

Bipolar tissue sealant device decreases hemoglobin loss in multilevel spine surgery

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BACKGROUND: Traditional techniques for obtaining hemostasis during orthopedic surgery, such as conventional electrocautery and sealants, have limited clinical effectiveness in reducing hemoglobin (Hb) loss and requirement for transfusion. The bipolar tissue sealant device studied in this trial combines radiofrequency energy with saline irrigation to hemostatically seal both cut bone and soft tissue, potentially aiding hemostasis.

STUDY DESIGN AND METHODS: Sixty patients undergoing multilevel posterior lumbar instrumentation and fusion were randomly assigned to unipolar cautery alone (control group) or unipolar cautery plus use of the bipolar tissue sealant device (treatment group). Hb loss from the surgical field was measured (rather than estimated) and compared between the two groups. The primary hypothesis was that the treatment group would lose significantly less Hb than the control group.

RESULTS: The control group experienced a mean Hb loss of 102.4 g while the treatment group showed a significantly lower mean Hb loss of 66.2 g ($p = 0.0004$). No significant difference was found between groups with respect to secondary endpoints including length of surgery, number of red blood cell units transfused, number of total blood component units transfused, transfusion avoidance, length of stay, or serious adverse events.

CONCLUSION: Use of a bipolar tissue sealant device in addition to unipolar cautery significantly decreased Hb loss during multilevel, posterior lumbar spinal instrumentation and fusion when compared with unipolar cautery alone.

Lumbar spinal instrumentation and fusion is associated with significant blood loss often requiring allogeneic transfusion.^{1,2} Numerous studies across diverse patient populations indicate that red blood cell (RBC) transfusion is associated with a range of deleterious sequelae including pulmonary edema, renal failure, multiorgan failure, myocardial infarction, infection, increased hospital stay, and death.³⁻⁶ Notably, the Cochrane systematic review of multiple randomized trials found that liberal blood transfusion versus a more restrictive strategy is associated with a 20% increase in mortality and 56% increase in ischemic events.⁷ However, concerns associated with the risk of RBC transfusion are tempered by the increasing realization that anemia is a clinical predictor of adverse outcome.^{8,9} Therefore, recent strategies for patient blood management have focused on optimizing preoperative hemoglobin (Hb) levels and decreasing intraoperative Hb loss in an effort to avoid the anemia that triggers allogeneic transfusion in the perioperative period.¹⁰ Traditional techniques for obtaining hemostasis, such as conventional electrocautery and sealants, have limited clinical effectiveness in spine surgery. Particularly in revision surgery and cases involving several levels, bleeding control with monopolar cautery leads to charring and tissue damage. Conventional bipolar cautery can be time-consuming and difficult to apply over large surfaces. Deep

ABBREVIATION: CL(s) = confidence limit(s).

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areas can be difficult to see and control, resulting in significant blood loss before hemostasis is obtained. Even though there can be major intraoperative and postoperative blood loss with spinal surgery, techniques to achieve better hemostasis and minimize blood loss have not been extensively studied. The Aquamantys bipolar tissue sealant device (Medtronic Advanced Energy, LLC, Portsmouth, NH) combines radiofrequency energy with saline irrigation to hemostatically seal both cut bone and soft tissue. The use of saline with this device prevents tissue temperatures from increasing to more than 100°C. This prevents burning and charring tissues associated with the use of conventional electrocautery where temperatures can exceed 300°C. By operating at a much lower temperature, this bipolar sealing device changes the mechanism of hemostasis from the creation of a blood coagulum plug to a mechanical closure of vessels by shrinking the vascular collagen. By shrinking vascular collagen, the Aquamantys technology may provide superior cut bone and soft tissue hemostasis. The use of saline irrigation also provides an additional advantage by evenly conducting energy to the tissues enabling the treatment of oozing from bone or multiple bleeding vessels over a broad area of cut surfaces.

