Relationship Between Hypothermia and Blood Loss in Adult Patients Undergoing Open Lumbar Spine Surgery

Nicholas S. Tedesco, DO; Frederick P. Korpi, DO; Vanessa K. Pazdernik, MS; and Jeffrey M. Cochran, DO

From the Department of Orthopedics at the Ohio University Heritage College of Osteopathic Medicine at Athens and Affinity Medical Center in Massillon, Ohio (Drs Tedesco, Korpi, and Cochran), and Research Support at the A.T. Still University-School of Osteopathic Medicine in Arizona (Mesa) (Ms Pazdernik). Dr Korpi was affiliated with the A.T. Still University-Kirksville College of Osteopathic Medicine in Missouri at the time of this study.

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Address correspondence to Nicholas S. Tedesco, DO, Ohio University Heritage College of Osteopathic Medicine at Athens, Affinity Medical Center, 875 8th St NE, Massillon, OH 44646-8503.

E-mail: nicholas.tedesco@gmail.com

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Context: Intraoperative blood loss during open lumbar spine surgery is associated with adverse events and is a contributor to higher medical costs. Intraoperative hypothermia has been shown to increase blood loss and postoperative allogeneic blood transfusion rates in other realms of orthopedic surgery, but it has not been studied extensively in patients undergoing spine surgery.

Objective: To determine whether a clinically relevant association exists between intraoperative core body temperature and blood loss or transfusion rates in adult patients undergoing open lumbar spine surgery.

Methods: In this retrospective medical record review, the surgical records of 174 adult patients who underwent open, nonmicroscopically assisted lumbar spine surgery performed by a single surgeon at a single institution were evaluated. Maximum, minimum, and average temperature, hypothermic temperature, and temperature range parameters were compared with intraoperative, total, and net blood loss and blood transfusion parameters. Additional patient demographic and perioperative characteristics were compared with blood loss and transfusion parameters to determine potential confounders. Analysis of variance, Spearman rank correlation, and generalized multiple linear regression analysis were performed to test for an association between temperature and blood loss or allogeneic transfusion rates. Statistical significance was set at $P \leq .05$.

Results: After implementation of exclusion criteria, 160 patient records and 168 surgical procedures were included in the analysis. For patients whose temperature decreased to a hypothermic level at some point during the procedure, hypothermic maximum temperature was protective against blood loss on bivariate analysis ($P \leq .02$), but this finding lost significance after multivariate regression analysis ($P > .09$). Temperature range was associated with increased blood loss on bivariate analyses ($P < .001$) but also lost significance after adjusting for covariates in regression analysis ($P \geq .65$). Surgery type ($P \leq .001$) and operative time ($P \leq .001$) were the most robust predictors of increased blood loss ($P = .005$) and were significantly associated with temperature ($P < .001$).

Conclusion: No effect was found on perioperative blood loss from any temperature parameter or hypothermia in adult patients who underwent lumbar spine surgery once covariates were controlled for with multivariate analysis. One possible interpretation of these results is that the effect of temperature on blood loss can be explained by its strong relationship to the confounders of operative time and surgery type.

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Intraoperative blood loss is expected during any open surgical procedure, with harmful sequelae proportional to the amount of blood lost. Postoperative anemia due to hemodilution from perioperative intravenous fluid administration and blood loss from surgical dissection can lead to complications ranging from mild dizziness to death.[1] Many preventive and palliative strategies exist to mitigate postoperative anemia. The standard treatment for patients with symptomatic or excessive postoperative anemia is allogeneic blood transfusion. However, this treatment does not come without its own complications, some of which can be fatal.[1,2]

According to a 2010 review,[3] blood loss in adult patients undergoing spine surgery continues to be a major problem despite multiple available treatment strategies. The authors of the study also noted a lack of quality evidence supporting minimization of intraoperative hypothermia as a means of decreasing intraoperative blood loss and its related complications.[3]

Clinical[4-8] and basic science[9-20] research supports the association between core hypothermia and increased surgical blood loss. Mild hypothermia, defined as core body temperature between 34°C and 36°C, has been shown to increase blood loss and transfusion requirements in patients undergoing total hip replacement.[5] The same study also showed that maintaining intraoperative normothermia reduced blood loss and allogeneic blood transfusions.[5] This result was supported by another study,[6] which showed that maintaining a tympanic membrane temperature greater than 36.5°C during total hip replacement reduced intraoperative blood loss and allogeneic blood transfusion. In a review by Rajagopalan et al,[7] mild hypothermia independently increased blood loss by an average of 16% and the relative risk for transfusion by an average of 22%. The authors also found that strict maintenance of normothermia within a narrow range reduced blood loss and transfusion requirements.[7] Limited research is available investigating these relationships in orthopedic spine surgery.[3]

The purpose of the present study was to determine whether a clinically relevant association exists between intraoperative core body temperatures and perioperative blood loss or transfusion rates in adult patients undergoing open lumbar spine surgery. We hypothesized that hypothermia would result in a statistically significant increase in blood loss and allogeneic transfusion rates in these patients.

