G16: Does allogeneic blood transfusion increase the risk of postoperative infections in patients undergoing major orthopedic surgery?

Fatih Yıldız, Mustafa Şenyurt, Antony Palmer, Waleed A Al-Saadan, Nathanael Heckmann, Gabriele Tucci, Udo E Anyaehie, Jorge Negrete Corona, Kerem Başarır

Response/Recommendation:

Yes. Allogeneic blood transfusion is associated with an increased risk of postoperative infections, including surgical site infection (SSI)/periprosthetic joint infection (PJI) and systemic infections in patients undergoing major orthopedic surgery.

Level of Evidence: Moderate

Delegate Vote:

Rationale:

The risk of postoperative infections after major orthopedic surgeries is influenced by various factors, including patient-related, surgeon-related and perioperative factors [1]. Allogeneic blood transfusion (ABT) has been associated with potential adverse effects on the recipient's immune system, termed transfusion-related immunomodulation (TRIM) [2]. TRIM is thought to involve both cellular and humoral immune suppression, which could potentially increase the recipient's susceptibility to infection. For this reason, in recent years, patient blood management strategies, such as preoperative optimization of anemia, minimizing intraoperative blood loss, adopting restrictive transfusion triggers.

Conflicting results have been reported regarding the association between ABT and infection [3, 4]. Some studies found an increased risk of infection with ABT [5, 6], while others have not [7–9]. The International Consensus Meeting in 2018 recognized an increased risk of surgical site infection (SSI) associated with ABT compared to no transfusion or autologous transfusion, but concluded that there is no data to support withholding ABT in patients with symptomatic anemia as a strategy to prevent SSIs [10].

The relationship between ABT and infection risk in spinal surgery has been a subject of considerable investigation, yielding mixed results. Many studies have identified ABT as a significant risk factor for postoperative infection after instrumented spinal fusion [11–16]. Woods et al. found a significant association between the volume of ABT and SSI in lumbar spine surgery[17], and Zhang et al. further identified a dose-response relationship with an inflection point of 3 units [18]. These findings underscore the complexity of the relationship between ABT and infection risk in spinal surgery, highlighting the need to consider potential confounding factors such as patient comorbidities and surgical complexity when interpreting the study results [19].

In patients undergoing joint replacement surgery, the relationship between ABT and infection has been extensively studied, with results indicating that ABT may be associated with an increased risk of infection [6]. A meta-analysis by Kim et al. showed a mean risk ratio for infection after ABT of 1.71 (range, 1.23-2.40) in patients undergoing total hip or knee arthroplasty [20]. Berríos-Torres et al. conducted a meta-analysis for the Centers for Disease Control and Prevention (CDC) guidelines for the prevention of SSI, which examined the association between allogeneic and autologous blood transfusions and the risk of infection [21]. The study found that ABT was associated with increased odds of infection compared to no transfusion (odds ratio [OR]: 1.96, 95% confidence interval [CI] 1.46 to 2.63, $p < 0.01$, I2 = 0).

For the current systematic review and meta-analysis, we searched Pubmed, Embase and Scopus databases. Thirty-four studies were included after reviewing 497 articles by at least two independent reviewers. Fourteen of those studies investigated the relation between ABT and SSI or periprosthetic joint infection (PJI). The remaining 20 studies have results of the mixed data including SSI/PJI and systemic infections such as urinary tract infection and lower respiratory tract infection. Meta-analysis of those 34 articles showed that ABT is associated with an increased risk of infection compared to non-ABT (risk ratio [RR] = 1.94, 95% confidence interval [CI]: 1.59 to 2.37, $P < 0.01$, Fig. 1) [2, 4–6, 8, 9, 11–16, 19, 22–42]. Both arthroplasty and spine surgery, showed a trend of increased infection risk with ABT [2, 4–6, 8, 9, 11–16, 19, 22–42]. The analysis was further stratified by subgroups with different transfusion exposure, with one group having received no previous transfusion, and the other having received autologous blood. ABT was associated with a higher risk of infection in both non-transfused and allogenic non-exposed subgroups (Fig. 2) [2, 4–6, 8, 9, 11–16, 19, 22–42]. Subgroup analysis examining isolated SSI/PJI (RR = 2.23, 95% CI: 1.66 to 2.99, $P < 0.01$) and general infection (RR = 1.83, 95% CI: 1.41 to 2.36, $P < 0.01$) revealed a consistent association between ABT and increased risk (Fig.3). A separate meta-analysis evaluating the mean difference in the number of allogeneic blood units transfused between patients with and without infection revealed that patients with infection received a significantly higher number of units (mean difference [MD] = 1.02, 95% CI: 0.58–1.45, $I^2 = 64\%$, Fig. 4) [17, 18, 43–45]. This finding further supports the association between ABT and an increased risk of infection.

