European Review for Medical and Pharmacological Sciences 2022; 26: 7420-7430

Preoperative anemia and complications after total joint arthroplasty: a systematic review and meta-analysis

H.-C. ZHANG, Y. ZHANG, H.-B. DAI, D. WU, B. XU

Department of Orthopedics, Xiangtan Central Hospital, Xiangtan City, Hunan Province, China

Abstract. – OBJECTIVE: The purpose of this review was to collect data from the literature to assess the impact of preoperative anemia on complications after total joint arthroplasty (TJA).

MATERIALS AND METHODS: We conducted a literature search on the websites of PubMed, Scopus, CENTRAL, Embase, and Google Scholar for comparative TJA studies reporting complication rates based on the presence of anemia. The last search was conducted on the 15th of May 2022. Studies only on hip and knee replacements were eligible for inclusion.

RESULTS: Twelve studies with 1,463,813 patients published between 2012-2022 were included. Meta-analysis indicated that anemic patients had increased risk of mortality (OR: 2.85 95% CI: 1.89, 2.48 I^2=83% p<0.00001), wound complications (OR: 2.06 95% CI: 3.51, 2.48 I^2=99% p=0.008), cardiac complications (OR: 2.40 95% CI: 1.56, 3.68 I^2=98% p<0.0001), respiratory complications (OR: 2.46 95% CI: 1.10, 5.50 I^2=100% p=0.03), renal complications (OR: 2.84 95% CI: 1.39, 5.80 I^2=99% p=0.004), sepsis (OR: 3.93 95% CI: 1.15, 13.45 I^2=99% p=0.03), urinary complications (OR: 2.42 95% CI: 1.27, 4.59 I^2=100% p=0.007), and readmission rates (OR: 1.58 95% CI: 1.42, 1.76 I^2=66% p<0.00001) as compared to non-anemic patients undergoing TJA. Most results did not change on sensitivity analysis. There were some non-significant results on subgroup analysis based on joint type and definition of anemia.

CONCLUSIONS: Our review suggests that preoperative anemia leads to increased morbidity and mortality after TJA. Specifically, anemia increases the risk of wound, cardiac, respiratory, renal, and urinary complications along with a higher incidence of sepsis and readmissions. Results should be interpreted with caution due to the high heterogeneity in the meta-analyses.

Key Words:

Hemoglobin, Joint replacement, Hip arthroplasty, Knee arthroplasty, Surgery, Complications.

Introduction

Total joint arthroplasty (TJA) is one of the most common elective orthopedic surgeries performed worldwide. While shoulder, elbow, wrist, and ankle arthroplasties are being performed around the globe, a major chunk of TJAs still consists of total hip arthroplasty (THA) and total knee arthroplasty (TKA). Advances in prosthesis designs with well-developed perioperative protocols have catapulted the number of TJAs in the past decade[1]. Research from the USA suggests that the numbers are expected to increase by a further 85% by 2030[2].

For any commonly performed surgical procedure, there should be efforts directed to minimize postoperative patient morbidity to reduce healthcare expenditure and improve patient satisfaction. THA and TJA have been shown to achieve high functional success rates, however, one should note that these are major and complex surgical procedures that carry a significant risk of postoperative systemic and local complications[3]. Research suggests that medical complications after THA and TJA can result in further healthcare expenditure of 22,775$ and 24,183$ respectively[4]. In this context, the importance of perioperative patient optimization by identifying and treating modifiable risk factors responsible for postoperative complications cannot be underestimated[5].

Anemia is defined as a hematocrit of <36% or hemoglobin levels <13 g/dl in men and <12 g/dl in women[6]. Data suggest that approximately 1/3rd of the world population suffers from anemia with higher prevalence in low and middle-income countries[7]. A systematic review[8] has found that around 15-33% of patients undergoing TJA are anemic. The importance of recognizing anemia

Corresponding Author: Yu Zhang, MD; e-mail: h58214911430118@126.com

can be gauged from the fact that several scholars[9] have identified anemia as an important risk factor for postoperative complications after different surgical procedures. Furthermore, in the recent past, there has been a spurt of studies reporting the association between anemia and complications after TJA[10-12]. However, we are unaware of any systematic review which has aimed to collect published data and present comprehensive evidence. Thus, we planned and designed this systematic review and meta-analysis to compile data from studies to assess the impact of preoperative anemia on postoperative complications after TJA.

Materials and Methods

Search and Eligibility

We first registered the protocol of our review on PROSPERO (No. CRD42022331454). The PRISMA guidelines were followed during the reporting of our study[13]. Next, we conducted a literature search on the websites of PubMed, Scopus, CENTRAL, Embase, and Google Scholar for studies reporting medical complications in patients undergoing major TJA with or without preoperative anemia. The search was initiated from the inception of the databases and the last date was 15th May 2022. Two reviewers were independently involved in the search which was restricted to English-language publications only. We used the following search terms, namely, "arthroplasty", "joint", "knee", "hip", "replacement", "anemia", and "hemoglobin". Further details are provided in the **Supplementary Table I**. The search results were consolidated and deduplicated for initial screening by article titles and abstracts. Only studies relevant to the review were extracted and matched against the eligibility criteria.

The primary eligibility criteria were formatted based on PECOS guidelines. We included studies conducted on patients undergoing TKA or THA (*Population*) and comparing those with preoperative anemia (*Exposure*) and without preoperative anemia (*Comparison*) and reporting any of the following outcomes: mortality, wound /cardiac/ respiratory/renal/thromboembolic/sepsis/urinary complications, or readmissions. All types of comparative study designs were eligible for inclusion. There was no restriction on the definition of anemia for inclusion in the review.

We excluded studies which: (1) were based on postoperative anemia levels; (2) did not group patients into anemia and controls; (3) did not report any of the relevant outcomes; (4) had overlapping data. If studies were using the same data source, we included the article with the largest sample size.

In the final stage, the full-text articles were screened based on the eligibility criteria, and those fulfilling the same were included. Any differences in study selection were resolved by consulting the third reviewer. Lastly, we also hand-searched the reference list of included studies and previous reviews to look for any missed articles.

Data Management

Using an Excel spreadsheet, the following data were gathered from the studies: details of study authors, publication year, study location, the database used, study type, joint studied, the definition of anemia, sample size, mean age, gender details, body mass index, and outcome data.

We assessed the risk of bias using the Newcastle-Ottawa scale (NOS)[14] which has three domains, namely, study population, comparability, and outcomes. Every study was evaluated based on predetermined questions. The maximum score achievable is nine.

