4-1-2018

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Global Spine Journal
2018, Vol. 8(2) 198-207

DOI: 10.1177/2192568217747572
journals.sagepub.com/home/gsj

Blood Transfusion and Postoperative Infection in Spine Surgery: A Systematic Review

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Abstract

Study Design: Systematic review.

Objectives: Allogeneic blood transfusion-related immunomodulation may relatively suppress the immune system, heightening the risk of infection following spine surgery. This systematic review seeks to determine whether allogeneic blood transfusion increases the risk of postoperative infection and whether there are any factors that modify this association.

Methods: PubMed, Cochrane Central Register of Controlled Trials, and reference lists from included studies were searched from inception to April 20, 2017 to identify studies examining the risk of infection following allogeneic blood transfusion in adult patients receiving surgery for degenerative spine disease.

Results: Eleven retrospective cohort or case-control studies, involving 8428 transfusion patients and 43 242 nontransfusion patients, were identified as meeting the inclusion criteria. Regarding surgical site infection (SSI), the results were mixed with roughly half reporting a significant association. There was an association between allogeneic transfusion and urinary tract infection (UTI) and any infection, but not respiratory tract infection. There was no statistical modifying effect of lumbar versus thoracic surgery on the association of allogeneic transfusion and SSI, though subgroup analyses in 3 of 4 studies reported a statistical association between transfusion and postoperative infections, including SSI, UTI, and any infection within the lumbar spine.

Conclusions: This systematic review failed to find a consistent association between allogeneic transfusion and postoperative infection in spine surgery patients. However, these studies were all retrospective with a high or moderately high risk of bias. To properly examine this association an observational prospective study of sufficient power, estimated as 2400 patients, is required.

Keywords

allogeneic blood transfusion, postoperative infection, spine, complications

Introduction

The United States has seen a growing rate of allogeneic blood transfusion in the context of spine surgery.[1,2] Intraoperative blood loss necessitates the transfusion of allogeneic blood to avoid perioperative anemia, itself identified as an independent risk factor in perioperative morbidity and mortality.[3,4] However, there exist consequential trade-offs between the risks and benefits of allogeneic blood transfusion versus anemia in terms of their effects on perioperative outcomes.[3,4]

Although the adverse effects of allogeneic blood transfusion on postoperative infection in the context of spine surgery have been demonstrated, the low power and uncontrolled potential

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confounds of many of these studies has limited the interpretation of their data. The aim of this systematic review is to evaluate the association between allogeneic transfusion and postoperative infection in spine surgery patients, as well as the many modifying risk factors. We sought to answer the following key questions: (1) Does allogeneic blood transfusion increased the risk of postoperative infection in patients undergoing spine surgery compared with no blood transfusion? (2) Are there any factors that modify the risk of infection associated with allogeneic blood transfusion?

Materials and Methods

Study Design: Systematic Review

Information Sources and Search. PubMed, Cochrane Central Register of Controlled Trials, and reference lists from included studies were searched from inception to April 20, 2017. Search strategy can be found in the Supplemental Online Material.

Eligibility Criteria

Inclusion criteria. (1) Adult patients receiving surgery for degenerative spine disease and (2) comparative studies comparing the risk of infection in those with allogeneic blood transfusion versus no blood transfusion.

Exclusion criteria. (1) More than or equal to 20% of patients who received spine surgery for trauma or cancer, (2) $\geq$20% of patients who received autologous blood instead of allogeneic blood, (3) outcomes other than infection, and (4) case series.

Data Identification and Extraction. Articles were selected for inclusion and data was extracted by 2 investigators (CF, JRD). Discrepancies were resolved through discussion. The following data items were recorded: study author, study design, study demographics (sample size, age, sex), data source, spine segment treated, timing of transfusion, covariates analyzed, odds ratio from both univariate and multivariate models comparing infection in those receiving blood transfusion versus no transfusion.

Outcomes. Surgical site infection, urinary tract infection, respiratory tract infection, sepsis.

Analysis and Synthesis of Results

Qualitative synthesis and meta-analysis. Because of the likelihood of confounding, the primary analysis used adjusted versus crude odds ratios. For meta-analysis, we performed a logarithmic transformation of the adjusted odds ratios and confidence intervals. The corresponding standard errors were then computed. Next the studies were pooled and weighted according to the inverse of their respective variances, which were derived from the standard errors. A random effects model was assumed. Final values were exponentiated back to and presented in their original scale. Calculations and figures were done with RevMan v. 5.2.