The majority of literature relating to blood loss and blood management involves retrospective database review of transfusion requirements, estimated blood loss, and change in measured Hb levels during the study period. Because transfusion therapy is considered to be standard of care, high-quality randomized prospective trials investigating transfusion avoidance and clinical outcome as endpoints are limited.^{11,12} The measurement of Hb concentration as a surrogate for necessity of transfusion is complicated by the effect of clinical transfusion decisions to give allogeneic blood for reasons other than a fixed Hb trigger. The resultant increase in Hb level after allogeneic RBC transfusion makes change in Hb level in the perioperative period an unreliable marker for blood loss. Estimates of blood loss by providers in the operating room are inaccurate.¹³⁻¹⁵ Therefore, use of a less subjective measurement of blood loss such as direct measurement of the Hb mass lost from the surgical field would better quantify the impact of an intraoperative intervention designed to reduce surgical bleeding. The objective of this prospective, randomized, single-blind, single-center clinical trial was to assess the effect of the Aquamantys bipolar tissue sealant device on intraoperative Hb loss during multilevel posterior lumbar instrumentation and spinal fusion.

MATERIALS AND METHODS

The investigational protocol was approved by the Duke University Investigational Review Board (Durham, NC), as well as registered with ClinicalTrials.gov (NCT01300559). After granting informed consent, 60

adult patients (age ≥ 18 years) undergoing elective, multilevel, posterior lumbar decompression and fusion with Dr William Richardson were randomly assigned into two groups. All patients suffered from degenerative conditions of the spine including spinal stenosis, spondilolisthesis, and degenerative scoliosis. Unipolar electrocautery was used for intraoperative coagulation in one group (control group) and the Aquamantys device plus unipolar electrocautery (treatment group) in the other. The Aquamantys device was used to control soft tissue bleeding predominantly in the muscle and from pars bleeders. Bone wax was used to control bleeding on decorticated bone. Exclusion criteria consisted of existing spinal cord injury with neurologic deficit or previously diagnosed coagulopathy, preoperative Hb of less than 11 g/dL, prothrombin time/international normalized ratio of greater than 1.3, partial thromboplastin time of more than 40, and platelet (PLT) count of less than 100×10^3 . Patients were also excluded if taking non-aspirin medications producing a bleeding diathesis undetectable by screening labs such as clopidogrel or ticlopidine within 7 days of surgery or valproic acid (associated with thrombocytopenia). All patients received general endotracheal anesthesia with surgery performed in the prone position. Hypotensive anesthesia was not used in this predominantly elderly population of patients. Subfascial drains were placed for postoperative use.

Hb concentrations were measured with a point-of-care testing device (Hemocue, Hemocue and Dronfield, Derbyshire, UK). Intraoperatively, shed blood was preferentially aspirated from the surgical field into a cell salvage device (Cobe Laboratories, Aurora, CO) containing citrate as anticoagulant. Heparinized saline was added to wall suction containers to prevent clotting of any blood aspirated into wall suction. Blood removed from the field in surgical sponges was recovered by immediately soaking the sponges in a container of citrated normal saline. Before processing the salvaged blood from the cell saver device, collected blood was mixed by agitation of the collection container and Hb concentration (g/dL) was measured from an aliquot of the salvaged blood via a sampling port inserted at the base of the collection chamber using sterile technique. Volume (dL) of the salvaged blood was measured by use of the gradations on the side of the collection chamber. Volume and concentration allowed calculation of Hb mass in the shed blood (volume in dL \times Hb concentration in g/dL = Hb mass in g). All salvaged blood was processed and the RBCs in saline were returned to the patient. Upon completion of surgery all surgical sponges soaked in citrated saline were wrung into the soak container. The soak solution was then added to the sanguinous solution in the wall suction containers. After mixing, Hb concentration was measured and total volume of fluid in the wall suction container was recorded from

the gradations on the side of the canister before discard. Hb loss in surgical sponges and wall suction was then calculated as above. Intraoperative surgical time as well as the amount and date of preoperative autologous donation were recorded. Preoperatively, patient Hb was measured. Postoperatively, Hb and the number of transfused units were recorded for the first 5 postoperative days. The study was not controlled for autologous predonation. Therefore, transfusion of either an allogeneic or an autologous RBC unit was counted as a transfusion event for analysis.

The two groups were compared for primary and secondary endpoints. The primary hypothesis was that use of the Aquamantys coagulation system in addition to unipolar cautery results in less intraoperative Hb loss compared with unipolar cautery alone during multilevel spinal decompression and fusion surgery. Secondary endpoints included transfusion of allogeneic blood products, hospital length of stay, operative time, and adverse event rate. These endpoints were compared after determination of the primary outcome. Because postoperative Hb levels are altered by clinical transfusion decisions, which were uncontrolled in this study, change in Hb concentration was not analyzed as a secondary endpoint. Adverse events were monitored and defined as any undesirable clinical occurrence in any enrolled study patient during study participation.