Statistical Analysis

The review was conducted using "Review Manager" (RevMan, version 5.3; Nordic Cochrane Centre [Cochrane Collaboration], Copenhagen, Denmark; 2014). Complication data were extracted and pooled using an odds ratio (OR) with 95% confidence intervals (CI). The analysis was carried out using a random-effects model. We assessed inter-study heterogeneity using the I^2 statistic. I^2=25-50% meant low, 50-75% meant medium, and more than 75% meant substantial heterogeneity. As <10 studies were available for each meta-analysis, funnel plots were not generated. A sensitivity analysis was performed to examine the impact of each study on the overall results. One study was removed and the pooled effect estimate was recalculated for the remaining studies. Sub-group analysis was carried out based on joint type and definition of anemia. p-value <0.05 was statistically significant.

Results

The search results found at each level is presented in Figure 1. There were 3392 unique articles screened by the reviewers and 38 were selected

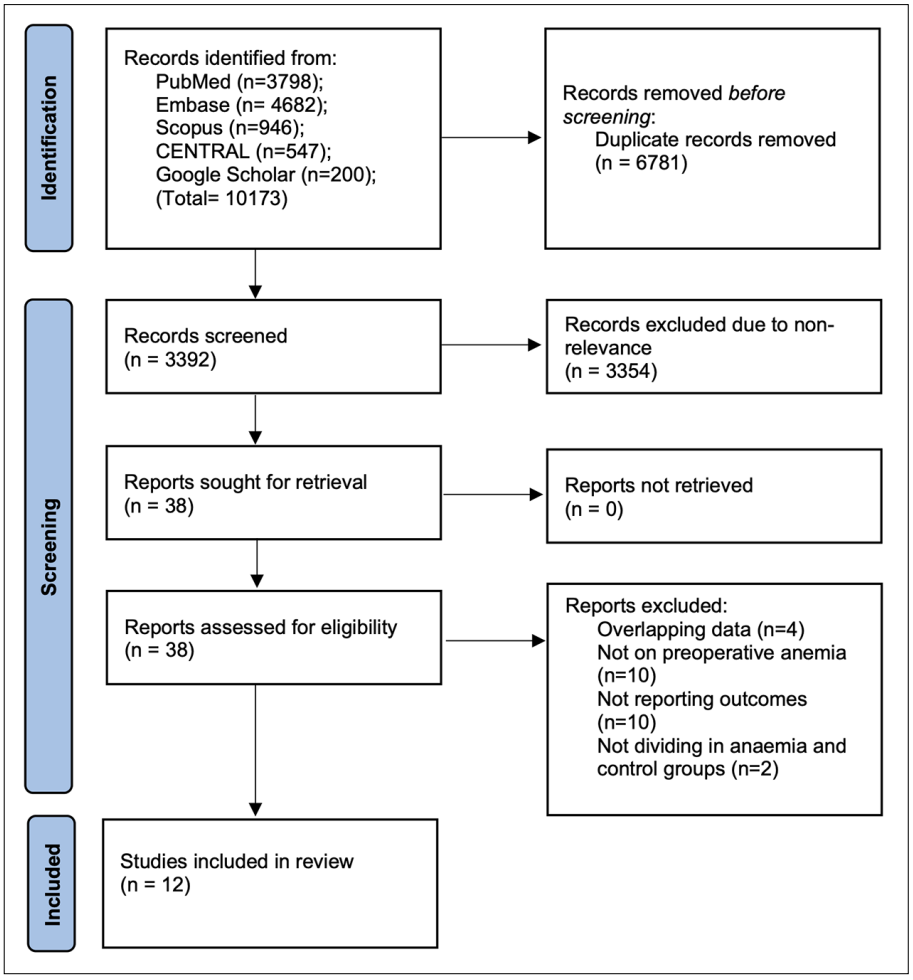

Figure 1. Study flow chart.

for full-text analysis. Of these, 12 articles fulfilled the inclusion criteria and were incorporated in this review[10-12,15-23].

Study details are presented in Table I. Most of the studies were published in the past two years. Furthermore, most of the data were from the USA, with the remaining were published from Denmark, Brazil, and Canada. Four studies[10,12,18,22] were on THA, two[11,20] on TKA and the remaining[15-17,19,23] included a mix of THA and TKA. Of the last group, only one study[21] reported separate outcomes for THA and TKA. Two studies[12,21] included only patients undergoing revision arthroplasty. Anemia was defined based on hematocrit values in three studies[11,21,22], six studies[10,15-17,19,23] used hemoglobin levels while the remaining[12,18] identified anemic patients based on ICD codes. Four studies[10,11,21,22] segregated anemic patients based on the severity of the condition. However, during the meta-analysis, these groups were combined into a single group of anemic patients to maintain homogeneity with the remaining studies. The sample size varied across the included studies. The total number of patients in the 12 studies was 1,463,813. The NOS scores are presented in Table I. All of them except for two studies[17,23], achieved a score of 8.

Meta-Analysis

Pooled analysis indicated that anemic patients had increased risk of mortality as compared to controls (OR: 2.85 95% CI: 1.89, 2.48 I^2=83% p<0.00001) (Figure 2). Similarly, we noted that anemic patients had an increased risk of wound complications (OR: 2.06 95% CI: 3.51, 2.48 I^2=99% p=0.008) (Figure 3), cardiac complications (OR: 2.40 95% CI: 1.56, 3.68 I^2=98% p<0.0001) (Figure 4), respiratory complications (OR: 2.46 95% CI: 1.10, 5.50 I^2=100% p=0.03) (Figure 5), and renal complications (OR: 2.84 95% CI: 1.39, 5.80 I^2=99% p=0.004) (Figure 6) as compared to non-anemic patients undergoing TJA. However, there was no evidence of higher

Table I. Details of included studies.