Methods

After obtaining approval from the local institutional review board, we generated a database of patients aged 18 years or older who had open, nonmicroscopically assisted lumbar intersegmental decompression, decompressive laminectomy, instrumented fusion, noninstrumented fusion, or anterior or posterior interbody fusion operations. Two authors (N.S.T. and F.P.K.) retrospectively and independently reviewed the hospital records of all cases performed by the same surgeon (J.M.C.) at a single institution between January 2010 and March 2013. All adult patients were included in the study, and those with inadequate documentation of study variables were excluded.

To test our study hypothesis, maximum temperature (T_{max}), minimum temperature (T_{min}), and average temperature (T_a) were measured via esophageal probe every 15 minutes during the procedure. Temperature range (T_r) was calculated as $T_{max} - T_{min}$. Intraoperative blood loss, total blood loss with postoperative drain output factored in, and net blood loss after transfusion (intraoperative autogenous via Cell Saver [Haemonetics] or postoperative allogeneic) were also recorded. Intraoperative blood loss was estimated for all operations using the amount of fluid suctioned during the procedure minus any irrigation used. When a surgical sponge was used, the sponge was weighed to estimate the amount of blood soaked up, with 1 g of additional weight from a dry sponge corresponding to 1 mL of blood. To test for associations with blood loss, temperature variables were analyzed both as continuous

(ie, in °C) and as binary categorical (ie, hypothermic levels ≤36.5°C were or were not reached).

To avoid possible spurious associations, information for secondary variables related to patient demographic and other perioperative characteristics was collected and compared with the blood loss parameters. For demographic characteristics, information was collected on patient age, sex, race, body mass index (BMI), smoking history, preoperative anticoagulant use, and preoperative nonsteroidal anti-inflammatory drug (NSAID) use. Patient comorbidities that are known risk factors for increased blood loss, including liver disease and known bleeding diatheses, were also recorded. For perioperative characteristics, information was collected on primary diagnosis; surgery type; whether the procedure was a surgical revision; operative time; number of spinal segments involved; maximum, minimum, and average intraoperative mean arterial pressure (MAP); incidental durotomy; use of deep wound drains; iliac crest bone grafting; perioperative surgical site infection; perioperative mortality; length of hospital stay; and discharge disposition (eg, home, subacute rehabilitation facility).

Specific procedures were in place for some of the secondary variables at the institution where the surgical procedures were performed. For instance, any patients taking anticoagulants were asked to stop taking those medications in accordance with each medication's recommendation, such that the target international normalized ratio would be less than 1.4 by the time of surgery. To avoid excessive blood loss due to platelet dysfunction, NSAID use was halted 14 days preoperatively, but patients taking a cardioprotective dose of 81 mg of aspirin daily could continue taking that medication up until the day of the procedure. The autologous blood collection system was used in patients with an anticipated greater intraoperative blood loss (ie, those undergoing instrumented fusions, interbody fusions, and multilevel decompressive laminectomies). Allogeneic blood transfusion was reserved for patients with symptomatic postoperative anemia. Deep wound drains were subjectively reserved for patients who had greater intraoperative blood loss or longer operative times. No suction was applied to the drains if an incidental durotomy occurred intraoperatively.

All study data were entered into a spreadsheet and confirmed by each author reviewing the medical record data during patient database generation. Descriptive statistics were presented as frequencies for the categorical variables of maximum, minimum, and average hypothermic temperature (core body temperature ≤36.5°C was or was not reached); autogenous and allogeneic transfusion (transfusion was or was not performed); sex; smoking history; preoperative anticoagulant use; preoperative NSAID use; primary diagnosis; surgery type; whether the procedure was a surgical revision; number of spinal segments involved; incidental durotomy; use of deep wound drains; iliac crest bone grafting; perioperative surgical site infection; perioperative mortality; length of hospital stay; and discharge disposition. Descriptive statistics were presented as mean and range for the continuous variables of maximum, minimum, and average core body temperature (°C); temperature range; intraoperative, total, and net blood loss; autogenous and allogeneic transfusion (mL); age; BMI; operative time; and maximum, minimum, and average intraoperative MAP.

A *t* test, 1-way analysis of variance (ANOVA), and Spearman rank correlation were used to test for associations between secondary variables and temperature with blood loss. The Welch *t* test and ANOVA were used when equal variance was not satisfied. The Spearman rank correlation was used because the blood loss data were skewed to the right, and this test can assess the strength of both linear and nonlinear relationships. For statistically significant results, estimates and 95% CIs were reported. The Tukey multiple comparisons tests were used as needed in ANOVA analyses to control the type I experimental error rate at α=.05. Categories with statistically significant differences indicated by the Tukey test were presented as mean (SD).

A generalized multiple linear regression analysis was carried out to test the association between temperature and blood loss while controlling for demographic or perioperative secondary variables. Neither categorical factors of deep wound drains nor transfusions were considered plausible risk factors because they were reactions to blood loss or factors occurring after the procedure, such as hospital length of stay. Body mass index, preoperative anticoagulant use, surgery type, operative time, number of spinal segments involved, and incidental durotomy were covariates included in all 3 regression models. Further, age, preoperative NSAID use, primary diagnosis, and maximum MAP were included in the model that fit intraoperative blood loss. The model that fit total blood loss included age, preoperative NSAID use, and perioperative surgical site infection, and sex was included in the model fitting net blood loss.