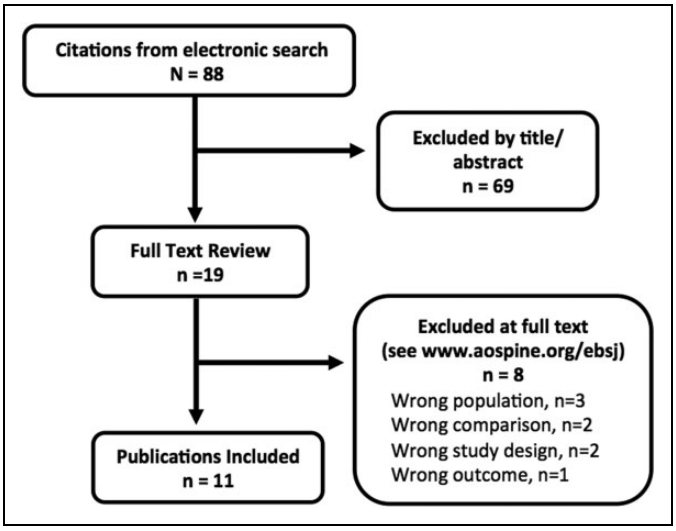

Figure 1. Study selection.

Results

Study Selection and Characteristics

We identified 19 of 88 studies as potentially meeting inclusion criteria. After full-text review of the 19 studies, 8 were excluded (wrong population, n = 3; wrong comparison, n=2; wrong study design, n = 2; and wrong outcome, n = 1) (Figure 1). Citations and a comprehensive list of reasons for exclusion can be found in the Supplemental Online Material. The remaining 11 met inclusion criteria and were retained. These studies involved 8428 patients who received a transfusion and 43 242 who did not. They are composed of 6 retrospective cohort studies[5-10] and 5 retrospective case-control studies.[11-15] All studies have moderately high or high risk of bias, class of evidence (CoE) III or IV (see Supplemental Online Material for CoE evaluation). Characteristics of the included studies are summarized in Table 1.

Does allogeneic blood transfusion increase the risk of postoperative infection in patients undergoing spine surgery compared with no blood transfusion?

Surgical Site Infection. With regard to surgical site infection (SSI), results from 10 low-quality studies are mixed; 3 studies report a significant association between allogeneic blood transfusion and infection,[7,8,10] 4 report no significant association,[12-15] 1 study describes an association within certain patient subgroups but not in others[5] and 2 do not report multivarariate analysis[6,11] (Table 2).

Urinary Tract Infection. Two low-quality studies[7,8] found a significant association between allogeneic transfusion and urinary tract infection (UTI), pooled odds ratio 2.4 (95% CI, 1.6-3.5) (Figure 2).

Respiratory Tract Infection. Two low quality studies[7,8] failed to find an association between allogeneic transfusion and

Table 1. Study Characteristics.

First Author (Year), Design	Population	Data Source	Timing of transfusion	Surgery	Infection outcomes	Covariates		Results, OR (95% CI)
Aoude (2016), retrospective cohort Level of evidence: III	N = 13 695 Age: 59.6 years (± 13.5) Male: 44% Transfusion N = 2407 No transfusion N = 11 288	American College of Surgeons National Surgical Quality Improvement Program (ACS-NSQIP) database 2010-2013	Timing: Intraoperative, and postoperative	Lumbar (n =13 170) and thoracic (n = 525) with or without interbody fusion Approach: anterior, posterior, and posterolateral	Superficial, deep, or organ/space SSI as defined by CDC F/U: ≤30 days	• Age • Gender • Race • BMI • Smoking • Diabetes • Dyspnea • COPD • CHF • Dialysis • Steroids • ASA class • Hypertension • In/outpatient	• Functional status prior surgery • Multilevel surgery • Operation time • Elective surgery • Return to operating room • Preoperative hematocrit • Preoperative platelet count • Preoperative WBC • Preoperative serum creatinine • Preoperative BUN • Preoperative serum sodium • Bleeding disease • Length of surgery	*SSI lumbar spine:* Deep infection aOR 2.44 (1.55-3.83) Superficial infection aOR 1.52 (1.03-2.26) *SSI thoracic spine:* Deep infection aOR 0.56 (0.11-3.01) Superficial infection aOR 0.94 (0.31-2.81)
Apisarnthanarak (2003), retrospective matched case-control Level of evidence: IV	N = 60 Age: 57.7 years (24-85) Male: 47% Cases: n = 13 Controls: n = 47	Community hospital (St Louis, Missouri) January 1, 1998 to June 30, 2000	Timing: Intraoperative and postoperative	Laminectomy, spinal fusion, or both Approach: unknown	Superficial, deep, or organ/space SSI as defined by CDC F/U: ≤30 days	• Age • Gender • Race • BMI • Malnutrition • Dural tear • C-arm • Propofol • Irrigation • Ambulation • Clotting agents • Corticosteroids • Surgery level • Diabetes • Smoking • Incontinence • Glucose level • ASA class • Tumor removal	• Skin preparation techniques • Hypothermia during surgery • Procedure type • Procedure duration • Instrumentation for fusion • Allograft/autograft • Glue to cement dural patch • Use of operating microscope • Drain use & type • Surgical personnel • Number/type of transfusions • No. days in ICU • Bathing/showering in hospital • Discharge to rehabilitation • Prophylactic antibiotics • Prophylactic antibiotics • Hospitalization duration • Underlying malignancy • Spinal cord compression • Previous spinal surgery	*SSI:* OR[a] = 1.33 (0.32-5.55)
Fisahn (2017), retrospective cohort Level of evidence: III	N = 56 Age: 65.4 years (±12.4) Male: 35.7% No transfusion n = 20 Transfusion n = 36	Swedish Medical Center, Seattle, WA 2012-2015	Timing: Perioperative	Spine fusion of at least 8 levels Approach: posterior	Any infection (UTI, wound infection, pneumonia, *Clostridium difficile*, sepsis) F/U: ≤90 days	• Age • Smoker • Gender • BMI • Diabetes • Steroid use • Level of surgery • Drain usage	• Vancomycin powder (2 mg topical application) • Intraoperative shock • Other interventions/ outcomes • Starting/ending hematocrit • Estimated blood loss • Transfused units • Length of surgery	*SSI:* OR, aOR not calculable *Any infection:* OR = 5.09 (0.93-50.85) aOR = 3.5 (0.58-20.9)