Study	Location	Database	TJA type	Groups	Definition of anemia (men)	Definition of anemia (women)	Sample size	Mean age (years)	Male gender (%)	Mean BMI (kg/m^2)	NOS score
Sicat 2022[10]	USA	NYU Langone health	Hip	Mild anemia Moderate anemia Severe anemia Normal	11-12.9 8-10.9 < 8 ≥ 13	11-11.9 8-10.9 < 8 ≥ 12	34 445 292 576	59.1 66.6 67 64.9	14.7 26.3 47.3 51.2	28 ± 6.5 28.3 ± 6.1 29.4 ± 6.4 29.5 ± 6.5	8
Neuwirth 2022[11]	USA	NSQIP (2006-2016)	Knee	Mild Severe Normal	27-36% HCT < 27% > 36%	27-36% HCT < 27% > 36%	20291 549 177393	NR	18.6 33.7 40.2	NR	8
Sylla 2021[12]	USA	PearlDriver (2005-2014)	Hip (revision)	Anemia Normal	ICD Codes	ICD Codes	15508 77440	NR	45.1 45	NR	8
Sequeira 2021[16]	USA	PearlDriver (2005-2014)	Hip	Anemia Normal	ICD Codes	ICD Codes	82983 331932	NR	33.9 33.9		8
Duarte 2021[15]	Brazil	Centro de Hemoterapia Celular em Medicina (2018-2020)	Hip and Knee	Anemia Normal	< 13 ≥ 13	< 12 ≥ 12	72 162	74 68.8	37.5 44.4	NR	6
Bailey 2021[17]	Canada	University of Ottawa (2012-2017)	Hip and Knee	Anemia Normal	< 13 ≥ 13	< 12 ≥ 12	817 4524	70.4 63.7	38.1 46.1	30.6 ± 6.7 31.1 ± 7	8
Mathew 2020[18]	USA	PearlDriver (2005-2014)	Knee	Anemia Normal	ICD Codes	ICD Codes	94053 470264	NR	27.8 27.8	NR	8
Gu 2020[19]	USA	NSQIP (2006-2017)	Hip (revision)	Mild Moderate-severe Normal	33-39% HCT < 33% > 39%	33-36% HCT < 33% >36%	2206 1097 5629	67 68.7 64.8	14.1 32.4 60.2	29.9 ± 7.2 28.7 ± 6.5 30.5 ± 6.5	8
Gu 2020*[19]	USA	NSQIP (2006-2017)	Knee (revision)	Mild Moderate-severe Normal	33-39% HCT < 33% > 39%	33-36% HCT < 33% > 36%	3515 736 9062	65.7 69.3 64.5	8.7 74.9 48.5	33.8 ± 7.7 32.8 ± 8.4 33.5 ± 7.3	8
Grosso 2020[20]	USA	NSQIP (2006-2016)	Hip	Mild Severe Normal	27-36% HCT < 27% > 36%	27-36% HCT < 27% > 36%	13214 541 116528	NR	24 38.3 47.3	NR	8
Viola 2014[21]	USA	The Rothman Institute at Thomas Jefferson University	Hip and Knee (including revision)	Anemia Normal	< 13 ≥ 13	< 12 ≥ 12	2576 10987	66.1 63.1	41 44.6	29.9 ± 6.9 30.3 ± 6.4	6
Jans 2014[22]	Denmark	NR	Hip and Knee (2010-2011)	Anemia	< 13 Normal	< 12 ≥ 13	662 ≥ 12	NR 4503	39.4	NR 43.7	8
Greenky 2012[23]	USA	Jefferson University	Hip and Knee	Anemia Normal	< 13 ≥ 13	< 12 ≥ 12	2991 12231	65.9 63.1	37.9 43.8	29.7 ± 8.3 30.3 ± 10.7	8

TJA, total joint arthroplasty; BMI, body mass index; NOS, Newcastle Ottawa scale; NR, not reported; NSQIP, National Surgical Quality Improvement. Program database; HCT, hematocrit; ICD, international classification of diseases. *Same study reporting separate outcomes.

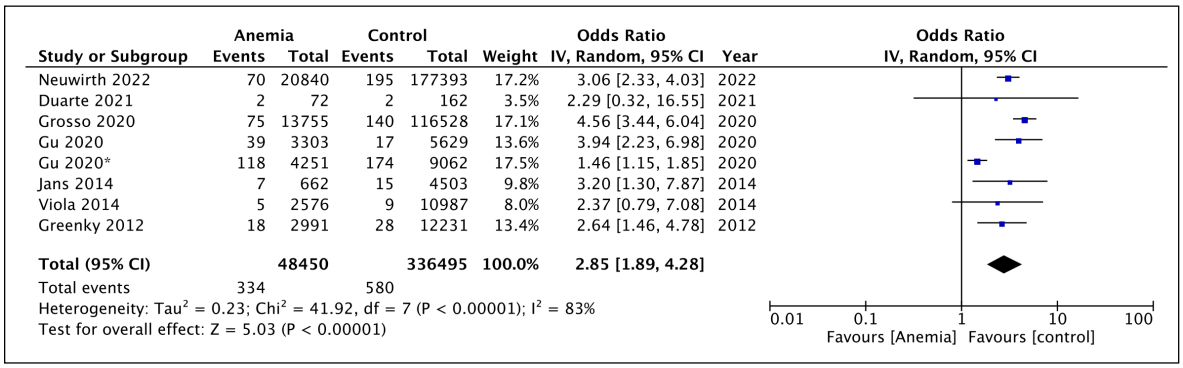

Figure 2. Meta-analysis of mortality in patients with and without anemia.

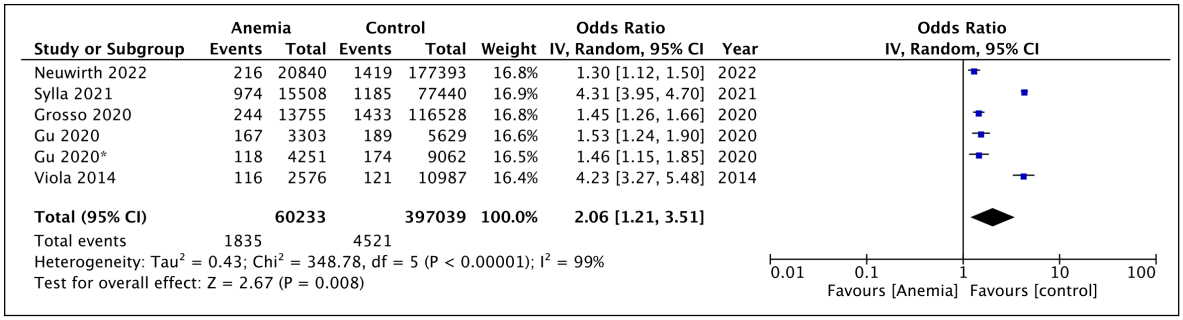

Figure 3. Meta-analysis of wound complications in patients with and without anemia.

