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RESEARCH ARTICLE

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Association between malnutrition status and total joint arthroplasty periprosthetic joint infection and surgical site infection: a systematic review meta-analysis

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Abstract

Background Malnutrition is a state resulting from lack of intake or uptake of nutrition. Investigating the association between malnutrition and postoperative complications is essential for enhancing patient outcomes in total joint arthroplasty (TJA). This meta-analysis aimed to investigate the impact of malnutrition on the incidence of surgical site infections (SSIs) and periprosthetic joint infections (PJIs) following TJA.

Methods The data were searched from databases including PubMed, Embase, Web of Science, and Cochrane Library inception through July 19 2023, without time restrictions. Inclusion criteria focused on studies examining malnutrition as a risk factor for SSIs and PJIs postarthroplasty, providing sufficient data for calculating odds ratios (ORs) and 95% confidence intervals (CIs). Methodological quality was assessed using the Newcastle–Ottawa Scale, and statistical analyses were executed in Stata version 17.

Results A total of 1,025 articles were screened, and 9 studies satisfying the predefined inclusion criteria were consequently selected for this meta-analysis. Studies indicated that malnutrition is significant factor to the heightened incidence of both SSIs and PJIs following TJA procedures. Our pooled results yielded aggregated ORs of 2.60 for SSIs and 3.44 for PJIs, with respective 95% CIs of 2.10–3.10 and 2.35–4.53. The heterogeneity of malnutrition as a risk factor for postoperative SSI was $I2 = 0.0\%$ ($p = 0.592$), and for PJI was $I2 = 0.0\%$ ($p = 0.422$). Egger's linear regression test showed no significant publication bias ($p > 0.05$).

Conclusions Malnutrition is a significant risk factor for SSIs and potentially PJIs in patients undergoing TJA. Preoperative optimization strategies targeted at malnourished patients are suggested to minimize postoperative complications clinically.

Keywords Arthroplasty, Malnutrition, Surgical Site infections, Periprosthetic Joint infections, Meta-analysis

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Background

The annual incidence rate of primary Total Hip Arthroplasty (THA) and Total Knee Arthroplasty (TKA) continues to rise. Based on data from 2000 to 2014, primary THA is projected to grow by 71%, reaching 635,000 procedures by 2030, while primary TKA is projected to grow by 85%, reaching 1.26 million procedures by 2030 in U.S [1]. These joint replacement surgeries have become essential interventions for end-stage degenerative joint diseases, offering renewed mobility and improved quality of life. However, the postoperative phase is fraught with various complications, each capable of prolonging hospital stay, escalating healthcare costs, reducing patient satisfaction, and potentially culminating in surgical failure and prosthetic revision. Among the panoply of postoperative complications, surgical site infections (SSIs) and periprosthetic joint infections (PJIs) are particularly deleterious [2, 3]. SSIs are infections that occur during or after surgery, and PJIs refer to acute or chronic infections caused primarily by bacteria or fungi that usually occurs after artificial joint replacement [4–6]. Current research suggests that the incidence rate of PJIs following hip and knee arthroplasties fluctuates between 1% and 2%, a range that signifies a substantial clinical burden and increase of in-hospital mortality [7–9]. There are reports even suggesting that total knee arthroplasty revision will be an immense burden on future health care systems over the next 30 years [10, 11]. Early identification and prevention of SSIs and PJIs are pivotal in augmenting the overall success rates of joint replacement surgeries [12, 13].

Malnutrition has been implicated in a myriad of adverse surgical outcomes, encompassing impaired wound healing, increased susceptibility to SSIs, and a heightened risk for PJIs [14]. Underlying mechanisms include but are not limited to lymphopenia, compromised immunological functions against infections, and reduced collagen synthesis that impedes wound healing [15, 16]. Owing to the insidious and often subclinical nature of malnutrition, with overt signs and symptoms evading easy detection, various diagnostic methodologies have been devised. Laboratory parameters such as serum albumin levels, transferrin, and total lymphocyte count serve as widely employed indicators for assessing the nutritional status of surgical patients [17, 18].

The extant literature has ventured into the arena of exploring the relationship between malnutrition and postoperative complications. Therefore, it is essential to consolidate available evidence through a systematic review and meta-analysis. This will elucidate whether a direct correlation exists between malnutrition and the incidence of SSIs and PJIs postjoint replacement surgery, thus providing a foundational rationale for the implementation of targeted nutritional interventions as a part of preoperative and postoperative care.