(continued)

Table 1. (continued)

First Author (Year), Design	Population	Data Source	Timing of transfusion	Surgery	Infection outcomes	Covariates		Results, OR (95% CI)
Janssen (2015), retrospective cohort Level of evidence: III	N = 3721 Age: 55 years (16) Male: 53% Transfusion n = 293 No transfusion n = 3428	Massachusetts General Hospital Research Patient Data Registry 2001-2013	Timing: 7 days prior up to 30 days after operation	Laminectomy and/or arthrodesis of lumbar spine Approach: anterior, posterior	• SSI • RTI • Endocarditis • Meningitis • UTI • Central venous line F/U: ≤90 days	• Age • Gender • Race • BMI • Comorbidities • Tobacco use • Obesity • CHF	• Hemoglobin • Operative treatment • Renal disease • Duration of surgery • Single vs multilevel • Anterior/posterior approach • Year of surgery • Chronic pulmonary disease • Chronic diabetes	*SSI:* aOR 2.6 (1.3-5.3) *Any infection:* aOR 2.6 (1.7-3.9) *UTI:* aOR 2.2 (1.3-3.9) *Pneumonia* aOR 2.3 (0.96-5.3)
Kato (2016),[b] retrospective propensity-matched cohort study Level of evidence: III	N = 8550 Age ≥70 years: 70.4% Male: 63% No transfusion n = 4275 Transfusion n = 4275	Japanese Diagnosis Procedure Combination database (includes 82 academic hospitals) July 1 to December 31 each year 2007-2010 January 1, 2011 to March 31, 2012	Timing: Perioperative	Laminectomy, laminoplasty and/or fusion surgery of the lumbar spine Approach: unknown	• SSI • RTI • UTI • Sepsis • F/U: NR	• Gender • Age • Diagnoses • Length of stay • Diabetes • Hemodialysis • Cell saver use	• Volume transfused • Cardiovascular disease • Cerebrovascular disease • Decompression or fusion • Duration of anesthesia • Type of hospital	*SSI:* OR 2.87 (2.47-3.33) aOR 1.88 (1.40-2.50) *RTI:* OR 2.55 (1.94-3.32) aOR 1.12 (0.74-1.69) *UTI:* OR 3.07 (2.32-4.02) aOR 2.52 (1.50-4.24) **Sepsis:** OR 0.87 (0.79-0.91) aOR 3.01 (0.97-9.33)
Maragakis (2009), retrospective case-control Level of evidence: IV	N = 208 Age: 55 years (19-88) Male: 49% Cases: n = 104 Controls: n = 104	Johns Hopkins Hospital 2001-2004	Timing: preoperative, intraoperative, and postoperative	Laminectomy and/or fusion of lumbar spine Approach: various	Superficial, deep, or organ/space SSI as defined by CDC F/U: ≤30 days	• Age • Gender • Smoking • Diabetes • Cardiac disease • Obesity • ASA score • Karnofsky score • FiO_2 <50% • Dural tear • Instrumentation • CSF leak	• Emergent/urgent surgery • Razor shaving before surgery • Antimicrobial prophylaxis • Intraoperative nitrous oxide • Perioperative glucose >126 mg/dL • Lowest intraoperative temperature • Intraoperative infusion rate • Procedure duration • Lumbar-sacral level of surgery • Posterior surgical approach • Previous spinal surgery • European descent	*SSI:* OR: 6.7 (3.6-13.0) aOR for covariates: NS
Olsen (2003), retrospective case-control Level of evidence: IV	N = 219 Male: 59.4% Cases: n = 41 Controls: n = 178	Barnes-Jewish Hospital, Washington University School of Medicine, 1996-1999	Timing: Intraoperative and postoperative	Cervical, lumbar, thoracic, lumbosacral, multiple level laminectomy and/or fusion Approach: anterior, posterior, and other	Superficial, deep, or organ/space SSI as defined by CDC F/U: NS	• Age • Gender • Race • BMI • Smoking • Diabetes • Prior spinal op • Incontinence • ASA class • Steroids • Paralysis • Skin antisepsis • Level of op	• Spinal cord compression • Chemotherapy or irradiation • Recent injury/trauma • Preoperative hospitalization • Razor shaving vs clipping • Prophylactic antibiotics • Laminectomy vs fusion • Allograft vs autograft • Instrumentation • Resection of tumor	*SSI:* Unadjusted OR: 5.6 (2.6-12.2) aOR for covariates: NR