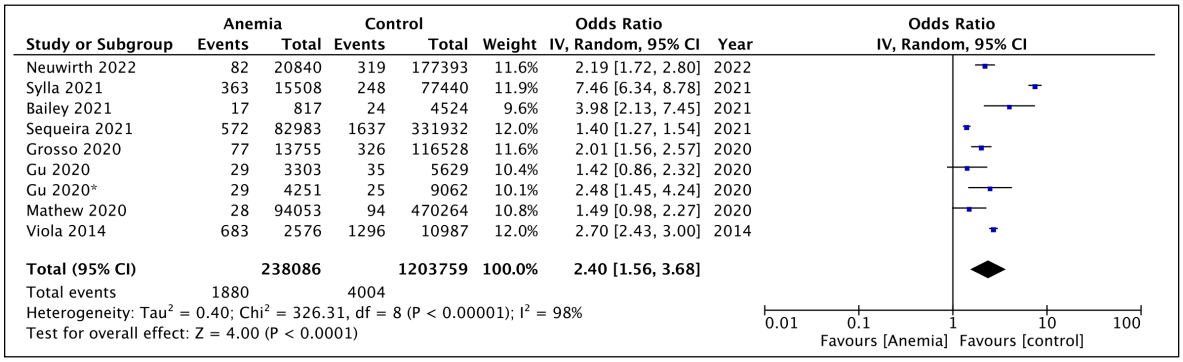

Figure 4. Meta-analysis of cardiac complications in patients with and without anemia.

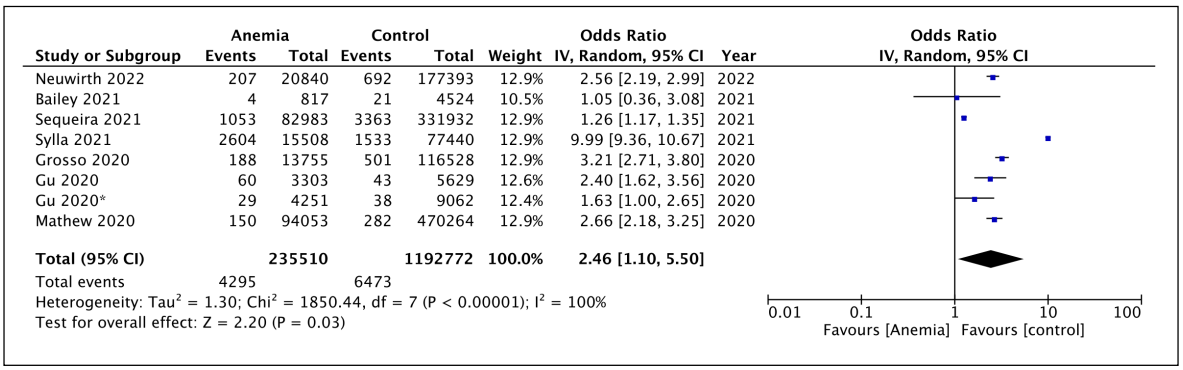

Figure 5. Meta-analysis of respiratory complications in patients with and without anemia.

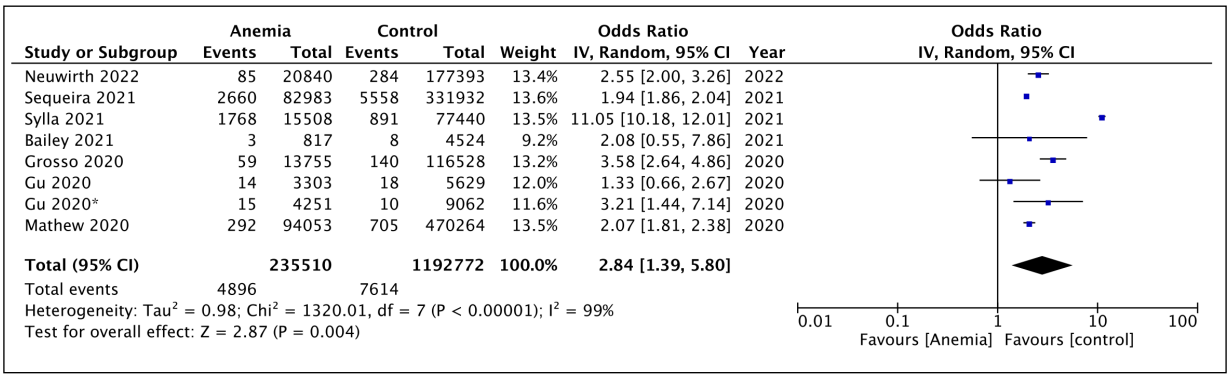

Figure 6. Meta-analysis of renal complications in patients with and without anemia.

risk of thromboembolic complications amongst anemic patients (OR: 1.45 95% CI: 0.83, 2.56 I^2=0% p=0.2) (Figure 7). Meta-analysis also indicated increased risk of sepsis (OR: 3.93 95% CI: 1.15, 13.45 I^2=99% p=0.03) (Figure 8) and urinary complications (OR: 2.42 95% CI: 1.27, 4.59 I^2=100% p=0.007) (Figure 9) amongst anemic patients. Also, the incidence of readmissions was also significantly higher in anemic patients as compared to controls (OR: 1.58 95% CI: 1.42, 1.76 I^2=66% p<0.00001) (Figure 10).

Sensitivity Analysis

Outcome of respiratory complications were non-significant on exclusion of Neuwirth et al[11] (OR: 2.44 95% CI: 0.97, 6.15 I^2=100% p=0.06). Sensitivity analysis also indicated an increased risk of thromboembolic complications in anemic patients on the exclusion of Sylla et al[12] (OR: 1.15 95% CI: 1.01, 1.31 I^2=69% p=0.04). Also, on the exclusion of Grosso et al[22] we noted no difference in the risk of sepsis (OR: 4.55 95% CI: 0.97, 21.27 I^2=99% p=0.05) between the

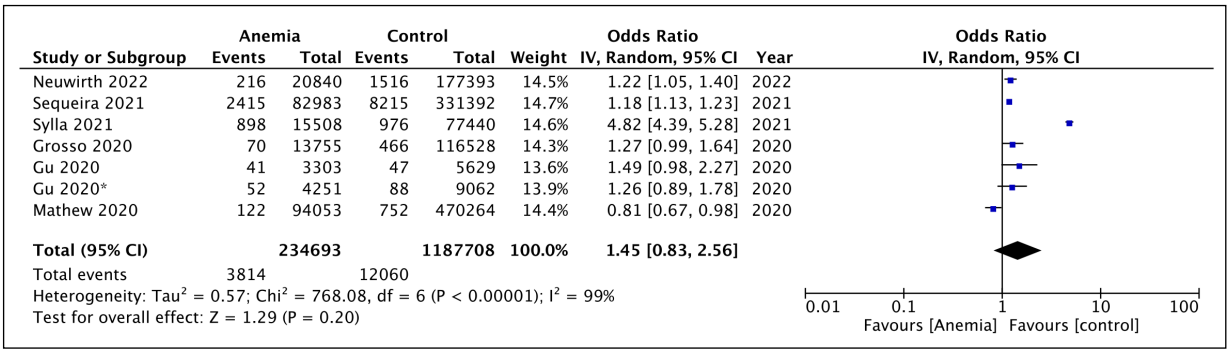

Figure 7. Meta-analysis of thromboembolic complications in patients with and without anemia.