Materials and methods

Search strategy

In the conduct and documentation of this meta-analysis, strict compliance was maintained with the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guidelines, as stipulated in their most recent version [19]. The methodological rigor of this work is scaffolded upon the PICO (Patient, Intervention, Comparison, Outcome) construct, delineating four core dimensions: Patient cohort (P)- This part needs to state the inclusion criteria comprised of patients who underwent primary THA and TKA; The Interventional variable (I) being the antecedent or subsequent state of malnutrition defined as indicate albumin levels <3.5 g/dl, transferrin levels <200 mg/dl, or total lymphocyte counts $<1500/\text{mm}^3$; the Comparison group (C) involving patients in a nutritionally stable condition who underwent comparable surgical interventions; and the Outcome metrics (O) centring on the postoperative incidence of SSIs and PJIs.

For the purposes of literature retrieval, an exhaustive search was executed across four preeminent electronic medical databases—PubMed, Embase, Web of Science, and Cochrane Library—on July 19, 2023, with no temporal restrictions imposed. The search protocol encompassed strategically chosen key terms, including but not limited to "joint replacement surgery," "arthroplasty," "malnutrition," "surgical site infections," and "periprosthetic joint infections." This lexicon was meticulously curated to mirror the extensive remit of the PICO construct and to facilitate the all-encompassing aggregation of germane studies for inclusion in this meta-analysis. No linguistic barriers were set for the search. Additionally, a manual scrutiny of reference lists within pertinent articles was conducted to identify any supplementary studies that may contribute to the meta-analysis.

Inclusion criteria and exclusion criteria

Inclusion criteria: (1) Study Population: The research must focus on patients who have undergone joint replacement surgery including total hip and knee arthroplasties, specifically assessing whether malnutrition is a risk factor for SSIs; (2) Outcome Measures: The studies must either provide raw data for odds ratios (ORs) and their corresponding 95% confidence intervals (CIs) or furnish sufficient dichotomous data from which ORs and 95% CIs can be calculated; (3) Diagnostic Criteria for Surgical Site Infections: Studies must use diagnostic criteria for SSIs that align with the established United States criteria for hospital-acquired infections [20]; (4) Malnutrition Definition: The identification of malnutrition should be based on laboratory findings that indicate albumin levels < 3.5 g/dl, transferrin levels < 200 mg/dl, or total lymphocyte counts < 1500/mm^3 [18]; and (5) Most Recent Data: For multiple studies involving the same cohort, the most recently published study with the most comprehensive and complete case data will be included.

The exclusion criteria were as follows: (1) Duplicate Publications: Studies that are duplicated in journals and conference proceedings will be excluded; (2) Incompatible Study Designs: Exclusion of literature types such as reviews, case–control studies, and case reports, which do not align with the required study design for this meta-analysis; (3) Insufficient Data: Studies that do not provide enough information to calculate or extract the OR and 95% CI; (4) Low Quality Studies: Studies with a low-quality score, as measured by the Newcastle–Ottawa Scale (NOS), with a score of 6 or less will be excluded from this meta-analysis.

Data extraction

Data extraction for this meta-analysis was conducted independently by two evaluators, who subsequently cross-verified their findings. Any discrepancies will be resolved through discussion among reviewers, with a third reviewer consulted if necessary. The data points for extraction include. The data points targeted for extraction include the following: publication date, country of origin, title of the study, author names, study design, target population, definition of malnutrition, type of joint replacement surgery performed, associated risk factors, number of postoperative infections, number in the negative control group, and OR and their corresponding 95% CI. In cases where pertinent data are absent from the published report, we will reach out to the primary investigators of the original study via email to request the unpublished data. This process adheres to established protocols to ensure methodological rigor and consistency in the meta-analysis.