(continued)

Table 1. (continued)

First Author (Year), Design	Population	Data Source	Timing of transfusion	Surgery	Infection outcomes	Covariates	Results, OR (95% CI)
						• Microscope • Dural tear • Other current ops • Intraoperative hypothermia • Postoperative CSF leak • Duration of procedure • Intraoperative drugs	
Olsen (2008), retrospective case-control Level of evidence: IV	N = 273[c] Age: 52.4 years (15.2-94.4) Male: 47.6% Cases: n = 36 Controls: n = 192	Barnes-Jewish Hospital, Washington University School of Medicine, 1998-2002	Timing: Perioperative	Laminectomy, discectomy and/or arthrodesis of the spine Approach: unknown	Superficial, deep, or organ/space SSI as defined by CDC F/U: 1 year	• BMI • Diabetes • Diagnosis • ASA class • IV steroids • Cervical level • Drains • Posterior approach • Prophylactic antibiotics • Number of vertebral levels • Duration of procedure • Nerve root compression • Resident surgeons • Postoperative incontinence • Pre- or postoperative incontinence	*SSI:* Unadjusted OR: 3.4 (1.6-7.4) aOR for covariates: NR
Triulzi (1992), retrospective cohort Level of evidence: III	N = 49[d] Age 32.2 years Male: 46% Transfusion n = 24 No transfusion n = 25	Department of Pathology and Laboratory Medicine, Transfusion Medicine and Laboratory Hematology Units, University of Rochester Medical Center November 1988 to May 1990	Timing: Unknown	Spinal fusion procedures Approach: anterior, posterior	In-hospital infections F/U: in-hospital	• Age • Gender • Diagnosis • Blood loss • Surgeon • WBC count • WBC differential • Culture results • Length of hospitalization • Kind and amount of transfusions • Kind and amount of blood loss • Transfusion history • Days of fever $\geq 38^{\circ}$ c • Days on antibiotics • Duration of surgery • Surgical procedure • Admission Hcts • Postoperative day 7 Hcts	*In-hospital:* Results, OR (95% CIs) *Infections:* OR[e] 6.32 (0.61-310.8)
Veeravegu (2009), retrospective cohort Level of evidence: III	N = 24 774 Age <60 years: 66% Male: 95% No transfusion n = 23 629 Transfusion n = 1143	Veterans Affairs' NSQIP database 1997-2006	Timing: Intraoperative	Spinal decompression, fusion, or instrumentation Approach: unknown	Superficial and deep wound infection F/U: $\leq$30 days	• Age • Gender • Race • Weight loss • Diabetes • Alcohol use • Hct • WBC • Creatine • Smoker • Fusion or instrumentation • Operative duration • Disseminated cancer • ASA class • Preoperative sepsis • Emergency • Bleeding disorder • Steroid use • Functional status	*SSI:* OR = 2.13 (1.62-2.75) aOR = 1.42 (1.07-1.90)
Woods (2013), retrospective matched case-control Level of evidence: IV	N = 147 Age: 61 years (23-83) Male: 49% Cases: n = 56 Controls: n = 91	University of Pittsburgh Medical Center 2005-2009	Timing: Intraoperative and postoperative	Lumbar laminectomy and instrumented fusion (88%) Approach: anterior and posterior	Superficial, deep, or organ/space SSI as defined by CDC (spinal or iliac crest) F/U: $\leq$30 days	• Age • Gender • BMI • Smoking • Diabetes • IBCG • Preoperative hemoglobin • Volume of intraoperative blood loss • Revision procedure • BMP-2 and allograft • Charlson Comorbidity • Length of surgery	*SSI:* aOR 1.25 (0.55-2.97) Transfusion volume associated with SSI aOR 4.00 (1.96-8.15)

Abbreviations: aOR, adjusted odds ratio; ASA, American Society of Anesthesiologists; BMI, body mass index; BUN, blood urea nitrogen; CHF, congestive heart failure; COPD, chronic obstructive pulmonary disease; CSF, cerebrospinal fluid; FiO_2, fraction of inspired oxygen; Hcts, hematocrit; NR, not reported; OR, unadjusted or crude odds ratio; RTI, respiratory tract infection; SSI, surgical site infection; CDC, Centers for Disease Control and Prevention; WBC, white blood cell.