In conclusion, the present systematic review and meta-analysis demonstrated a significant association between ABT and increased risks of SSI/PJI and systemic infections in the context of major orthopedic surgery. This observation remained consistent across various subgroups and surgical categories, including arthroplasty and spine surgery. Patients with infection received a higher number of allogeneic blood units, suggesting a possible dose response relationship.

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Figures

Fig.1:

Study or Subgroup	with allo. Events	with allo. Total	without allo. Events	without allo. Total	Weight	Risk Ratio IV, Random, 95% CI
Subgroup = Artroplasty						
Basora et al.2010 [126]	38	575	28	335	3.2%	0.79 [0.49; 1.26]
Jiang et al.2024 [139]	29	10057	40	10057	3.1%	0.72 [0.45; 1.17]
Maempel et al.2016 [144]	10	262	21	2022	2.5%	3.68 [1.75; 7.72]
Pedersen et al.2009 [135]	41	9063	22	18974	3.1%	3.90 [2.33; 6.55]
Poultsides et al.2018 [26]	36	4110	81	13849	3.3%	1.50 [1.01; 2.21]
Taneja et al.2019 [115]	82	3098	372	24798	3.6%	1.76 [1.39; 2.23]
Triantafyllopoulos et al.2018 [44]	37	4558	117	31936	3.4%	2.22 [1.53; 3.20]
WeberEWG et al.2005 [186]	10	92	8	352	2.2%	4.78 [1.94; 11.77]
Innerhofer et al.2005 [238]	13	122	8	186	2.3%	2.48 [1.06; 5.80]
Drosos et al.2012 [82]	13	71	14	177	2.6%	2.31 [1.15; 4.68]
Vamvakas et al.1995 [204]	10	108	2	312	1.2%	14.44 [3.22; 64.89]
Shander et al.2009 [179]	6	162	17	872	2.1%	1.90 [0.76; 4.75]
Newman et al.2014 [182]	14	836	18	2516	2.6%	2.34 [1.17; 4.69]
Rosencher et al.2003 [224]	146	1369	212	2455	3.7%	1.23 [1.01; 1.51]
Friedman et al.2014 [52]	392	5864	646	8215	3.8%	0.85 [0.75; 0.96]
Bierbaum et al.1999 [183]	105	1519	293	7963	3.7%	1.88 [1.51; 2.33]
Total (95% CI)		41866		125019	46.4%	1.87 [1.38; 2.53]
Heterogeneity: $Tau^2 = 0.2932$; $Chi^2 = 134.37$, df = 15 ($P < 0.01$); $I^2 = 89\%$						
Subgroup = Spine						
Carson et al.1999 [215]	286	5524	151	4074	3.7%	1.40 [1.15; 1.69]
Eisler et al.2022 [21]	150	4098	250	15061	3.7%	2.21 [1.81; 2.69]
Elsamadicy et al.2017 [388]	19	60	24	100	3.1%	1.32 [0.79; 2.20]
Fisahn et al.2017 [31]	13	36	2	20	1.4%	3.61 [0.90; 14.42]
Haase et al.2023 [75]	21	139	9	227	2.5%	3.81 [1.80; 8.08]
Johnston et al.2006 [137]	90	1068	160	2503	3.6%	1.32 [1.03; 1.69]
Kato et al.2016 [88]	385	5289	1971	79361	3.8%	2.93 [2.64; 3.26]
Kurra et al.2022 [100]	13	197	3	92	1.6%	2.02 [0.59; 6.93]
O'Malley et al.2021 [67]	142	1625	258	6064	3.7%	2.05 [1.69; 2.50]
PaulinoPereira et al.2016 [153]	178	774	94	492	3.7%	1.20 [0.96; 1.50]
Shen et al.2014 [123]	12	39	5	63	2.0%	3.88 [1.48; 10.16]
Zaw et al.2017 [30]	38	133	66	114	3.5%	0.49 [0.36; 0.67]
Falsetto et al.2022 [39]	161	1992	112	1992	3.6%	1.44 [1.14; 1.81]
Johnson et al.2017 [37]	14	603	2	360	1.2%	4.18 [0.96; 18.28]
Janssen et al. 2015 [23]	62	293	170	3428	3.6%	4.27 [3.27; 5.56]
Triulzi et al.1992 [200]	12	24	14	85	2.8%	3.04 [1.63; 5.67]
Innerhofer et al.1999 [167]	26	197	8	188	2.5%	3.10 [1.44; 6.68]
Kim et al.2022 [80]	474	77258	293	116778	3.8%	2.45 [2.11; 2.83]
Total (95% CI)		99349		231002	53.6%	2.01 [1.53; 2.65]
Heterogeneity: $Tau^2 = 0.2765$; $Chi^2 = 229.21$, df = 17 ($P < 0.01$); $I^2 = 93\%$						
Total (95% CI)		**141215**		**356021**	**100.0%**	**1.94 [1.59; 2.37]**
Heterogeneity: $Tau^2 = 0.2745$; $Chi^2 = 468.68$, df = 33 ($P < 0.01$); $I^2 = 93\%$						
Test for subgroup differences: $Chi^2 = 0.12$, df = 1 ($P = 0.72$)						