Quality assessment

The methodological quality of the studies incorporated into our meta-analysis will be meticulously appraised by a pair of autonomous reviewers utilizing the Newcastle–Ottawa Scale [21]. This scale is a recognized instrument designed to evaluate studies through nine individual criteria, grouped into three essential domains: selection, comparability, and outcome measures. These domains facilitate an in-depth analysis of potential biases existing within the evaluated studies. Subsequent to this exhaustive quality assessment, each included study will receive a numerical rating that spans from 0 to 9. Interpretation of these scores is delineated as follows: studies with a score ranging from 0 to 3 are categorized as low quality, those with scores between 4 and 6 are classified as moderate quality, and studies garnering a score between 7 and 9 are considered to be of high methodological quality. This approach adheres to standardized best practices in meta-analysis, ensuring both reliability and validity in our evaluation.

Statistical analyses

Interstudy heterogeneity was evaluated through chi-square statistical tests and expressed using the I^2 metric. An I^2 value below 50% coupled with a p value of 0.10 or greater was indicative of negligible heterogeneity, thus warranting the application of a fixed-effects model for the estimation of the aggregated effect size. Conversely, an I^2 value of 50% or greater or a corresponding p value below 0.10 indicated the presence of substantial heterogeneity. Under conditions of significant statistical heterogeneity, a random-effects model was employed for effect size amalgamation. Subgroup and sensitivity analyses were conducted to isolate and mitigate the underlying sources of heterogeneity. Sensitivity analyses were executed to assess the stability and resilience of our findings, examining the impact of individual studies on the cumulative effect size by iteratively excluding each study and recalculating the aggregated outcome. To identify any prospective publication bias, funnel plot symmetry was scrutinized. A balanced distribution of data points on either side of the funnel plot's vertex would imply a diminished probability of the results being skewed by publication bias. For a quantitative assessment of publication bias, Egger's linear regression test was utilized. All statistical inferences were made based on two-sided tests, and a p value less than 0.05 was considered statistically significant. Statistical analyses were performed utilizing Stata version 17 (StataCorp, College Station, TX, USA) in compliance with rigorous meta-analytical standards.

Results

Search results and study selection

In the preliminary search across electronic databases, a total of 1,025 pertinent articles were identified. Following the elimination of duplicate publications and a rigorous evaluation of titles and abstracts in accordance with predefined inclusion and exclusion criteria, 32 relevant articles were isolated. Upon subsequent full-text review, 23 of these articles were disqualified, culminating in the inclusion of 9 studies for the meta-analysis [21–30]. The sequential flow of the literature selection procedure, along with the resulting number of articles at each stage, is graphically depicted in Fig. 1, adhering to established meta-analytical guidelines.

Study characteristics

The included studies span the years 2015 to 2020 and encompass a geographically diverse set of research locales, including the United States, Spain, Mexico, and