Generalized linear models were used with a γ response distribution and log link because the parametric data on raw blood loss were skewed to the right. Potential confounders were eliminated only if $P>.20$.[21] The proportion of variance explained by the predictors was reported as the square of the estimated correlation measure between the response and predicted values.[22] Subsequent testing of the relationship between each temperature measure and current blood loss measure was performed. The relationship between each of the covariates included in the final model and temperature was assessed using both χ^2 tests and ANOVA. SAS software (version 9.3) was used for all analyses. Statistical significance was set at $P\leq.05$.

Results

Fourteen of 174 patients (182 operations) were excluded from our analyses because of incomplete intraoperative temperature documentation. Data from 168 operations on 160 patients were included. Six patients had 2 operations and 1 patient had 3 operations during the study period; however, each of these patients had more than 180 days between the operations. Each of these surgical procedures was considered an independent event during analysis; statistical results did not change when analyses used data on only 1 operation per patient.

When temperature was examined as a continuous variable on bivariate analysis, Spearman rank correlation analyses indicated no association between T_{max}, T_{min}, or T_a and intraoperative, total, or net blood loss (all $P\geq.06$). However, T_r had a significant positive correlation with all 3 blood loss parameters ($\rho\geq0.28$; all $P<.001$) (*Table 1*).

When temperature was examined as a binary variable (≤36.5°C), patients with hypothermic T_{max} had less total blood loss than those without (–151 mL [95% CI, –284 to –19 mL]; $P=.03$) (*Table 2*). Evidence was not statistically significant for intraoperative blood loss and net blood loss ($P=.08$ and $P=.06$, respectively). Conversely, patients with hypothermic T_{min} had more blood loss in all 3 parameters (all $P\leq.05$). On further investigation, 18 patients recorded both T_{max} and T_{min} greater than 36.5ºC (group 1), and 64 patients had T_{max} greater than 36.5°C but T_{min} less than or equal to 36.5°C (group 2). The remaining 86 patients had both T_{max} and T_{min} less than or equal to 36.5°C (group 3). When T_{min} was greater than 36.5°C, these differences in intraoperative, total, and net blood loss between group 1 and group 2 were negative, and group 1 had lower but not significant levels of blood loss ($P=.17$, $P=.25$, and $P=.45$, respectively). When T_{min} was less than or equal to 36.5°C, differences between group 2 and group 3 were positive, and group 2 had significantly greater levels of blood loss (130 mL [95% CI, 19-222 mL], 242 mL [95% CI, 106-377 mL], and 148 mL [95% CI, 44-251 mL]; $P=.02$, $P<.001$, and $P=.01$, respectively). Owing to the larger sample size of group 2, the main effect of groups 1 and 2 vs group 3 was positive, which is not useful in the presence of an interaction. There was no significant difference between group 1 and group 3 in intraoperative, total, or net blood loss ($P=.35$, $P=.25$, and $P=.45$, respectively). Hypothermic T_a had no correlation with any of the blood loss parameters (all $P\geq.89$).

Table 1.
Test Statistics by Blood Loss and Body Temperature of Adult Patients Undergoing Open Lumbar Spine Surgery (N=160)[a]

Body Temperature Group	Mean (SD) Body Temperature, °C	Test Statistics[b] by Blood Loss: Intraoperative ρ	Intraoperative *P* Value	Total ρ	Total *P* Value	Net ρ	Net *P* Value
Maximum (n=86)	36.5 (0.63)	0.09	.23	0.14	.08	0.15	.06
Minimum (n=150)	35.8 (0.74)	−0.11	.17	−0.08	.30	−0.04	.61
Average (n=126)	36.2 (0.59)	0.05	.54	0.07	.37	0.08	.28
Range	0.69 (0.64)	0.30	<.001	0.33	<.001	0.28	<.001

[a] Six patients underwent 2 surgical procedures and 1 underwent 3 procedures, for a total of 168 surgical procedures.
[b] Test statistics calculated using Spearman rank correlation and *t* tests.

The number of surgical procedures in which an intraoperative autogenous transfusion was necessary was 66 (39%), with a mean volume of 268 mL transfused. Procedures requiring this type of transfusion had significantly greater mean levels in all 3 blood loss parameters (all $P<.001$). Nonzero autogenous transfusion volume was positively correlated with all 3 blood loss parameters (all $P<.001$). In 4 operations (2%), allogeneic transfusion was required, with a mean volume of 525 mL transfused. Patients who required this type of transfusion had greater average levels of intraoperative and net blood loss ($P=.047$ and $P=.03$, respectively).