[a] Calculated from Apisarnthanarak et al,[11] table 2.

[b] Demographic information and unadjusted OR based on cohort of 79 361 patients without transfusion and 5,289 with transfusion. aOR based on propensity matched cohort

[c] Demographic information based on cohort that included a group receiving autologous blood transfusion. However, the ORs for Olsen 2008 are for allogeneic blood only (cases: n = 15, controls: n = 33) compared with no transfusion (cases: n = 21, controls: n = 159).

[d] Population characteristics given for 102 patients comprised of 3 arms; allogeneic arm (n=24), autologous blood (n=60) and no transfusion (n=25). The total, N=109, represents the number of surgeries as 7 patients had a subsequent operation.

[e] Calculated from Triulzi et al,[9] figure 1.

Table 2. Association (Crude and Adjusted Odds Ratio and 95% Confidence Interval) Between Allogeneic Blood Transfusion and Infection in Spine Surgery (*P* Value for Adjusted Odds Ratio Only).

First Author	Transfusion Timing	Surgery	Infection	Crude OR (95% CI)	Adjusted OR (95% CI)	*P*
Janssen 2015	Periop	L +/−	SSI	—	2.6 (1.3-5.3)	.007
Kato 2016	Periop	L +/−	SSI	2.9 (2.5-3.3)	1.9 (1.4-2.5)	<.001
Fisahn 2017	Periop	Sp +	SSI	Not calculable	Not calculable	
Woods 2013	Intra, postop	L +/−	SSI	—	1.3 (0.5-2.9)	.37
Olsen 08	Periop	Sp +/−	SSI	3.4 (1.6-7.3)	ns	>.05
Apisarnthanarak 2003	Intra, postop	Sp +/−	SSI	1.3 (0.3-5.5)	—	
Maragakis 2009	Periop	Sp +/−	SSI	6.7 (3.5-12.7)	ns	>.05
Olsen 2003	Intra, postop	C, L, T, LS +/−	SSI	5.6 (2.6-12.1)	ns	>.05
Veeravegu 2009	Intraop	Sp +/−	SSI	2.1 (1.6-2.8)	1.4 (1.1-1.9)	<.05
Aoude 2016						
Deep	Intra, postop	L +/−	SSI	2.8 (1.8-4.4)	2.4 (1.6-3.8)	<.001
Superficial	Intra, postop	L +/−	SSI	1.5 (1.0-2.3)	1.5 (1.03-2.3)	<.037
Deep	Intra, postop	T +/−	SSI	0.5 (0.1-2.7)	0.6 (0.1-3.0)	.495
Superficial	Intra, postop	T +/−	SSI	1.2 (0.4-3.5)	0.9 (0.3-2.8)	.914
Janssen 2015	Periop	L +/−	Any	—	2.6 (1.7-3.9)	<.001
Fisahn 2017	Periop	Sp +	Any	5.1 (0.9-50.1)	3.5 (0.6-20.9)	.172
Janssen 2015	Periop	L +/−	UTI	—	2.2 (1.3-3.8)	.004
Kato 2016	Periop	L +/−	UTI	—	2.5 (1.5-4.2)	<.001
Triulzi 1992	Unknown	Sp +	In hospital	6.3 (0.6-310)	—	

Abbreviations: C, cervical; L, lumbar; LS, lumbosacral; ns, not significant (adjusted OR not reported); OR, odds ratio; T, thoracic; Sp, spinal; SSI, surgical site infection; UTI, urinary tract infection. +, with fusion; +/−, with or without fusion.

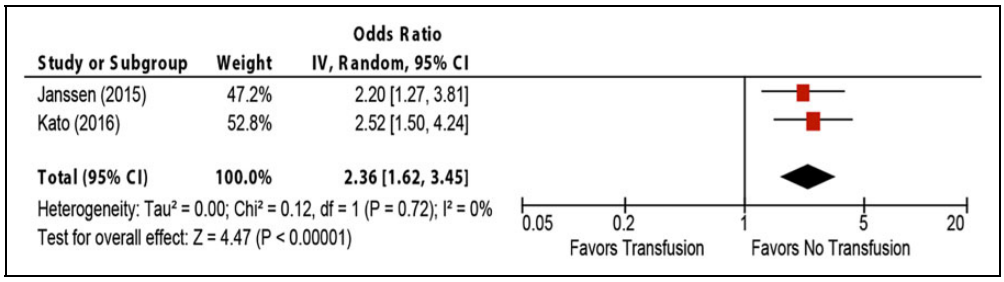

Figure 2. The association of allogeneic blood transfusion and urinary tract infection in spine surgery.