Statistical analysis

A difference in Hb loss of 30 g was considered clinically important as this represents the Hb content of half of a unit of allogeneic whole blood from a donor with a Hb level between 13 and 15 g/dL. Based on pilot data, it was estimated that 29 patients per group would provide 90% power with $\alpha = 0.01$ to distinguish such a difference between groups. Therefore, the randomized study was planned for 60 patients. Study groups were compared for demographic characteristics with *t* tests, Wilcoxon rank-sum tests, and categorical chi-square tests as appropriate. Descriptive statistics are presented as mean \pm standard deviation (SD) or count and percent. The primary hypothesis of Hb loss in this randomized trial was tested with a *t* test at a significance level of 0.05 after verifying assumptions of normality and homogeneity of variance. Secondary endpoints were tested with *t* tests or rank-sum tests for numeric outcomes and with chi-square tests for categorical outcomes, at a significance level of 0.05. To further characterize the treatment effect, multivariable modeling was done with analysis of covariance, testing potential effects of race, sex, age, body mass index, length of surgery, number of levels involved, and the two-way interactions of these terms with group. For analysis, number of levels was categorized as two ($n = 48$) versus three to five ($n = 12$).

RESULTS

The demographics of the study population are contained in Table 1. Randomization resulted in 30 participants in each group with no significant difference identified between groups.

Figure 1 illustrates the primary endpoint of Hb loss for both groups. The control group experienced a mean Hb loss of 102.4 ± 39.6 g while the treatment group showed a significantly lower mean Hb loss of 66.2 ± 35.3 g ($p = 0.0004$), a mean difference of 36.3 g with 95% confidence limits (CLs) of 17 to 56 g. In the multivariable analysis of covariance, Aquamantys treatment demonstrated a significant effect ($p < 0.0001$), along with simultaneous effects of length of surgery ($p < 0.0002$) and number of levels involved ($p = 0.0002$). The effect of length of surgery was consistent in both groups (interaction $p = 0.1031$). However, a significant treatment interaction with level ($p = 0.0450$) indicated a more marked effect of treatment in procedures involving more than two levels (Fig. 2). In two-level cases, the estimated Hb loss was 20.7 g lower with Aquamantys, and in cases with more than two levels, it was 58.3 g lower. These treatment differences were significant in both categories of surgical level (two levels, $p = 0.0141$; three to five levels, $p = 0.0007$). The model R^2 was 0.585. Significance of treatment was confirmed in separate subanalyses on the two categories of level.

Table 2 contains comparison data for secondary endpoints. No significant difference was found between groups with respect to length of surgery, RBC units transfused, total blood component units transfused, transfusion avoidance, or length of stay. There were three adverse events in each study group. Adverse events in the treatment group included serous wound drainage without evidence of infection, a dural tear, and a wound hematoma. Adverse events in the control group included a urinary tract infection, atrial fibrillation, and fever with a gout flare. None of the adverse events were life-threatening or resulted in persistent or significant disability.

DISCUSSION

In this study, use of the Aquamantys bipolar sealant device in addition to unipolar cautery showed significantly lower Hb loss from the surgical field compared with use of unipolar cautery alone (Fig. 1). Based on the average screening Hb level of 13.8 g/dL for the study population, a 450-mL unit of whole blood from this patient group would contain 62.1 g of Hb. Therefore, the control group lost an average of 0.58 unit-equivalents of Hb more than the treatment group. The mean number of RBC units administered in the control group was 1.33. For a procedure with a mean RBC administration rate of 1.33 units per patient, a reduction in Hb loss of 0.58 unit-equivalents per case would be clinically significant as part of a patient blood