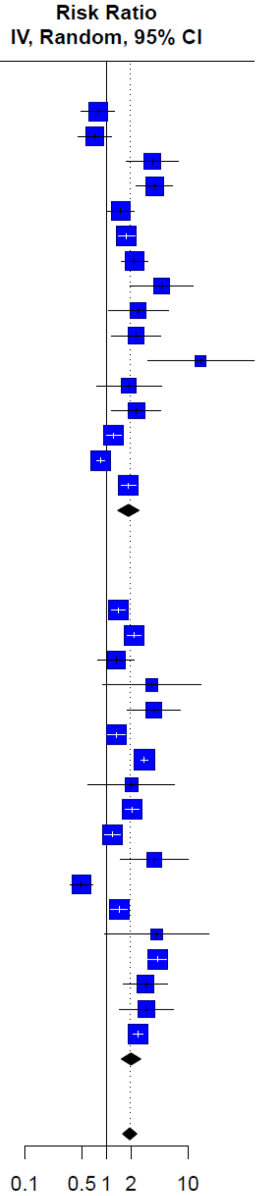

Fig. 2:

Study or Subgroup	with allo. Events	with allo. Total	without allo. Events	without allo. Total	Weight	Risk Ratio IV, Random, 95% CI
Subgroup = Event with none transfused						
Basora et al.2010 [126]	38	575	28	335	3.2%	0.79 [0.49; 1.26]
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Zaw et al.2017 [30]	38	133	66	114	3.5%	0.49 [0.36; 0.67]
Total (95% CI)		53685		216274	69.0%	1.88 [1.46; 2.44]
Heterogeneity: $Tau^2 = 0.3170$; $Chi^2 = 269.17$, df = 22 ($P < 0.01$); $I^2 = 92\%$						
Subgroup = Allogenic non−exposed						
Bierbaum et al.1999 [183]	105	1519	293	7963	3.7%	1.88 [1.51; 2.33]
Drosos et al.2012 [82]	13	71	14	177	2.6%	2.31 [1.15; 4.68]
Friedman et al.2014 [52]	392	5864	646	8215	3.8%	0.85 [0.75; 0.96]
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Vamvakas et al.1995 [204]	10	108	2	312	1.2%	14.44 [3.22; 64.89]
Total (95% CI)		87530		139747	31.0%	2.04 [1.48; 2.82]
Heterogeneity: $Tau^2 = 0.2077$; $Chi^2 = 155.88$, df = 10 ($P < 0.01$); $I^2 = 94\%$						
Total (95% CI)		**141215**		**356021**	**100.0%**	**1.94 [1.59; 2.37]**
Heterogeneity: $Tau^2 = 0.2745$; $Chi^2 = 468.68$, df = 33 ($P < 0.01$); $I^2 = 93\%$						
Test for subgroup differences: $Chi^2 = 0.15$, df = 1 ($P = 0.70$)						