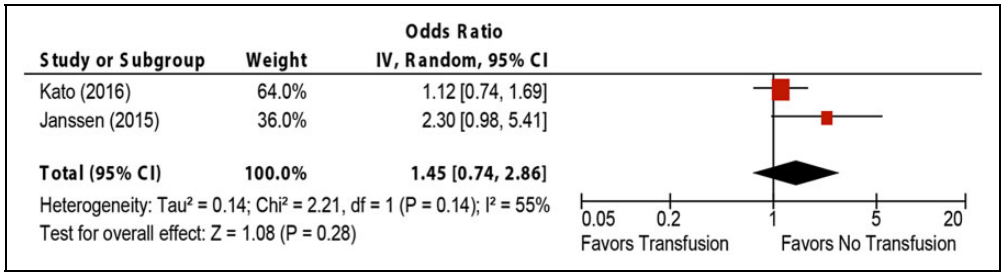

Figure 3. The association of allogeneic blood transfusion and respiratory tract infection.

respiratory tract infection (RTI), pooled odds ratio 1.5 (95% CI, 1.7-2.9) (Figure 3).

Any Infection. Two low-quality studies assessed the association between allogeneic blood transfusion and any infection. Any infection is defined as an SSI, RTI, UTI, sepsis, and *Clostridium difficile* in one study by Fisahn et al,[6] and SSI, RTI, UTI, endocarditis, meningitis, and central venous line infection in a second study by Janssen et al.[7] Pooling the studies result in a significant association, pooled odds ratio 2.6 (95% CI, 1.8-4.0) (Figure 4).

In-Hospital Infection. One small low-quality study did not find an association between allogeneic blood transfusion and in-hospital infection, crude odds ratio, 6.3 (95% CI, 0.6-310).

Are There Any Factors That Modify the Risk of Infection Associated With Allogeneic Blood Transfusion?

One study stratified SSI results by spine segment, lumbar and thoracic. There was no statistical difference between the

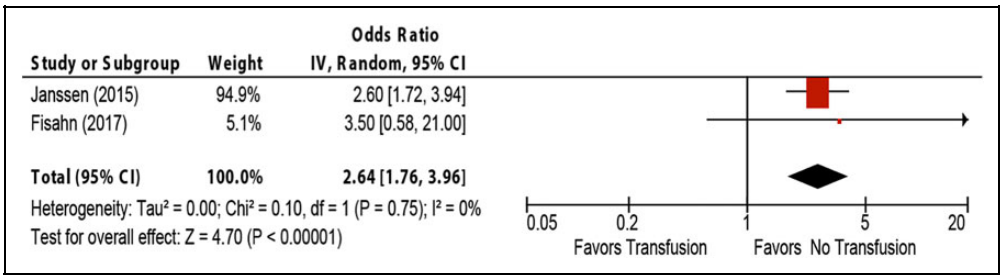

Figure 4. The association of allogeneic blood transfusion and any infection in spine surgery.

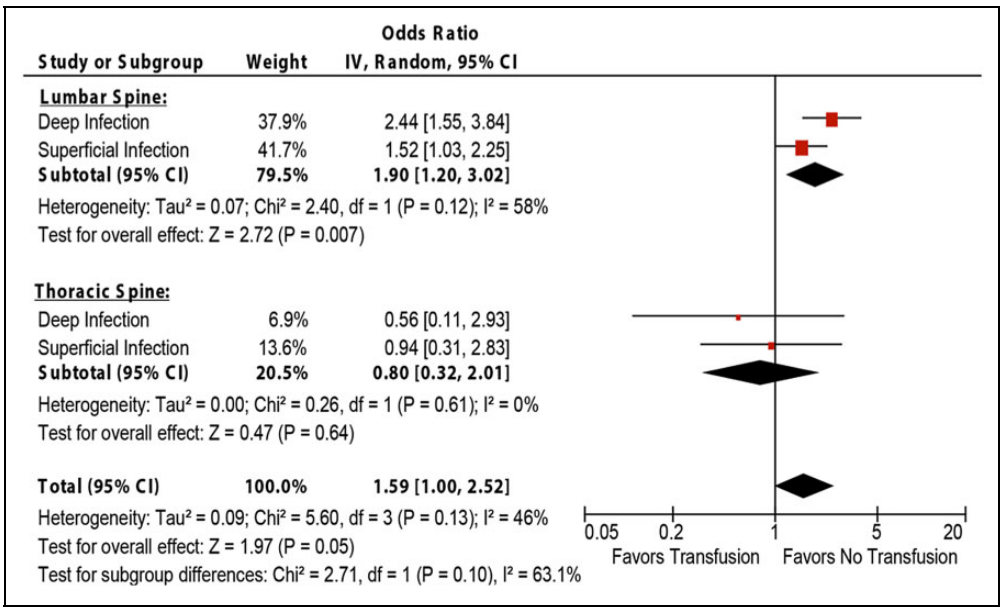

Figure 5. Subgroup analysis comparing the association of allogeneic blood transfusion and surgical site infection (SSI) between spine surgery of the lumbar and thoracic spines.