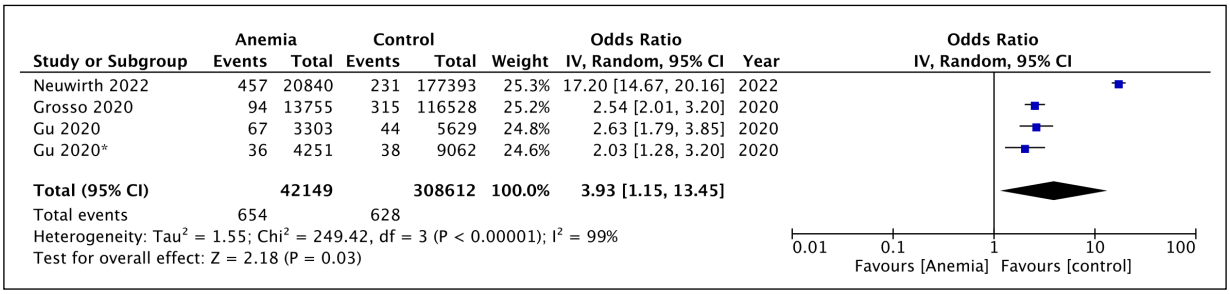

Figure 8. Meta-analysis of sepsis in patients with and without anemia.

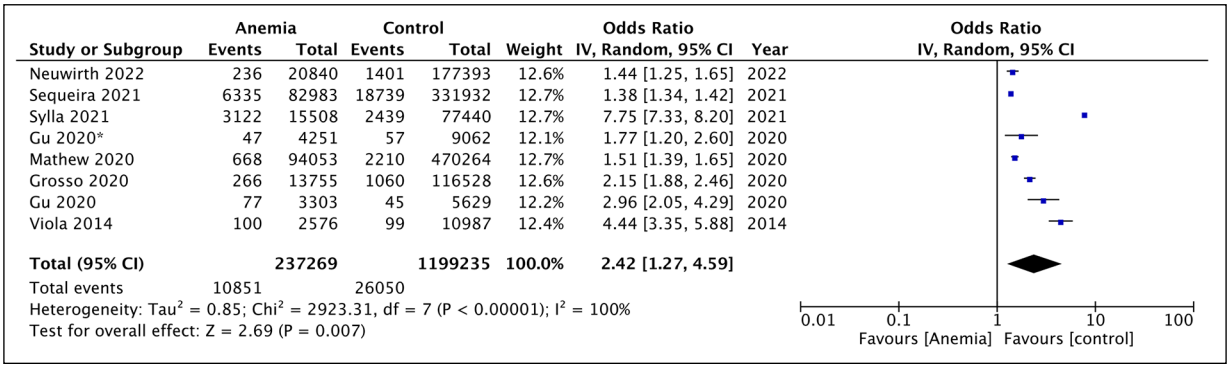

Figure 9. Meta-analysis of urinary complications in patients with and without anemia.

two groups. All the remaining outcomes did not change on sensitivity analysis.

Sub-Group Analysis

Results of the subgroup analysis are presented in Table II. The outcomes of mortality, sepsis, and readmission were unchanged on subgroup analysis. The remaining results were unstable with non-significant results in one or more subgroups.

Discussion

In the past decade, several researchers have recognized the impact of anemia on surgical outcomes and have reported a detailed association between preoperative anemia and postoperative complications for a variety of surgical procedures[24-26]. Abt et al[24] in a recent study on 1,193 head and neck cancer patients have reported a significantly increased risk of complications and mortality with anemia. Tohme et al[25] in a retrospective study of 12,987 patients undergoing hepatectomy with 32.8% anemic patients noted a significantly higher risk of postoperative morbidity and mortality amongst those with anemia. A recent meta-analysis of 22 studies by Padmanabhan et al[26] has shown that anemic patients undergoing cardiovascular surgery are at an increased risk of mortality, acute kidney injury, stroke, and infection as compared to non-anemic patients. Fowler et al[9] in a meta-analysis published in 2016 included 24 studies with varying surgical procedures to demonstrate that anemia was a cause of increased mortality, acute kidney injury, and infections in the surgical population. Thus, there seems to be a broad consensus in the literature that anemia is directly associated with poor postoperative outcomes after most surgical procedures. However, it must be recognized that every surgical procedure has its unique characteristics, risks, and complication rates. The complexity of the surgical procedure can have a major role in the rate of postoperative complications in anemic patients. TJA of the major joints (TKA and THA) is one of the most common procedures performed

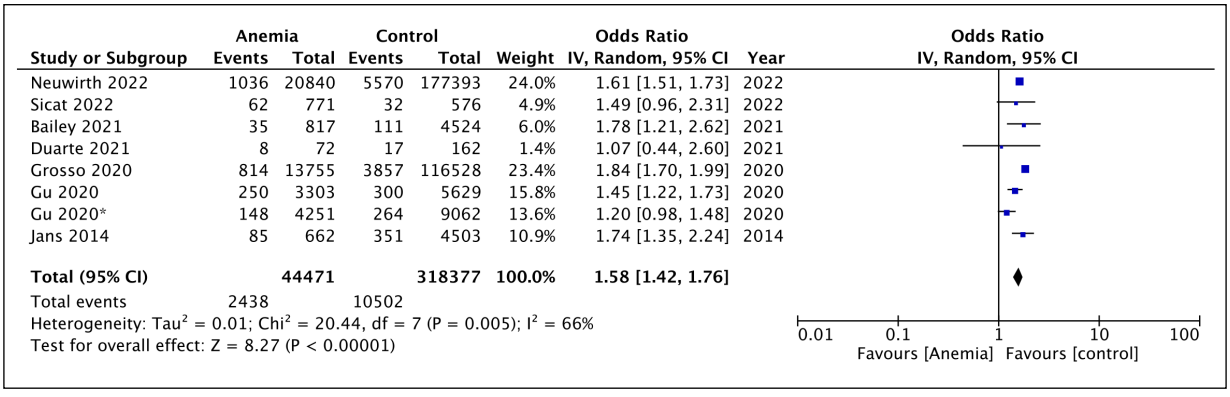

Figure 10. Meta-analysis of readmission rates in patients with and without anemia.