TABLE 1. Demographics of study population*

Treatment	Mean	SD	Median	Range	Count	%	p value	Test
Age (years)								
Control	61.8	10	64	40-80			0.7824	t test
Treatment	62.6	11.3	61.5	46-86				
Height (in.)								
Control	66.6	3.9	65	61.8-74.5			0.5244	Rank sum
Treatment	66	4.3	65.3	60-77				
Weight (lb)								
Control	187	38	186	116-254			0.5375	t test
Treatment	181	35	182	115-245				
BMI								
Control	29.4	4.7	28.5	20.1-39.5			0.8040	t test
Treatment	29.1	4.7	28.3	19.7-38.9				
Preop Hb (g/dL)								
Control	13.9	1.5	14.1	11.8-17.1			0.8399	t test
Treatment	13.8	1.4	13.6	11.1-17.1				
Surgery time (min)								
Control	219	41	214	147-294			0.2184	t test
Treatment	206	43	208	93-277				
Number of screws used								
Control	6.1	1.1	6	4-8			0.2548	Rank sum
Treatment	6.5	1.2	6	6-10				
Number of spinal levels involved								
Control	2.4	0.8	2	2-5			0.6335	Rank sum
Treatment	2.4	0.9	2	2-5				
Caucasian								
Control					24	80	1.0000	Chi-square
Treatment					24	80		
Female sex								
Control					19	63.3	0.5796	Chi-square
Treatment					22	73.3		
Revision procedure								
Control					11	36.7	0.1954	Chi-square
Treatment					17	56.7		
Two spinal levels involved								
Control					23	76.7	0.748	Chi-square
Treatment					25	83.3		
Three to five spinal levels involved								
Control					7	23.3		
Treatment					5	16.7		

* Characteristics of 60-patient study population (n = 30 control, n = 30 treatment).

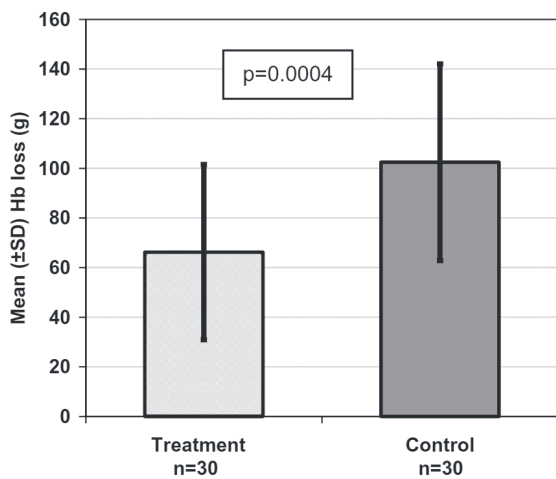


Fig. 1. Mean (\pm SD) mass of measured intraoperative Hb loss by treatment group.

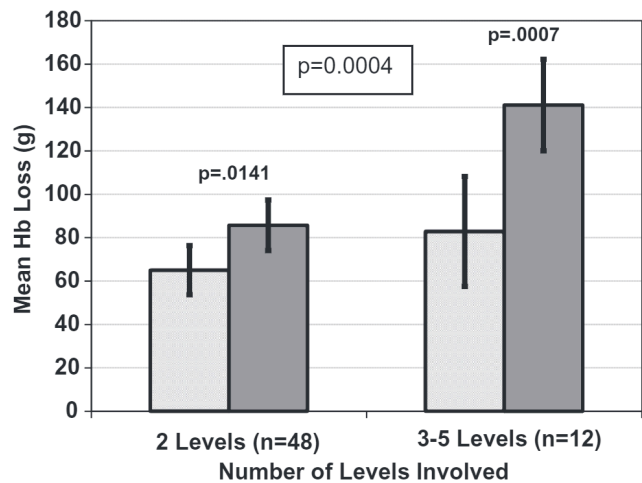


Fig. 2. Model-estimated mean mass of measured intraoperative Hb loss with 95% CLs, accounting for duration of surgery (210 min for estimation). Estimates by treatment group within number of levels involved. (□) Treatment; (■) control.

TABLE 2. Study outcomes by treatment

Treatment	Median	Mean	SD	95% CL		Range	Count	%	p value*	Test
				Lower	Upper					
Hb loss (g)										
Control	91.3	102.4	39.6	87.6	117.2	55.5-197.3			0.0004	t test
Treatment	64.9	66.2	35.3	53	79.4	14.4-174.1				
Surgery time (min)										
Control	214	219	41	204	235	147-294			0.2184	t test
Treatment	208	206	43	189	222	93-277				
Number of RBC units given										
Control	1.5	1.33	1.32	0.84	1.83	0-4			0.0760	Rank sum
Treatment	0	0.77	1.1	0.35	1.18	0-4				
Total number of blood products given										
Control	2	1.6	1.73	0.95	2.25	0-7			0.0777	Rank sum
Treatment	0	0.87	1.11	0.45	1.28	0-4				
Postop length of stay (days)										
Control	4	4.5	2.2	3.7	5.3	3-14			0.8189	Rank sum
Treatment	4	4.4	1.5	3.8	4.9	1-8				
Transfusion avoidance (count, percent)										
Control							11	36.7	0.1954	Chi-square
Treatment							17	56.7		