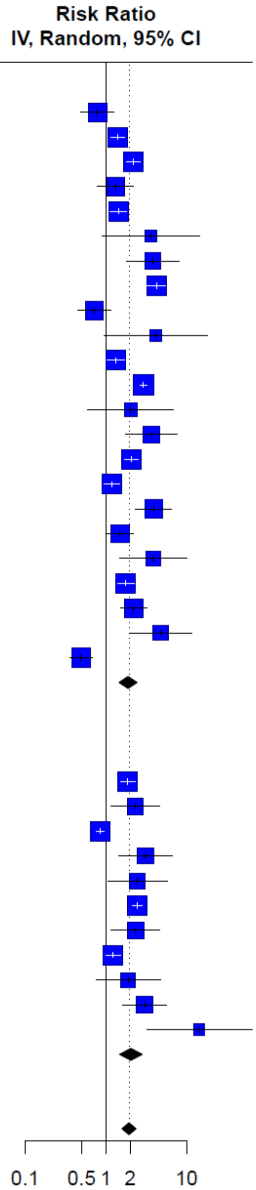

Fig. 3:

Study or Subgroup	with allo. Events	with allo. Total	without allo. Events	without allo. Total	Weight	Risk Ratio IV, Random, 95% CI
Subgroup = SSI/PJI						
Basora et al.2010 [126]	38	575	28	335	3.2%	0.79 [0.49; 1.26]
Drosos et al.2012 [82]	13	71	14	177	2.6%	2.31 [1.15; 4.68]
Haase et al.2023 [75]	21	139	9	227	2.5%	3.81 [1.80; 8.08]
Johnson et al.2017 [37]	14	603	2	360	1.2%	4.18 [0.96; 18.28]
Kim et al.2022 [80]	474	77258	293	116778	3.8%	2.45 [2.11; 2.83]
Kurra et al.2022 [100]	13	197	3	92	1.6%	2.02 [0.59; 6.93]
Maempel et al.2016 [144]	10	262	21	2022	2.5%	3.68 [1.75; 7.72]
Newman et al.2014 [182]	14	836	18	2516	2.6%	2.34 [1.17; 4.69]
Shen et al.2014 [123]	12	39	5	63	2.0%	3.88 [1.48; 10.16]
Taneja et al.2019 [115]	82	3098	372	24798	3.6%	1.76 [1.39; 2.23]
Triantafyllopoulos et al.2018 [44]	37	4558	117	31936	3.4%	2.22 [1.53; 3.20]
Total (95% CI)		87636		179304	29.0%	2.23 [1.66; 2.99]
Heterogeneity: $Tau^2 = 0.1405$; $Chi^2 = 29.65$, df = 10 ($P < 0.01$); $I^2 = 66\%$						
Subgroup = General Infection						
Bierbaum et al.1999 [183]	105	1519	293	7963	3.7%	1.88 [1.51; 2.33]
Carson et al.1999 [215]	286	5524	151	4074	3.7%	1.40 [1.15; 1.69]
Eisler et al.2022 [21]	150	4098	250	15061	3.7%	2.21 [1.81; 2.69]
Elsamadicy et al.2017 [388]	19	60	24	100	3.1%	1.32 [0.79; 2.20]
Falsetto et al.2022 [39]	161	1992	112	1992	3.6%	1.44 [1.14; 1.81]
Fisahn et al.2017 [31]	13	36	2	20	1.4%	3.61 [0.90; 14.42]
Friedman et al.2014 [52]	392	5864	646	8215	3.8%	0.85 [0.75; 0.96]
Innerhofer et al.1999 [167]	26	197	8	188	2.5%	3.10 [1.44; 6.68]
Innerhofer et al.2005 [238]	13	122	8	186	2.3%	2.48 [1.06; 5.80]
Janssen et al. 2015 [23]	62	293	170	3428	3.6%	4.27 [3.27; 5.56]
Jiang et al.2024 [139]	29	10057	40	10057	3.1%	0.72 [0.45; 1.17]
Johnston et al.2006 [137]	90	1068	160	2503	3.6%	1.32 [1.03; 1.69]
Kato et al.2016 [88]	385	5289	1971	79361	3.8%	2.93 [2.64; 3.26]
O'Malley et al.2021 [67]	142	1625	258	6064	3.7%	2.05 [1.69; 2.50]
PaulinoPereira et al.2016 [153]	178	774	94	492	3.7%	1.20 [0.96; 1.50]
Pedersen et al.2009 [135]	41	9063	22	18974	3.1%	3.90 [2.33; 6.55]
Poultsides et al.2018 [26]	36	4110	81	13849	3.3%	1.50 [1.01; 2.21]
Rosencher et al.2003 [224]	146	1369	212	2455	3.7%	1.23 [1.01; 1.51]
Shander et al.2009 [179]	6	162	17	872	2.1%	1.90 [0.76; 4.75]
Triulzi et al.1992 [200]	12	24	14	85	2.8%	3.04 [1.63; 5.67]
Vamvakas et al.1995 [204]	10	108	2	312	1.2%	14.44 [3.22; 64.89]
WeberEWG et al.2005 [186]	10	92	8	352	2.2%	4.78 [1.94; 11.77]
Zaw et al.2017 [30]	38	133	66	114	3.5%	0.49 [0.36; 0.67]
Total (95% CI)		53579		176717	71.0%	1.83 [1.41; 2.36]
Heterogeneity: $Tau^2 = 0.3227$; $Chi^2 = 418.52$, df = 22 ($P < 0.01$); $I^2 = 95\%$						
Total (95% CI)		**141215**		**356021**	**100.0%**	**1.94 [1.59; 2.37]**
Heterogeneity: $Tau^2 = 0.2745$; $Chi^2 = 468.68$, df = 33 ($P < 0.01$); $I^2 = 93\%$						
Test for subgroup differences: $Chi^2 = 1.00$, df = 1 ($P = 0.32$)						