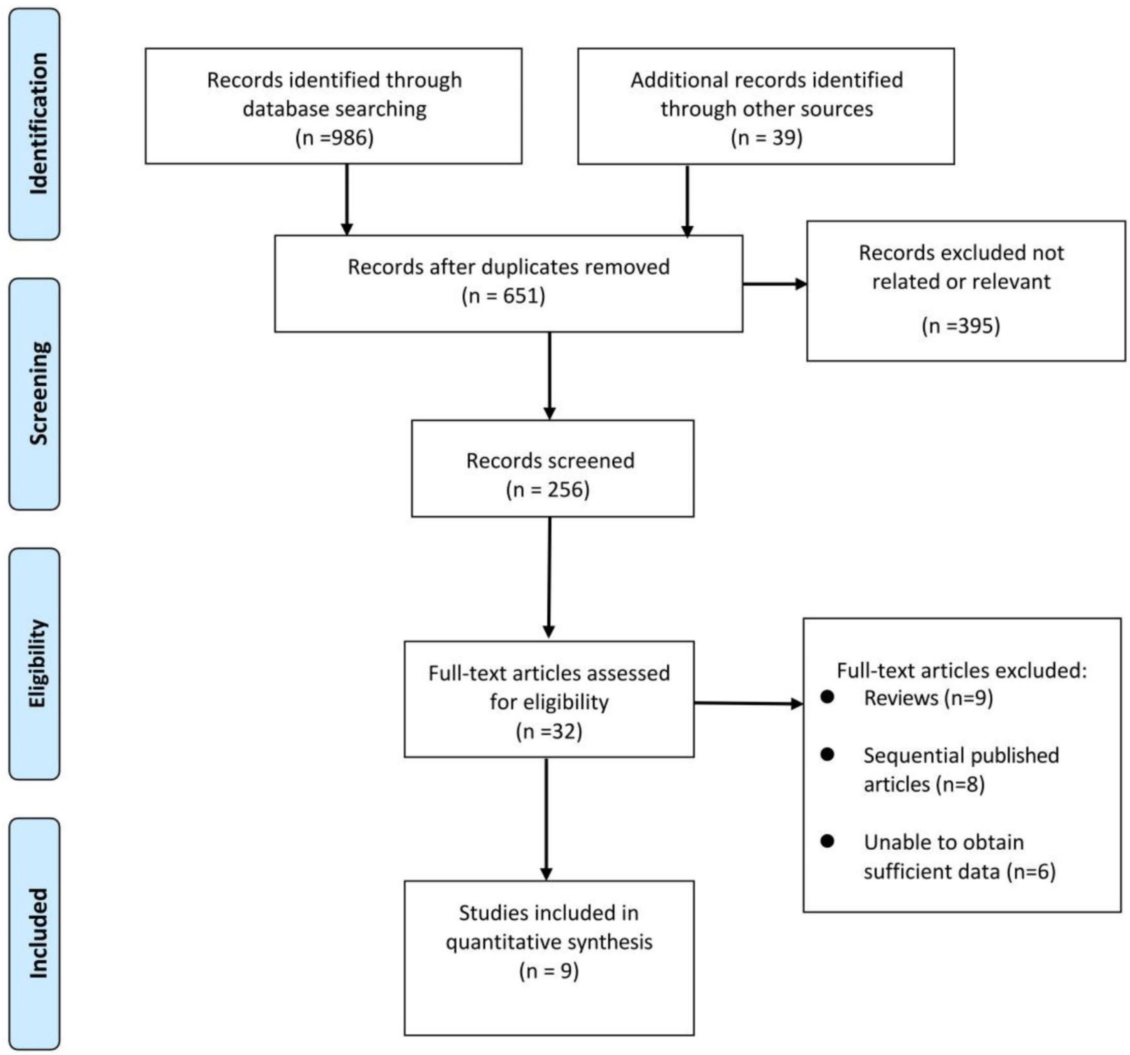

Fig. 1 Selection process of included studies

Korea. All studies employed a retrospective cohort design to investigate the relationship between different types of total joint arthroplasty (TJA)—namely, hip and knee arthroplasty—and subsequent infection rates, either SSIs or PJIs. In terms of sample size, the studies vary significantly, ranging from as few as 75 to as many as 114,379 subjects. This disparity in sample size adds a layer of heterogeneity that may be important for the interpretation of the ORs and their associated 95% CIs. The OR values across the studies notably varied as well, extending from 1.38 to 34.8. Likewise, the corresponding 95% CIs display a wide range, indicating differing levels of precision and reliability among the studies (Table 1).

Results of quality assessment

Each study included in our meta-analysis underwent a rigorous evaluation of its methodological integrity via the NOS. On this scale, a subset of two studies attained

Table 1 Characteristics of studies included in the meta-analysis

Author	Year	Research Design	Country	Joint Replacement Type	Infection Type	Sample Size	OR Value	95% CI
Hijas-Gomez et al.	2020	Retrospective Cohort	Spain	Hip Arthroplasty	SSI	18,808	34.8	2.14–565.10
Ryan et al.	2018	Retrospective Cohort	USA	Hip Arthroplasty; Knee Arthroplasty	SSI; PJI	48,751; 7,966	2.47; 3.10; 1.92; 1.60	1.88–3.24; 1.84–5.25; 1.44–2.55; 0.81–3.18
Haro-Gomez et al.	2018	Retrospective Cohort	Mexico	Hip Arthroplasty	SSI	75	6.12	1.17–31.87
Roche et al.	2018	Retrospective Cohort	USA	Knee Arthroplasty	SSI	114,379	2.72	2.60–2.84
Blevins et al.	2018	Retrospective Cohort	USA	Total joint arthroplasty	PJI	8,796	4.69	2.42–9.08
Kamath et al.	2017	Retrospective Cohort	USA	Knee Arthroplasty	SSI; PJI	4,551	2.48; 3.79	1.74–3.53; 2.31–6.21
Courtney et al.	2016	Retrospective Cohort	USA	Total joint arthroplasty	PJI	670	18.75	3.57–98.29
Morey et al.	2016	Retrospective Cohort	Korea	Knee Arthroplasty	PJI	3,169	1.38	0.30–6.36
Yi et al.	2015	Retrospective Cohort	USA	Total joint arthroplasty	PJI	375	5.85	1.31–26.05