Table II. Subgroup analysis.

Variable	Groups	Studies	Odds ratio	I^2 (%)	*p*-value
Mortality					
Joint	Hip only	2	4.43 (3.44, 5.70)	0	< 0.001
	Knee Only	2	2.11 (1.02, 4.36)	94	0.04
	Mixed	4	2.70 (1.74, 4.19)	0	< 0.001
Definition of anemia	HCT	3	2.95 (1.66, 5.22)	93	0.0002
	Hemoglobin	4	2.70 (1.74, 4.19)	0	< 0.001
Wound complications					
Joint	Hip only	3	2.13 (0.94, 4.81)	99	0.07
	Knee Only	2	1.34 (1.19, 1.52)	0	< 0.001
	Mixed	1	4.23 (3.27, 5.48)	-	-
Definition of anemia	HCT	3	1.41 (1.30, 1.53)	0	< 0.001
	Hemoglobin	1	4.23 (3.27, 5.48)	-	-
	ICD code	1	4.31 (3.95, 4.70)	-	-
Cardiac complications					
Joint	Hip only	3	2.81 (0.96, 8.24)	98	0.06
	Knee Only	3	2.02 (1.55, 2.63)	33	< 0.001
	Mixed	2	2.89 (2.16, 3.86)	31	< 0.001
Definition of anemia	HCT	3	2.05 (1.75, 2.39)	0	< 0.001
	Hemoglobin	1	2.70 (2.43, 3.00)	-	-
	ICD code	3	2.51 (0.71, 8.81)	99	0.15
Respiratory complications					
Joint	Hip only	4	3.14 (0.87, 11.34)	100	0.08
	Knee Only	3	2.47 (2.08, 2.95)	42	< 0.001
	Mixed	1	1.05 (0.36, 3.08)	-	-
Definition of anemia	HCT	3	2.57 (2.07, 3.20)	66	< 0.001
	Hemoglobin	1	1.05 (0.36, 3.08)	-	-
	ICD code	3	3.22 (0.69, 15.07)	100	0.14
Renal complications					
Joint	Hip only	4	3.24 (1.01, 10.42)	100	0.05
	Knee Only	3	2.28 (1.90, 2.73)	34	<0.001
	Mixed	1	2.08 (0.55, 7.86)	-	-
Definition of anemia	HCT	3	2.66 (1.89, 3.74)	60	< 0.001
	Hemoglobin	1	2.08 (0.55, 7.86)	-	-
	ICD code	3	3.55 (1.06, 11.81)	100	0.04
Thromboembolic complications					
Joint	Hip only	4	1.82 (0.74, 4.49)	100	0.19
	Knee Only	3	1.06 (0.79, 1.43)	83	0.68
Definition of anemia	HCT	3	1.25 (1.12, 1.40)	0	0.001
	ICD code	3	1.67 (0.59, 4.74)	100	0.34
Sepsis*					
Joint	Hip only	2	6.78 (1.08, 42.71)	99	0.04
	Knee Only	2	2.43 (1.97, 2.98)	0	< 0.001
Urinary complications					
Joint	Hip only	4	2.87 (0.96, 8.60)	100	0.06
	Knee Only	3	1.50 (1.40, 1.61)	0	< 0.001
	Mixed	1	4.44 (3.35, 5.88)	-	-
Definition of anemia	HCT	3	1.96 (1.46, 2.64)	87	< 0.001
	Hemoglobin	1	4.44 (3.35, 5.88)	-	-
	ICD code	3	2.53 (0.79, 8.16)	100	0.12
Readmission					
Joint	Hip only	3	1.64 (1.35, 1.98)	69	< 0.001
	Knee Only	2	1.42 (1.06, 1.89)	86	0.02
	Mixed	3	1.71 (1.39, 2.10)	0	< 0.001
Definition of anemia	HCT	3	1.55 (1.35, 1.78)	84	< 0.001
	Hemoglobin	5	1.81 (1.69, 1.95)	0	< 0.001

HCT, hematocrit; ICD, international classification of diseases. *No subgroup analysis based on definition of anemia as all studies used HCT.

in orthopedics. To the best of our knowledge, our review is the first meta-analysis presenting how exactly anemia impacts postoperative complication rates in patients undergoing TJA.

Our systematic review was able to include 12 recently published studies[10,11,22,23,12,15-21] with approximately 1.4 million patients undergoing THA or TKA thereby providing evidence with high statistical power. The results demonstrated that anemic patients undergoing TJA had a 2.8 times increased risk of mortality as compared to non-anemic patients. These results are consistent with prior reviews[9] on other surgical procedures. Furthermore, the pooled analysis also demonstrated a statistically significant association between anemia and major systemic and wound complications. We noted a nearly two-fold increase in the risk of cardiac, respiratory, renal, urinary, and wound complications in anemic patients undergoing TJA. The risk of sepsis was increased by nearly four-fold while there were a 1.5 times increased risk of hospital readmissions in anemic patients. Only thromboembolic complications were not found to be increased in anemic patients. It should be noted that most of the results did not change on sensitivity analysis demonstrating a consistent effect of anemia on the rate of complications. Nonetheless, the outcomes of respiratory complications and sepsis turned non-significant on the exclusion of one study each. However, the resultant effect size was still >1 and the lower end of 95% CI was very close to zero indicating a higher risk of complications in anemic patients. We also noted that anemic patients had higher thromboembolic complications on the exclusion of one study, but the resultant OR was very small indicating only a 1.15 times increased risk of thromboembolic complications.

To maintain homogeneity of data, our review focused only on THA and TJA since these are the major and most common joints replaced worldwide. However, evidence indicates anemia leads to poor outcomes with other joint arthroplasties as well. Kashanchi et al[27] have shown that anemia increases the risk of all complications, cerebrovascular accident, readmission, reoperation, and nonhome discharge in patients undergoing total shoulder arthroplasty. Pollock et al[28] have recently demonstrated a higher risk of readmission, reoperation, wound complications, and surgical site infections in anemic patients undergoing total ankle arthroplasty. Similar results have been found for patients undergoing elbow arthroplasty as well[29].