A weak negative correlation was observed between age and intraoperative, total, and net blood loss ($\rho=-0.20$, $P=.009$; $\rho=-0.23$, $P=.003$; and $\rho=-0.20$, $P=.008$, respectively). There was a small but significant positive correlation between BMI and the blood loss parameters ($\rho=0.24$, $P=.002$; $\rho=0.27$, $P<.001$; and $\rho=0.27$, $P<.001$, respectively). There was a significant increase in intraoperative, total, and net blood loss between patients who had taken preoperative NSAIDs and those who had not (135 mL [95% CI, 48-222 mL], 200 mL [95% CI, 70-330 mL], and 128 mL [95% CI, 30-226 mL], respectively; all $P<.01$).

Primary diagnosis was significantly associated with total and net blood loss ($P=.02$ and $P=.008$, respectively). A primary diagnosis of spondylolisthesis was associated with the greatest amounts of blood loss. The Tukey post-hoc multiple comparison indicated that the mean (SD) total blood loss in patients with a primary diagnosis of spondylolisthesis (950 [550] mL) was significantly greater than in patients with a combination of primary diagnoses (630 [430] mL; adjusted $P=.045$) or acquired lumbar spinal stenosis (ALSS) (360 [310] mL; adjusted $P<.001$). Total blood loss in patients with combined diagnoses was also larger than ALSS (adjusted $P=.01$). Mean (SD) net blood loss was significantly greater for spondylolisthesis than ALSS (670 [320] mL vs 320 [270] mL, respectively; adjusted $P=.004$). Surgery type was also significantly associated with intraoperative, total, and net blood loss (all $P\leq.001$), with instrumented fusion (IF) and posterior lumbar interbody fusion (PLIF) having the greatest amounts of blood loss (*Figure 1*).

The Tukey post-hoc multiple comparison indicated that the mean (SD) intraoperative blood loss in patients who underwent IF (950 [550] mL) or PLIF (430 [290] mL) was significantly greater than in patients who underwent intersegmental decompression (ID) (170 [210] mL) (adjusted $P<.001$ and $P=.005$, respectively). Mean (SD) total blood loss was significantly greater in patients who underwent IF (830 [410] mL) or PLIF

Table 2.
Mean (SD) Blood Loss by Body Temperature of Adult Patients Undergoing Open Lumbar Spine Surgery (N=160)[a]

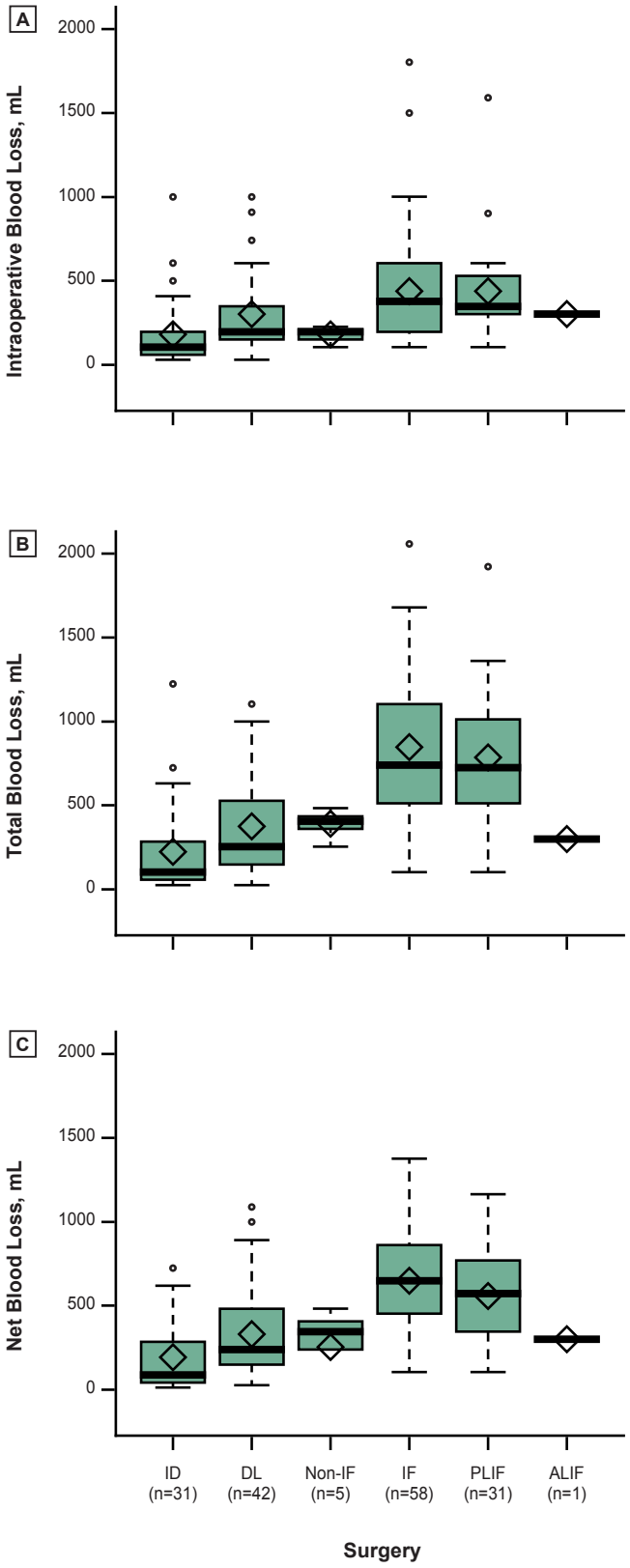
Body Temperature	Mean (SD) Blood Loss, mL		
	Intraoperative	Total	Net[b]
Maximum (n=86)			
Hypothermic	302 (222)	504 (358)	414 (293)
Nonhypothermic	381 (348)	655 (497)	508 (355)
P value	.08[c]	.03[c]	.06
Minimum (n=150)			
Hypothermic	358 (300)	608 (442)	478 (330)
Nonhypothermic	201 (164)	332 (290)	316 (265)
P value	.002[c]	.001[c]	.047
Average (n=126)			
Hypothermic	339 (281)	577 (431)	458 (333)
Nonhypothermic	346 (329)	581 (458)	467 (313)
P value	.90	.95	.87