"SSI" signifies Surgical Site Infection, while "PJI" represents Periprosthetic Joint Infection

"OR Value" is the Odds Ratio, capturing the relationship between exposure and outcome

"95% CI" is the 95% Confidence Interval, delineating the range in which the true effect size is likely to reside

Table 2 The quality assessment according to Newcastle-Ottawa Scale of each cohort study

Study	Selection				Comparability	Outcome			Total score
	Representativeness of the exposed cohort	Selection of the non -exposed cohort	Ascertainment of exposure	Demonstration that outcome	Comparability of cohorts	Assessment of outcome	Was follow-up long enough	Adequacy of follow up of cohorts	
Hijas-Gomez et al.	★	★	★	★	★★	★	★	★	9
Ryan et al.		★	★	★	★★	★	★	★	8
Haro-Gomez et al.	★	★		★	★	★	★	★	7
Roche et al.	★	★	★	★	★★	★		★	8
Blevins et al.	★	★	★	★	★★	★	★	★	9
Kamath et al.	★	★	★	★	★	★	★	★	8
Courtney et al.	★	★	★	★	★★	★	★	★	9
Morey et al.	★	★		★	★	★	★	★	7
Yi et al.	★	★	★	★	★★	★	★	★	9

a score of 7, another triad of studies achieved an 8-point rating, and a quartet of studies garnered the highest score of 9. No included studies implemented blinding protocols or exhibited evidence of allocation concealment. Likewise, an assessment of potential funding biases yielded no discernible imbalances among the studies considered. Notably, none of the studies were found to have incomplete outcome data, premature study termination bias, or baseline characteristic imbalances. The compiled risks of bias along with their corresponding ratios are systematically consolidated and presented in Table 2.

Meta-analysis of malnutrition as a risk factor for postoperative SSI

We conducted a meta-analysis of five studies exploring the relationship between malnutrition and the incidence of postoperative SSI following TJA. Heterogeneity testing revealed moderate heterogeneity among the included studies ($I^2=0.0\%$, $p=0.592$). Given this outcome, a fixed-effects model was deemed appropriate for the pooled analysis. The consolidated findings indicate a statistically significant association between malnutrition and elevated risk for developing SSI post-TJA. Compared to the well-nourished population, individuals with malnutrition demonstrated a higher likelihood of postoperative SSI, with an OR of 2.60 and a 95% CI ranging from 2.10 to 3.10 ($p=0.592$). It is noteworthy that the risk of postoperative SSI in malnourished patients was 2.6 times greater than that in their well-nourished counterparts. This underlines malnutrition as a significant risk factor for the onset of SSI following TJA (Fig. 2).