An important limitation of the review was the high heterogeneity in most of the meta-analyses. This was likely owing to the differences in the study populations, surgery type, anemia definition, and methods of the included studies. An attempt was made to reduce the heterogeneity using subgroup analysis. The first subgroup analysis was based on joint type. It was noted that the results of wound, cardiac, respiratory, renal, and urinary complications turned non-significant for one of the subgroups (hip only, knee only, or mixed). Nevertheless, the ORs were still on the higher side and the lower end of 95% CI was close to zero for most of these subgroups. Similarly, for the subgroup analysis based on anemia definition, non-significant results were seen for cardiac, respiratory, renal, and urinary complications in one or the other subgroups (hemoglobin, hematocrit, or ICD codes). Important to note is that the subgroup analysis significantly reduced the number of studies in each analysis, and this may have been an important factor for many of the non-significant results. The limitation of data also precluded a subgroup analysis based on the type of arthroplasty (primary and revision) and severity of anemia.

Since evidence strongly links preoperative anemia with postoperative complications, the next logical step is to screen and correct anemia to reduce the burden of complications. Indeed, elective orthopedic surgery has been one of the most appropriate procedures to implement preoperative anemia optimization programs[30]. However, anemia screening and correction are still not universally established with more than 70% of anemic patients not receiving any treatment for anemia before surgery[31]. Perioperative blood transfusion has been used to correct anemia in TJA patients, but it often leads to high morbidity and mortality[32,33]. Erythropoietin has also been utilized to optimize hemoglobin levels, but its high costs have restricted widespread use[34]. Since most of the patients are anemic due to iron deficiency, several studies have reported the use of iron supplements to correct preoperative anemia in TJA patients[31]. The meta-analysis by Scrimshire et al[31] has shown that iron treatment can reduce perioperative blood transfusions in TJA patients, but the overall quality of evidence is low. Furthermore, it is unclear how these interventions affect the different complications reported in our review. Future studies should explore this to generate higher-quality evidence.

Limitations

Our study has some limitations. Firstly, despite including a large number of studies with a high sample size, the review outcomes were not universally reported by all studies. This heterogeneity amongst studies limited our ability to assess the impact of anemia severity on the study outcomes. Secondly, the retrospective and observation nature of the data is another source of bias due to unmeasured confounding and selection bias. Thirdly, complications can be influenced by several factors including patients' age, comorbidities, surgical protocols, etc. These factors were not considered in our analysis. Fourthly, we could not assess the impact of perioperative transfusion on the complication rates due to the unavailability of adequate data from the included studies. Thus, the independent role of anemia on postoperative complications could not be established. Lastly, most of the data were from a single country and the results may not be generalizable to the global population.

Conclusions

Our review suggests that preoperative anemia leads to increased morbidity and mortality after TJA. Specifically, anemia increases the risk of wound, cardiac, respiratory, renal, and urinary complications along with a higher incidence of sepsis and readmissions. Results should be interpreted with caution owing to the high heterogeneity in the meta-analyses. Our results demonstrate a need for multicentric large-scale randomized controlled trials to assess the impact of anemia-based interventions in reducing complication rates after TJA.

Conflict of Interest

The Authors declare that they have no conflict of interests.

Acknowledgements

Not applicable.

Informed Consent

Not applicable.

Authors' Contribution

HZ and YZ conceived and designed the analysis; HD and DW collected the data; HD, DW and BX Performed the analysis; HZ and YZ wrote the paper.

Funding

Not applicable.

ORCID ID

HZ: 0000-0003-4125-3541; YZ: 0000-0002-5332-6026; HD: 0000-0003-4139-6956; DW: 0000-0001-5491-851X; BX: 0000-0002-0705-6256.

References

1) Patel A, Pavlou G, Mújica-Mota RE, Toms AD. The epidemiology of revision total knee and hip arthroplasty in England and Wales: a comparative analysis with projections for the United States. A study using the National Joint Registry dataset. Bone Joint J 2015; 97-B: 1076-1081.
2) Sloan M, Premkumar A, Sheth NP. Projected Volume of Primary Total Joint Arthroplasty in the U.S., 2014 to 2030. J Bone Joint Surg Am 2018; 100: 1455-1460.
3) Soffin EM, Wainwright TW. Hip and Knee Arthroplasty. Anesthesiol Clin 2022; 40: 73-90.
4) Clair AJ, Evangelista PJ, Lajam CM, Slover JD, Bosco JA, Iorio R. Cost Analysis of Total Joint Arthroplasty Readmissions in a Bundled Payment Care Improvement Initiative. J Arthroplasty 2016; 31: 1862-1865.
5) Wall C, de Steiger R. Pre-operative optimisation for hip and knee arthroplasty: Minimise risk and maximise recovery. Aust J Gen Pract 2020; 49: 710-714.
6) Beutler E, Waalen J. The definition of anemia: what is the lower limit of normal of the blood hemoglobin concentration? Blood 2006; 107: 1747-1750.
7) Chaparro CM, Suchdev PS. Anemia epidemiology, pathophysiology, and etiology in low- and middle-income countries. Ann N Y Acad Sci 2019; 1450: 15-31.
8) Spahn DR. Anemia and patient blood management in hip and knee surgery: a systematic review of the literature. Anesthesiology 2010; 113: 482-495.
9) Fowler AJ, Ahmad T, Phull MK, Allard S, Gillies MA, Pearse RM. Meta-analysis of the association between preoperative anaemia and mortality after surgery. Br J Surg 2015; 102: 1314-1324.
10) Sicat CS, Muthusamy N, Singh V, Davidovitch RI, Slover JD, Schwarzkopf R. Impact of Preoperative Anemia Severity on Primary Total Hip Arthroplasty Outcomes. J Arthroplasty 2022; 37: 721-726.
11) Neuwirth AL, Boddapati V, Held MB, Grosso MJ, Shah RP, Geller JA, Cooper HJ. Preoperative Anemia Is Associated With 30-Day Morbidity in Total Knee Arthroplasty. Orthopedics 2022; 45: e86-e90.
12) Sylla MM, Gruffi L, Roth ES, Rosato FE, Wong CHJ, Razi AE. How Does Iron Deficiency Anemia Impact Outcomes following Revision Total Hip Arthroplasty? Hip Pelvis 2021; 33: 140-146.