[a] Six patients underwent 2 surgical procedures and 1 underwent 3 procedures, for a total of 168 surgical procedures.
[b] Test statistics calculated using Spearman rank correlation and *t* tests.
[c] Welch analysis of variance.

(410 [560] mL) than in patients who underwent decompressive laminectomy (DL) (370 [310] mL) or ID (220 [260] mL) (both adjusted $P<.001$). Also, mean (SD) net blood loss was significantly greater in patients who underwent IF (650 [300] mL) than in patients who underwent DL (340 [270] mL, adjusted $P<.001$), non-IF (260 [260] mL, adjusted $P=.03$), or ID (200 [200] mL, adjusted $P<.001$). Mean (SD) PLIF (560 [300] mL) was also greater than DL (adjusted $P=.01$) and ID (adjusted $P<.001$). There was a strong correlation with operative time and the 3 blood loss variables ($\rho=0.66$, $P<.001$; $\rho=0.75$, $P<.001$; and $\rho=0.64$, $P<.001$, respectively) (*Figure 2*). Minimum intraoperative MAP was weakly correlated with less blood loss for all 3 parameters ($\rho=-0.19$, $P=.02$; $\rho=-0.24$, $P=.002$; and $\rho=-0.26$, $P<.001$, respectively).

There was a significant increase in intraoperative blood loss between patients who had an incidental durotomy vs those who did not (180 mL [95% CI, 69-290 mL]; $P=.01$). Similarly, a significant increase was observed in intraoperative, total, and net blood loss between patients who were given deep wound drains and those who were not (258 mL [95% CI, 189-328 mL] mL, 614 mL [95% CI, 533-696 mL], and 441 mL [95% CI, 375-508 mL], respectively; all $P<.001$). Patients with a perioperative surgical site infection had a significant increase in total blood loss only (743 mL [95% CI, 429-1057 mL]; $P<.001$). Hospital length of stay showed a positive correlation with all 3 blood loss parameters ($\rho=0.33$, $\rho=0.35$, and $\rho=0.28$, respectively; all $P<.001$).

No continuous or categorical temperature variable was significant after controlling for covariates as described above (all $P>.09$). In the multivariate analysis, the models explained 44%, 54%, and 44% of the variation in intraoperative, total, and net blood loss, respectively. The removal of procedure length, used in all



3 models, caused this proportion of variance explained by the predictors to decrease by 10%, 5%, and 4%, respectively, indicating a clinically significant independent effect of procedure length on the blood loss parameters. Removal of surgery type caused a 15% and 11% point drop in total and net blood loss, respectively. Removal of preoperative NSAID use caused a 5% and 7% point drop in intraoperative and net blood loss, respectively. Finally, BMI caused a 7% point drop in net blood loss. The remaining predictor variables each caused less than 3% point drop decreases. Categories of temperature were strongly related to both surgery type (χ^2=18.6; P=.005) and operative time (F=7.28; P<.001).

Discussion

In the present study, we failed to confirm any correlation with intraoperative core body temperature and perioperative blood loss. In several of our bivariate analyses, core body temperature range was positively correlated with blood loss. Also, the group of patients that experienced both hypothermic and nonhypothermic temperatures during the operation was associated with significantly more blood loss than those patients who always stayed above or below hypothermic levels. Additionally, the greater blood loss associated with nonhypothermic T_{max} depended on whether the patient had hypothermic T_{min}, because hypothermic T_{min} was associated with greater blood losses. However, all of these findings failed

Figure 1.
Bivariate analysis of surgery type and intraoperative blood loss (A), total blood loss (B), and net blood loss (C). Points less than the first quartile or greater than the third quartile by more than 1.5 times the interquartile (IQR) range are plotted separately. The horizontal line in the middle of each box indicates the median, and the top and bottom borders of the box mark the third and first quartiles, respectively. The whiskers above and below the box mark the maximum and minimum, respectively, of the subset of the data ranging between 1.5 × IQR below the first quartile and 1.5 × IQR above the third quartile. The mean is represented by the diamond.

to reach significance once confounders were accounted for with multivariate regression analysis.