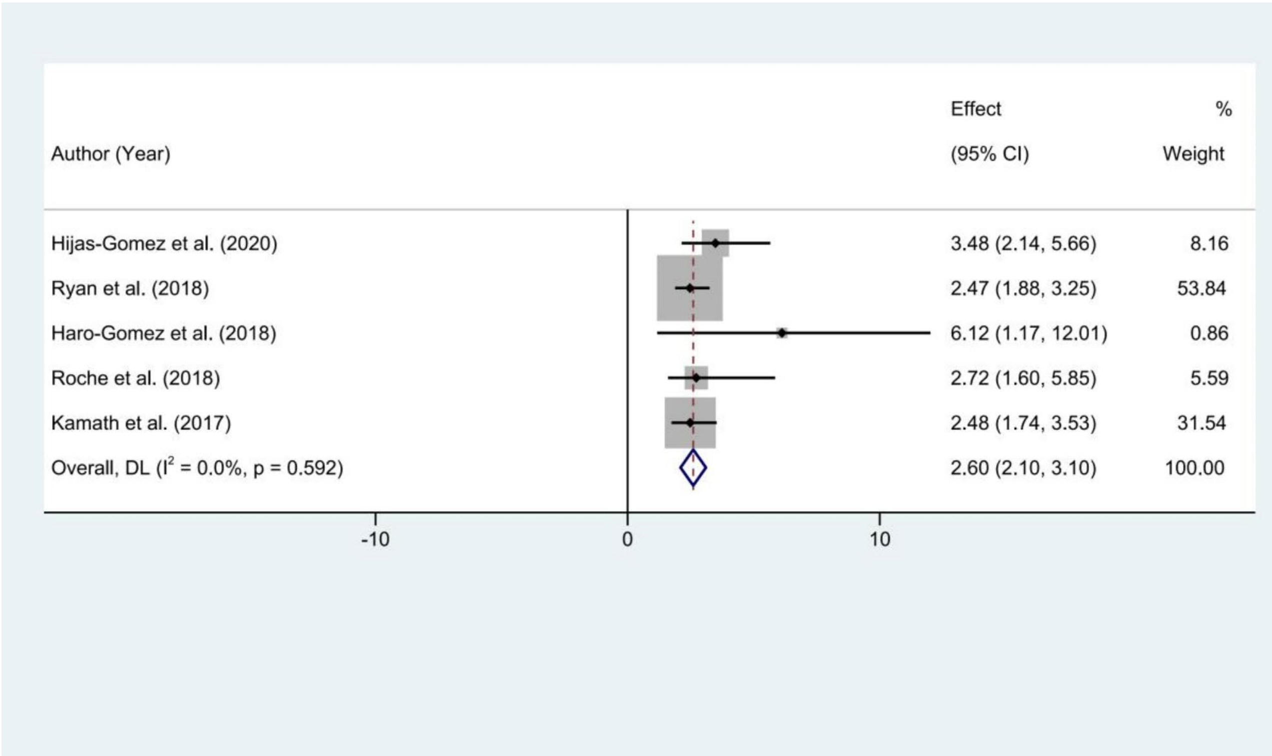

Fig. 2 Forest plots of malnutrition as a risk factor for postoperative surgical site infections

Meta-analysis of malnutrition as a risk factor for postoperative PJI

In accordance with the principles of rigorous meta-analysis, we conducted an integrated analysis of six studies evaluating the association between malnutrition and the incidence of postoperative PJI after TJA. A test for heterogeneity revealed moderate levels of heterogeneity across the studies ($I^2=0.0\%$, $P=0.422$). Consequently, a fixed-effects model was chosen for meta-analytic synthesis. Our results demonstrated a significant increase in the risk of postoperative PJI in malnourished patients compared to well-nourished cohorts. Specifically, the OR for the occurrence of PJI in malnourished patients was calculated to be 3.44, with a 95% CI ranging from 2.35 to 4.53 ($p=0.422$). This robust finding underscores malnutrition as a notable risk factor for PJI following joint replacement surgeries, lending quantifiable support to the call for preoperative nutritional assessment and intervention (Fig. 3).

Publication bias

In assessing the validity and robustness of our meta-analytic findings, we employed funnel plots to scrutinize the potential existence of publication bias. Symmetry observed in these plots (Fig. 4) offered initial reassurance of minimal bias. Further statistical validation was achieved using Egger's linear regression test, which failed to identify any statistically significant publication bias across diverse variables ($P>0.05$ in all cases). This absence of publication bias substantiates the robustness and reliability of our synthesized findings.

Discussion

SSIs and PJIs are two significant complications that arise post-TJA, which are closely related to the nutrition status, comorbidities, and smoking history of patients [4–6]. The associated morbidity and increased healthcare expenditure emphasize the importance of identifying modifiable risk factors that could mitigate these postoperative complications [4, 31]. Previous study revealed that the preoperative Controlling Nutritional Status (CONUT) score, which is calculated based on serum albumin, total cholesterol concentration, and total lymphocyte count, was found to be an independent risk factor for postoperative complications, highlighting the potential connection of malnutrition and postoperative complications [32]. Our meta-analysis rigorously evaluated the role of malnutrition as a risk factor for both SSI and PJI, yielding compelling evidence. For SSI, a pooled analysis of five studies revealed a 2.6-fold increase in risk among malnourished patients (OR=2.60; 95% CI: 2.10–3.10). Similarly, six studies were assessed for PJI, revealing an odds ratio (OR) of 3.44 (95% CI: 2.35–4.53). These findings are aligned with current pathophysiological understandings of infection mechanisms.