13) Page MJ, McKenzie JE, Bossuyt PM, Boutron I, Hoffmann TC, Mulrow CD, Shamseer L, Tetzlaff JM, Akl EA, Brennan SE, Chou R, Glanville J, Grimshaw JM, Hróbjartsson A, Lalu MM, Li T, Loder EW, Mayo-Wilson E, McDonald S, McGuinness LA, Stewart LA, Thomas J, Tricco AC, Welch VA, Whiting P, Moher D. The PRISMA 2020 statement: an updated guideline for reporting systematic reviews. BMJ 2021; 372: n71.

14) Wells GA, Shea B, O'Connell D, Peterson J, Welch V, Losos M, Tugwell P. The Newcastle-Ottawa Scale (NOS) for assessing the quality of nonrandomised studies in meta-analyses. Available at: http://www.ohri.ca/programs/clinical_epidemiology/oxford.asp. Accessed October 30, 2020.

15) Jans Ø, Jørgensen C, Kehlet H, Johansson PI; Lundbeck Foundation Centre for Fast-track Hip and Knee Replacement Collaborative Group. Role of preoperative anemia for risk of transfusion and postoperative morbidity in fast-track hip and knee arthroplasty. Transfusion 2014; 54: 717-726.

16) Greenky M, Gandhi K, Pulido L, Restrepo C, Parvizi J. Preoperative anemia in total joint arthroplasty: is it associated with periprosthetic joint infection? Clin Orthop Relat Res 2012; 470: 2695-2701.

17) Duarte GC, Catanoce AP, Zabeu JL, Ribeiro GN, Moschen M, de Oliveira NAG, Langhi DM, Marques Júnior JFC, Mendrone-Junior A. Association of preoperative anemia and increased risk of blood transfusion and length of hospital stay in adults undergoing hip and knee arthroplasty: An observational study in a single tertiary center. Health Sci Rep 2021; 4: e448.

18) Sequeira SB, Quinlan ND, Althoff AD, Werner BC. Iron Deficiency Anemia is Associated with Increased Early Postoperative Surgical and Medical Complications Following Total Hip Arthroplasty. J Arthroplasty 2021; 36: 1023-1028.

19) Bailey A, Eisen I, Palmer A; Ottawa Arthroplasty Blood Preservation Group,, Beaulé PE, Fergusson DA, Grammatopoulos G. Preoperative Anemia in Primary Arthroplasty Patients-Prevalence, Influence on Outcome, and the Effect of Treatment. J Arthroplasty 2021; 36: 2281-2289.

20) Mathew KK, Vakharia RM, Salem HS, Sodhi N, Anis HK, Roche MW, Mont MA. Is Iron Deficiency Anemia a Risk Factor for Poorer Outcomes in Primary Total Knee Arthroplasty? J Arthroplasty 2020; 35: 1252-1256.

21) Gu A, Chen AZ, Selemon NA, Tornberg H, Wei C, Fassihi SC, Campbell JC, Sculco PK. Preoperative Anemia Independently Predicts Significantly Increased Odds of Short-Term Complications Following Aseptic Revision Hip and Knee Arthroplasty. J Arthroplasty 2021; 36: 1719-1728.

22) Grosso MJ, Boddapati V, Cooper HJ, Geller JA, Shah RP, Neuwirth AL. The Effect of Preoperative Anemia on Complications After Total Hip Arthroplasty. J Arthroplasty 2020; 35: S214-S218.

23) Viola J, Gomez MM, Restrepo C, Maltenfort MG, Parvizi J. Preoperative anemia increases postoperative complications and mortality following total joint arthroplasty. J Arthroplasty 2015; 30: 846-848.

24) Abt NB, Tarabanis C, Miller AL, Puram SV, Varvares MA. Preoperative anemia displays a dose-dependent effect on complications in head and neck oncologic surgery. Head Neck 2019; 41: 3033-3040.

25) Tohme S, Varley PR, Landsittel DP, Chidi AP, Tsung A. Preoperative anemia and postoperative outcomes after hepatectomy. HPB (Oxford) 2016; 18: 255-261.

26) Padmanabhan H, Siau K, Curtis J, Ng A, Menon S, Luckraz H, Brookes MJ. Preoperative Anemia and Outcomes in Cardiovascular Surgery: Systematic Review and Meta-Analysis. Ann Thorac Surg 2019; 108: 1840-1848.

27) Kashanchi KI, Nazemi AK, Komatsu DE, Wang ED. The Impact of Preoperative Anemia on Complications After Total Shoulder Arthroplasty. J Am Acad Orthop Surg Glob Res Rev 2021; 5: e20.00136.

28) Pollock JR, Doan MK, Moore ML, Hassebrock JD, Makovicka JL, Deckey DG, Kile TA, Patel KA. 30-Day Outcomes for Total Ankle Arthroplasty in Patients With Anemia. Foot Ankle Int 2021; 42: 1463-1468.

29) Gordon AM, Ashraf AM, Sheth BK, Magruder ML, Conway CA, Choueka J. Anemia Severity and the Risks of Postoperative Complications and Extended Length of Stay Following Primary Total Elbow Arthroplasty. Hand (N Y) 2022: 15589447211073830.

30) Goodnough LT, Maniatis A, Earnshaw P, Benoni G, Beris P, Bisbe E, Fergusson DA, Gombotz H, Habler O, Monk TG, Ozier Y, Slappendel R, Szpalski M. Detection, evaluation, and management of preoperative anaemia in the elective orthopaedic surgical patient: NATA guidelines. Br J Anaesth 2011; 106: 13-22.

31) Scrimshire AB, Booth A, Fairhurst C, Kotze A, Reed M, McDaid C. Preoperative iron treatment in anaemic patients undergoing elective total hip or knee arthroplasty: a systematic review and meta-analysis. BMJ Open 2020;10: e036592.

32) Song K, Pan P, Yao Y, Jiang T, Jiang Q. The incidence and risk factors for allogenic blood transfusion in total knee and hip arthroplasty. J Orthop Surg Res 2019; 14: 273.

33) Danninger T, Rasul R, Poeran J, Stundner O, Mazumdar M, Fleischut PM, Poultsides L, Memtsoudis SG. Blood transfusions in total hip and knee arthroplasty: an analysis of outcomes. ScientificWorldJournal 2014; 2014: 623460.

34) Voorn VM, van der Hout A, So-Osman C, Vliet Vlieland TP, Nelissen RG, van den Akker-van Marle ME, Dahan A, Marang-van de Mheen PJ, van Bodegom-Vos L. Erythropoietin to reduce allogeneic red blood cell transfusion in patients undergoing total hip or knee arthroplasty. Vox Sang 2016; 111: 219-225.