* p value is from test comparing treatment groups. Test is statistical test used to compare groups.

management program designed to optimize preoperative Hb, decrease perioperative blood loss, and reduce exposure to allogeneic transfusion.¹⁰ Because both severity of anemia as well as transfusion of allogeneic RBCs are independently associated with poor outcome,¹⁶⁻¹⁸ measures that significantly reduce surgical blood loss, thereby increasing nadir Hb and triggering less transfusion, should directly benefit patients. Reduction of surgical blood loss also preserves coagulation factors and PLTs that cannot be recovered with current cell salvage techniques.

While the study was not powered to determine multiple endpoints, several trends are present, which suggest a clinically significant treatment effect in decreasing Hb loss. In our sample, the treatment group had a lower number of RBC units transfused ($p = 0.076$) and total blood components administered ($p = 0.078$) compared with control patients. Because this trial included patients with a posterior surgical approach only, and anterior as well as posterior surgical exposure is frequently used with procedures involving more than two levels, 80% of patients enrolled in this trial ($n = 48$) had two-level surgery only. With two-level surgery, equipment costs may not be justified without a significant reduction in allogeneic blood transfusion. Nevertheless, accounting for length of surgery, the adjusted model found a significant benefit of Aquamantys at each category of level and estimated a significantly greater Aquamantys benefit on Hb loss in cases involving more than two levels (Fig. 2). Therefore, it is likely that allogeneic transfusion would be significantly reduced by use of the bipolar sealant device with more extensive procedures (more than two levels) and that the expense of the equipment would be outweighed by the cost of transfusion.

As can be seen from the data in Table 1, the treatment and control groups are well matched, arguing that the ran-

domization procedure was effective. Double-blinding was not feasible for this trial as the surgeon required knowledge of the type of instrument used for the procedure. However, the surgeon and the principal investigator were blinded of the results of the Hb loss measurements until after study completion. The patient was blinded of treatment. Limitations of this trial are mainly related to small sample size. While a significant difference is present in Hb loss between treatment and control groups, other clinically significant differences in transfusion rate, length of stay, or surgical time could not be conclusively determined. Variability in surgical technique and transfusion practice was controlled because one surgeon performed all procedures in this trial and was primarily responsible for postoperative care. However, the ability to generalize the results to other surgical providers and institutions may be limited by the study design. While every attempt was made to measure all Hb lost during the surgical procedure, blood soaking into the drapes was not measured. Even though this variable could impact results, the surgeon made a conscious effort to recover all blood from the field and there is no reason to think this effect would differ between groups.

The study design did not control for preoperative autologous donation of RBCs. While the availability of autologous RBC may influence the secondary endpoint of transfusion decisions, it would be unlikely to impact the primary endpoint in this study. Autologous predonation was infrequent in the study population ($n = 4$) and was evenly divided between the treatment ($n = 2$) and control ($n = 2$) groups. All four patients predonating autologous RBCs received all of their predonated cells back in the perioperative period. While individual patients predonating RBCs may present with lower Hb when compared with their individual baseline Hb, patients were excluded if

they developed anemia with a Hb level of 11 g/dL before surgery. Because relatively anemic patients lose less Hb with each milliliter of blood loss, the potential effect of autologous predonation would tend to lessen the difference between the treatment and control groups with regard to Hb loss in this trial. The finding that the treatment and control groups showed a significant difference in Hb loss in spite of allowing autologous predonation actually strengthens the conclusion of this trial and makes the study more applicable to current practice.

Use of the Aquamantys bipolar sealant device in addition to unipolar cautery significantly decreased Hb loss during multilevel, posterior lumbar spinal instrumentation and fusion when compared with unipolar cautery alone. Further study of the device comparing rates of transfusion avoidance when used in complex spinal surgery involving more than two levels is indicated to confirm clinical significance of this device as part of a patient blood management plan.

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