subgroups, $P = .10$, possibly due to the small sample size and variability in the thoracic spine (Figure 5). Stratifying the results of all studies reporting SSI by spinal segment reveals that allogeneic blood transfusion is significantly associated with SSI in 3 of 4 studies in surgeries restricted to the lumbar spine. This is in contrast to only 1 of 5 studies reporting a significant association in studies of only the thoracic spine or in studies that likely include several segments (Table 3). The pattern is similar for UTI and any infection.

Evidence Summary (Table 4)

- Mixed results as to whether allogeneic blood transfusion is associated with SSI in spine surgery patients, strength of evidence *very low*.
- Allogeneic blood transfusion is associated with UTI; pooled odds ratio 2.4 (95% CI, 1.6-3.5), strength of evidence *low*.
- No association between allogeneic blood transfusion and RTI; pooled odds ratio 1.5 (95% CI, 0.7-2.9), strength of evidence *very low*.
- Allogeneic blood transfusion is associated with any infection; pooled odds ratio 2.6 (95% CI, 1.8-4.0), strength of evidence *very low*.
- Allogeneic blood transfusion was not significantly associated with SSI in a direct comparison when the surgery was performed in the lumbar spine compared with thoracic spine, strength of evidence *very low*.

Clinical Guidelines

American Association of Blood Banks' (AABB) recommendations[16]:

- Recommendation 1: The AABB recommends a restrictive red blood cell (RBC) transfusion threshold in which the transfusion is not indicated until the hemoglobin level is 7 g/dL for hospitalized adult patients who are hemodynamically stable, including critically ill patients, rather than a liberal threshold when the hemoglobin level is 10 g/dL (strong recommendation, moderate quality evidence). For patients undergoing orthopedic surgery or cardiac surgery and those with preexisting

Table 3. Association (Adjusted Odds Ratio and 95% Confidence Interval) Between Allogeneic Blood Transfusion and Infection in Spine Surgery Stratified by Surgery Segment.

First Author	Surgery Segment	Adjusted OR (95% CI)	*P*
SSI			
Aoude 2016			
Deep	Lumbar only	2.4 (1.6-3.8)	<.001
Superficial	Lumbar only	1.5 (1.03-2.3)	<.037
Janssen 2016	Lumbar only	2.6 (1.3 to 5.3)	.007
Kato 2016	Lumbar only	1.9 (1.4-2.5)	<.001
Woods 2013	Lumbar only	1.3 (0.5-2.9)	.37
Aoude 2016			
Deep	Thoracic only	0.6 (0.1-3.0)	.495
Superficial	Thoracic only	0.9 (0.3-2.8)	.914
Olsen 2008	Spinal	Nonsignificant	>.05
Maragakis 2009	Spinal	Nonsignificant	>.05
Olsen 2003	Spinal	Nonsignificant	>.05
Fisahn 2017	Spinal	Not calculable	–
Veeravegu 2009	Spinal	1.4 (1.1-1.9)	<.05
UTI			
Janssen 2015	Lumbar only	2.2 (1.3-3.8)	.004
Kato 2016	Lumbar only	2.5 (1.5-4.2)	<.001
RTI			
Janssen 2015	Lumbar only	2.3 (0.96-5.3)	>.05
Kato 2016	Lumbar only	1.1 (0.74-1.7)	>.05
Any infection			
Janssen 2015	Lumbar only	2.6 (1.7-3.9)	<.001
Fisahn 2017	Spinal	3.5 (0.6-20.9)	.172

cardiovascular disease, the AABB recommends a restrictive RBC transfusion threshold (hemoglobin level of 8 g/dL; strong recommendation, moderate quality evidence). The restrictive hemoglobin transfusion threshold of 7 g/dL is likely comparable to 8 g/dL, but randomized controlled trial (RCT) evidence is not available for all patient categories. These recommendations apply to all but the following conditions for which the evidence is insufficient for any recommendation: acute coronary syndrome, severe thrombocytopenia (patients treated for hematological or oncological disorders who at risk of bleeding), and chronic transfusion–dependent anemia.

- Recommendation 2: The AABB recommends that patients, including neonates, should receive RBC units selected at any point within their licensed dating period (standard issue) rather than limiting patients to transfusion of only fresh (storage length: <10 days) RBC units (strong recommendation, moderate quality evidence).

Discussion

We herein conducted a systematic review examining (*a*) whether allogeneic blood transfusion increases the risk of postoperative infection compared with no blood transfusion and (*b*) whether there are any factors that modify the risk of infection associated with allogeneic blood transfusion.