To our knowledge, only 2 other studies[4,23] have investigated the relationship between blood loss and core body temperature during spine surgery. In one study, patients who underwent elective spine surgery had an increased risk of infection with intraoperative hypothermia, but there was no association with blood loss and body temperature.[23] However, with only 70 patients in that study, the results may have been underpowered. A prospective, randomized controlled trial comparing blood loss in patients with and without an electrically heated body humidifier noted increased mean intraoperative blood loss and blood transfusion requirements in patients without the heated humidifier.[4] These findings support our bivariate results that suggested that temperature range was correlated with increased blood loss rather than absolute hypothermia or other temperature parameters. One possible explanation for this finding is that the body may up- and down-regulate specific clotting factors in response to temperature changes, but it is unable to keep up with extreme fluctuations in temperature, causing a wide temperature range to be more damaging than a lower absolute temperature. However, this speculation has yet to be confirmed in the basic science literature.

The mechanism by which hypothermia increases blood loss may be related to a multifactoral coagulopathy precipitated by subphysiologic body temperature.[9-18] Hypothermia has been shown to strongly inhibit multiple steps in the coagulation cascade, progressively prolonging the prothrombin and partial thromboplastin times with increasing hypothermia.[9-11] Hypothermia also appears to disrupt thrombin and fibrinogen synthesis.[12] Furthermore, there seems to be an inhibition of platelet activation through multiple mediators that is reversible with increases in temperature.[13-15]

Although hypothermia has been shown to disrupt platelet function,[11,16] coagulation protease activity is inhibited[16] and platelet aggregation is increased[17] at lower temperatures. Studies[4-8] that have found mild hypothermia correlated to increased operative blood loss suggest that clotting inhibition may outweigh the procoagulant effect of hypothermia with respect to platelet function, leading to a net decrease in clotting. This predilection for decreased clotting with mild hypothermia has been shown to have clinical significance.[4-7,18] However, we failed to confirm this conclusion because hypothermia failed to reach significance as a risk factor for blood loss once confounders were accounted for.

Perioperative fluid administration and, thus, hemodilution may independently exacerbate coagulopathy.[18,19] Perioperative fluid administration is required to maintain hydration status, electrolyte balance, and adequate blood pressure. Because restricting fluids is ill-advised, it is suggested that only a portion of perioperative coagulopathy could be mitigated by controlling core body temperature.[5-7] However, results of the present study failed to show any significance with any of our blood loss parameters, and hypothermic T_{min} and T_r lost their statistical significance after multivariate regression analysis. Preoperative NSAID use, BMI, surgery type, and increased operative time had the largest independent effects on blood loss. This result was evidenced by the largest decreases in predictive power of the model on blood loss after removal of these variables.

Although there was a significant association between incidental durotomy and intraoperative blood loss, it seems that the confounders of surgery type, whether the procedure was a surgical revision, patient comorbidities, and operative time may more accurately account for this association, because there was no significant association between incidental durotomy and total or net blood loss. These same factors may also account for the significant associations we observed between blood loss and perioperative surgical site infection rate and length of hospital stay.

It was expected that patients who had deep wound drains would have significantly greater blood loss parameters, owing to the additional recorded perioperative blood loss compared with those who did not have a drain.