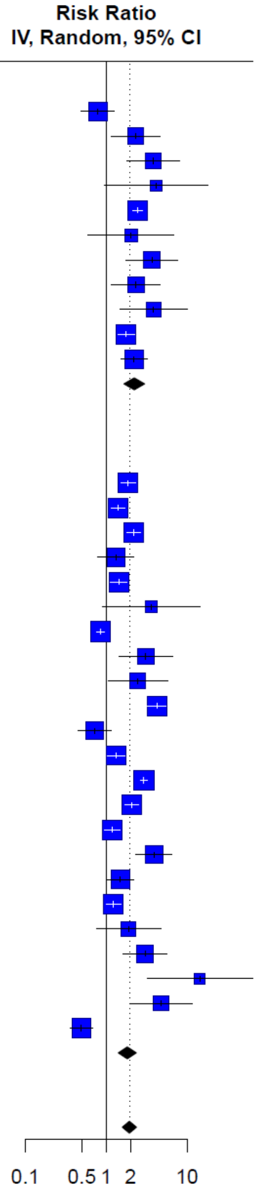

Fig. 4

Study	SSI Mean	SSI SD	SSI Total	non-SSI Mean	non-SSI SD	non-SSI Total	Weight	Mean Difference IV, Random, 95% CI
Woods et al.2013 [130]	2.89	2.3800	56	1.40	1.1900	91	18.0%	1.49 [0.82; 2.16]
Zhang et al.2024 [79]	2.40	1.9000	124	1.60	1.2000	248	25.7%	0.80 [0.43; 1.17]
Osterhoff et al.2015 [178]	1.20	1.7000	26	0.70	1.9000	218	17.3%	0.50 [−0.20; 1.20]
Christodoulou et al.2006 [169]	2.33	0.7410	8	0.67	1.4810	94	19.8%	1.67 [1.07; 2.26]
Everhart et al.2017 [157]	2.00	1.4810	22	1.33	0.7410	685	19.2%	0.67 [0.05; 1.29]
Total (95% CI)			**236**			**1336**	**100.0%**	**1.02 [0.58; 1.45]**
Heterogeneity: $Tau^2 = 0.1583$; $Chi^2 = 11.05$, df = 4 ($P = 0.03$); $I^2 = 64\%$