Addressing the first question, a body of very low strength evidence showed mixed results for an association between allogeneic blood transfusion and surgical site infection. This may be a result of confounding factors that are inherent to these different subgroups of patients, factors controlled for in some studies but not others. For example, 3 studies reporting no significant association controlled for American Society of Anesthesiologists (ASA) class[12-14] while 2 studies reporting a significant association did not.[7,8] The posterior approach has been shown to be a risk factor for postoperative infection.[17] Three studies in our review adjusted for approach[7,12,14] whereas others did not.[5,8,10,13,15]

Two low-strength studies found a significant association between allogeneic blood transfusion and UTI, yet no association was found between allogeneic blood transfusion and RTI.[7,8] The risk of any infection was significantly associated with allogeneic blood transfusions, but again with a very low strength of evidence.[6,7] The significant association between all infections and allogeneic blood transfusions found by Fisahn et al[6] was in a study population of only 56 patients, the smallest population to yield significant results in our series. When examining individual infection risks (eg, SSI, UTI) the association lost significance. However, the underlying assumption of the current clinical question is that allogeneic blood increases infection risk because of its systemic immunomodulatory effects. It is therefore appropriate to be pooling all postoperative infections to examine for an association with perioperative allogeneic transfusion.

Addressing the second question, a stratification of SSI data by spine segment, lumbar and thoracic, found allogeneic blood transfusion to be significantly associated with SSI in 3 of 4 studies in surgeries restricted to the lumbar spine. The increased potential for infection in the lumbar region may be due to its proximity to the perineal region, a significant potential source of infection.

Limitations

Studies included consisted only of low-quality retrospective studies with high or moderately high risk of bias. These studies are subject to confounding variables. In this review, every study reporting both univariate and multivariate analyses had important confounds as demonstrated by the large change in the odds ratio between the 2 analyses. Because of the retrospective designs, not all studies collected the same prognostic characteristics and potentially important information was omitted, such as volume of blood transfused. Prospective studies are needed, which identify and control for all important potential confounders for infection.

We estimate that 2400 patients will be needed in a prospective observational study to establish the relationship between autologous blood transfusions and the risk of SSI assuming an SSI risk of 2% in patients without transfusion, a power of 80%, and an effect size of 2.0.

Table 4. Evidence Summary Table.

Outcome	Follow-up	Studies N	Serious Risk of Bias	Serious Inconsistency	Serious Indirectness	Serious Imprecision	Conclusions	Quality
Key Question 1. Does allogeneic blood transfusion increased the risk of postoperative infection in patients undergoing spine surgery compared with no blood transfusion?								
Surgical site infection	Variable, mostly within 30 to 90 days	10 observational studies[5-8,10-15] N = 51 430	Yes (−1)	Yes (−1)	No	No	Mixed results, pooled ORs not calculable	Very low
Urinary tract infection	Variable, ≤ 90 days and unreported	2 observational studies[5,6] N = 12 271	No	No	No	No	Pooled aOR: 2.4 (95% CI, 1.6-3.5)	Low
Respiratory tract infection	Variable, ≤90 days and unreported	2 observational studies[5,6] N = 12 271	No	Yes (−1)	No	No	Pooled aOR: 1.5 (95% CI, 0.7-2.9)	Very low
Any infection	≤ 90 days	2 observational studies[5,10] N = 3 777	Yes (-1)	Yes (−1)	No	No	Pooled aOR: 2.6 (95% CI, 1.8-4.0)	Very low

Subgroup	Outcome	Follow-up	Studies N	Serious Risk of Bias	Serious Inconsistency	Serious Indirectness	Serious Imprecision	Conclusions	Quality
Key Question 2, Are there any factors that modify the risk of infection?									
Spine segment, lumbar vs thoracic or spinal	Surgical site infection	Variable, mostly within 30 to 90 days	10 observational studies[5-8,10-15] N = 51 430	Yes (−1)	No	No	No	No significant association in 1 study stratifying on spine segment Lumbar—aOR: 1.9 (95% CI, 1.2-3.0) Thoracic—aOR (95% CI 0.3-2.0) Test for heterogeneity across subgroups for all other studies could not be performed	Very low

Conclusion

This systematic review failed to find a consistent association between allogeneic transfusion and SSI in patients undergoing spinal surgery. However, the studies were all retrospective with a high or moderately high risk of bias. To understand the nature of the association between allogeneic blood transfusion and subsequent infection in spine surgery, appropriately designed and controlled prospective studies of sufficient power (n = 2400) are required.

Declaration of Conflicting Interests

The author(s) declared no potential conflicts of interest with respect to the research, authorship, and/or publication of this article.

Funding

The author(s) received no financial support for the research, authorship, and/or publication of this article.

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Supplemental Material

The supplemental material is available in the online version of the article.

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