remove tumor cells completely in vitro, showing that filtered blood is devoid of tumor cells and is hence safe. This knowledge found clinical application in the Departments of Urology and Epidemiology at the University of Miami, where they retrospectively

analyzed 769 patients who underwent radical retrograde prostatectomy, out of which 87 patients received cell-salvaged blood and the rest either received autologous transfusion, no transfusion, or were excluded from the study for various reasons. Davis and colleagues<sup>37</sup> found that the group which received cell-salvaged blood did not show any significant difference in tumor recurrence rates, compared to patients who received no blood or received pre-donated autologous transfusion. Catling and colleagues<sup>38</sup> showed that in 50 consecutive patients undergoing gynecologic surgery, no remaining viable nucleated malignant cells could be detected after blood had been passed through a combination of cell salvage and a Pall RS leucocyte depletion filter.<sup>43</sup>

Although there has been no direct evidence in the literature supporting the use of IOCS in spine tumor surgery, there is a reasonable prospect that in the future, IOCS systems, when used with an LDF filter, may also be successfully applied to spine tumor surgery without the fear of promoting further tumor dissemination. More research is urgently required in spine tumor surgery to replicate the success in using IOCS in gynecological and urological tumor surgery. In addition, the theoretical risk of reinfusion of salvaged blood containing tumor cells must be balanced against the recent reports of reduced disease recurrence rate and mortality in patients receiving salvaged blood and against the well-documented risks of homologous transfusion.

### CONCLUSION

In this review, we have given an overview of the blood conservation and replacement techniques available to spine surgeons when performing major spinal surgery. We have also focused on autologous blood transfusion, which when used effectively, can provide a viable alternative to homologous blood for replenishing perioperative blood loss in major spine surgery. Autologous blood transfusion has been shown to significantly reduce or even completely obviate the need for homologous transfusion. These methods may be used singly or in combination with other modalities as part of a blood conservation strategy to reduce homologous blood use. In particular, IOCS has been shown to be a reliable method of autologous blood transfusion, which is effective in reducing homologous blood transfusion demand in a cost-effective manner in almost any major spine surgery. Central to these renewed efforts to promote alternatives to homologous transfusion worldwide is the increasing recognition of adverse events associated with homologous blood transfusion, which may have adverse bearing on patient morbidity and mortality. As cell salvage has already been applied successfully to oncological surgery in other fields such as gynecological, urological, and hepatocellular malignancies, research is urgently needed to evaluate the feasibility and

safety of adopting cell salvage techniques for use in surgery for malignant spinal disorders.

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