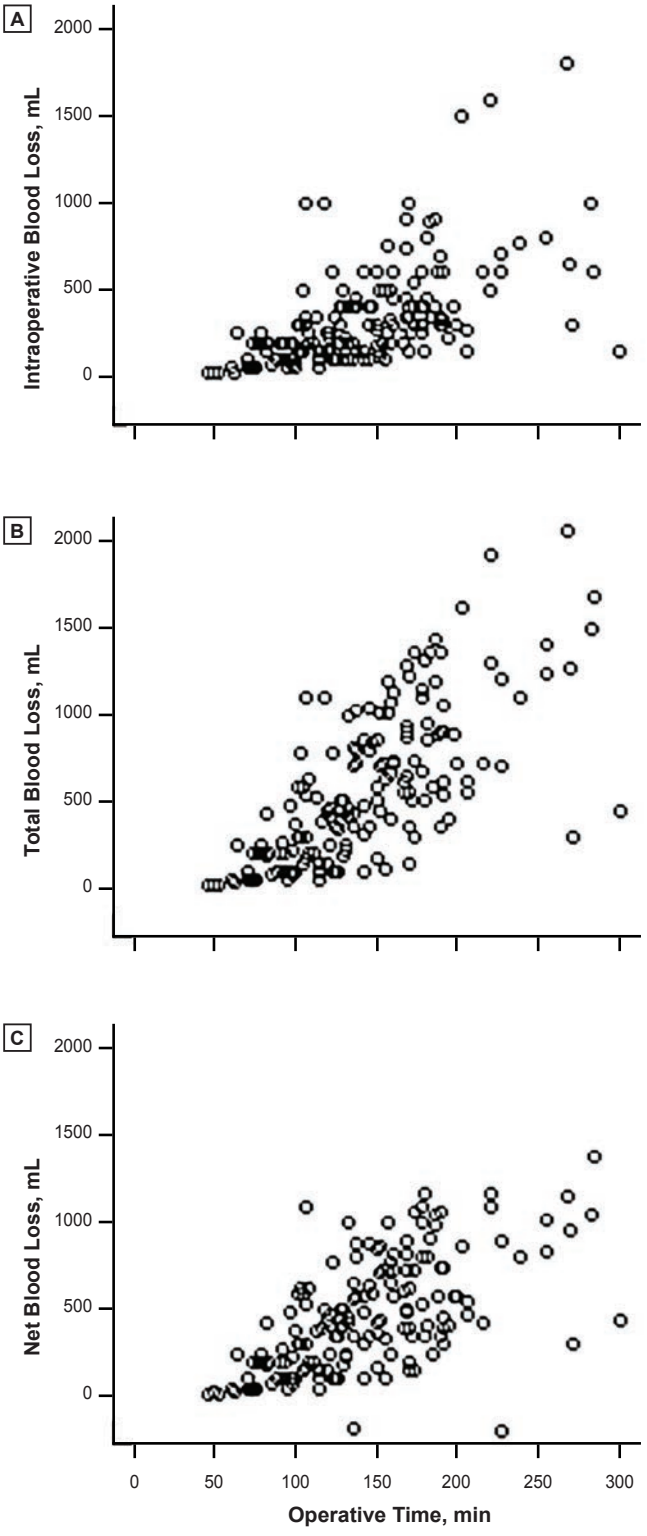


Figure 2.
Bivariate analysis of operative time and intraoperative blood loss (A), total blood loss (B), and net blood loss (C).

Our results supported this assumption. The presence or absence of a drain was accounted for in all patients during analyses of blood loss parameters by including those with (intraoperative, total, and net blood loss) and without (intraoperative and net blood loss only) the additional recorded drain output as separate cohorts. Suction was applied to all deep wound drains with the exception of patients with an incidental durotomy. Therefore, total blood loss may have been artificially decreased in these patients as a result of the lack of suction continuing to pull blood from the surgical site, potentially confounding their select results.

The present study had several limitations. Because this was a retrospective observational study, no direct causal conclusions could be made regarding the relationship between intraoperative core body temperature and perioperative blood loss or blood transfusion rates in adult patients who underwent lumbar spine surgery. Likewise, there was no control cohort or homogenization of specific perioperative measures. However, the same physician performed all operations at the same institution, and there were no major changes in techniques, instrumentation, preferred implants, or management strategies during the study period. Because of these similarities for all reviewed records, it seems probable that these variables did not affect the generalizability of our results.

Because there were only 4 allogeneic blood transfusions and 6 iliac crest bone graft procedures in the present study, we were unable to determine correlations of statistical significance with the primary variables. Additionally, only 2 patients were nonwhite, 1 patient had documented liver disease, and none had a known bleeding diathesis, precluding analysis of these potential confounders. Preadmission testing was not routinely performed on all patients. Therefore, undetected preoperative anemia could not be analyzed. A larger cohort of patients may have obviated these issues. Further, with no strict protocol on drain use or monitoring of preoperative cessation of NSAIDs and anticoagulants, the findings

regarding these variables may not be as reliable as other, more controlled study variables. There is likely additional intraoperative blood loss unaccounted for as a result of the methods used at our institution. However, we believe those methods represent current practice standards and any blood loss unaccounted for was not likely to substantially affect the primary outcome variables.

Additionally, because we only studied a specific group of adult patients who underwent specific types of lumbar spine surgery, results may not be generalizable to pediatric patients or patients undergoing microscopically assisted surgery, cervical or thoracic spine surgery, or fusions by means of alternative approaches to the lumbar spine. By limiting the type of patients included in the present study, we hoped to minimize potential confounding influences.

A future subgroup analysis may identify which NSAID is the biggest contributor to blood loss, how strictly patients follow the cessation protocol, or whether 81 mg of aspirin daily contributes to blood loss. Additional studies should investigate core body temperature and its relationship to operative blood loss, with close scrutiny of the statistical analyses and confounders accounted for in regression analysis of previous and future studies.

Conclusion

Although bivariate analysis suggested that hypothermia initially appeared to be correlated with blood loss, this association did not hold true when other variables were accounted for with multivariate regression analysis. In the present study, intraoperative core body maximum and minimum temperatures, average temperature, temperature range, and hypothermia did not have a significant effect on intraoperative, total, or net blood loss in adult patients who underwent open lumbar spine surgery. Surgery type and longer operative time seemed to have the greatest association with increased blood loss and were also associated with intraoperative core body temperature. Therefore, one possible interpretation of the results is that the effect of temperature on blood loss can be explained by its strong relationship to the confounders of surgery type and operative time. Increased BMI and preoperative NSAID use were additional significant independent predictors of increased blood loss, but to a lesser degree. Therefore, controlling the above confounders may have a more robust effect on blood loss than intraoperative normothermia.

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Author Contributions

Drs Tedesco, Korpi, Pazdernik, and Cochran provided substantial contributions to conception and design, acquisition of data, or analysis and interpretation of data; drafted the article or revised it critically for important intellectual content; and gave final approval of the version of the article to be published.

References

1. Kumar V, Abbas AK, Fausto N, Aster J. *Robbins and Cotran Pathologic Basis of Disease*. 8th ed. Philadelphia, PA: Saunders; 2010.
2. Leo A, Pedal I. Diagnostic approaches to acute transfusion reactions. *Forensic Sci Med Pathol*. 2010;6(2):135-145. doi:10.1007/s12024-009-9115-7.
3. Tse EY, Cheung WY, Ng KF, Luk KD. Reducing perioperative blood loss and allogeneic blood transfusion in patients undergoing major spine surgery. *J Bone Joint Surg Am*. 2011;93(13):1268-1277. doi:10.2106/JBJS.J.01293.
4. Lee HK, Jang YH, Choi KW, Lee JH. The effect of electrically heated humidifier on the body temperature and blood loss in spinal surgery under general anesthesia. *Korean J Anesthesiol*. 2011;61(2):112-116. doi:10.4097/kjae.2011.61.2.112.
5. Schmied H, Kurz A, Sessler DI, Kozek S, Reiter A. Mild hypothermia increases blood loss and transfusion requirements during total hip arthroplasty. *Lancet*. 1996;347(8997):289-292.
6. Winkler M, Akça O, Birkenberg B, et al. Aggressive warming reduces blood loss during hip arthroplasty. *Anesth Analg*. 2000;91(4):978-984.

7. Rajagopalan S, Mascha E, Na J,Sessler DI. The effects of mild perioperative hypothermia on blood loss and transfusion requirement. *Anesthesiology*. 2008;108(1):71-77.

8. Watts DD, Trask A, Soeken K, Perdue P, Dols S, Kaufmann C. Hypotherimic coagulopathy in trauma: effect of varying levels of hypothermia on enzyme speed, platelet function, and fibrinolytic activity. *J Trauma*. 1998;44(5):846-854.

9. Rohrer MJ, Natale AM. Effect of hypothermia on the coagulation cascade. *Crit Care Med*. 1992;20(10):1402-1405.

10. Wolberg AS, Meng ZH, Monroe DM III, Hoffman M. A systematic evaluation of the effect of temperature on coagulation enzyme activity and platelet function. *J Trauma*. 2004;56(6):1221-1228.

11. Michelson AD, MacGregor H, Barnard MR, Kestin AS, Rohrer MJ, Valeri CR. Reversible inhibition of human platelet activation by hypothermia in vivo and in vitro. *Thromb Haemost*. 1994;71(5):633-640.

12. Martini WZ. Coagulopathy by hypothermia and acidosis: mechanisms of thrombin generation and fibrinogen availability. *J Trauma*. 2009;67(1):202-208. doi:10.1097/TA.0b013e3181a602a7.

13. Valeri CR, Feingold H, Cassidy G, Ragno G, Khuri S, Altschule MD. Hypothermia-induced reversible platelet dysfunction. *Ann Surg*. 1987;205(2):175-181.

14. Kermode JC, Zheng Q, Milner EP. Marked temperature dependence of the platelet calcium signal induced by human von Willebrand factor. *Blood*. 1999;94(1):199-207.

15. Reed RL II, Bracey AW Jr, Hudson JD, Miller TA, Fischer RP. Hypothermia and blood coagulation: dissociation between enzyme activity and clotting factor levels. *Circ Shock*. 1990;32(2):141-152.

16. Scharbert G, Kalb ML, Essmeister R, Kozek-Langenecker SA. Mild and moderate hypothermia increases platelet aggregation induced by various agonists: a whole blood in vitro study. *Platelets*. 2010;21(1):44-48. doi:10.3109/09537100903420269.

17. Martini WZ, Pusateri AE, Uscilowicz JM, Delgado AV, Holcomb JB. Independent contributions of hypothermia and acidosis to coagulopathy in swine. *J Trauma*. 2005;58(5):1002-1009.

18. Gubler KD, Gentilello LM, Hassantash SA, Maier RV. The impact of hypothermia on dilutional coagulopathy. *J Trauma*. 1994;36(6):847-851.

19. Brohi K, Singh J, Heron M, Coats T. Acute traumatic coagulopathy. *J Trauma*. 2003;54(6):1127-1130.

20. Matsukawa T, Sessler DI, Sessler AM, et al. Heat flow and distribution during induction of general anethesia. *Anesthesiology*. 1995;82(3):662-673.

21. Budtz-Jørgensen E, Keiding N, Grandjean P, Weihe P. Confounder selection in environmental epidemiology: assessment of health effects of prenatal mercury exposure. *Ann Epidemiol*. 2007;17(1):27-35.

22. Zheng B, Agresti A. Summarizing the predictive power of a generalized linear model. *Stat Med*. 2000;19(13): 1771-1781.

23. Guest JD, Vanni S, Silbert L. Mild hypothermia, blood loss and complications in elective spinal surgery. *Spine J*. 2004;4(2):130-137.