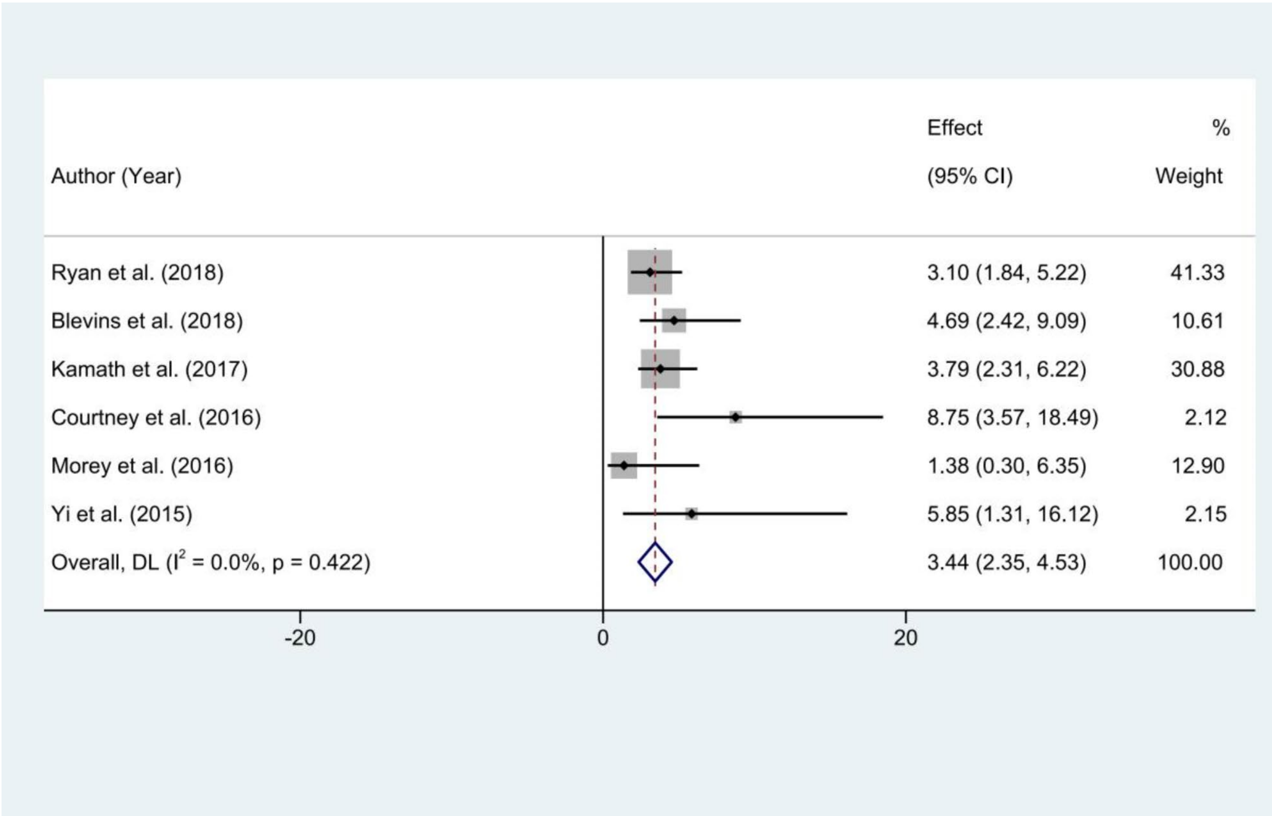

Fig. 3 Forest plots of malnutrition as a risk factor for postoperative periprosthetic joint infections

Malnutrition, including deficiencies in carbohydrates, proteins, fats, vitamins, and minerals, can perturb metabolic processes, thereby hampering the wound healing cascade [14]. Adequate nutritional status underpins a robust immune system that relies on a sufficient lymphocyte count to neutralize pathogens. Malnutrition contributes to reduced lymphocyte counts, elevating susceptibility to infections [31, 33]. Furthermore, malnutrition impairs collagen synthesis and fibroblast proliferation due to insufficient protein reserves, and decreased albumin levels exacerbate tissue edema and reduce oxygen tension. These deficits collectively compromise wound healing and the skin's protective barrier against underlying tissue colonization by pathogens, thereby amplifying the risk of SSIs [23]. Nutritional status is often evaluated through various measures, including serological tests, anthropometric measures, and standardized scoring systems. While anthropometric parameters such as calf and arm muscle circumference provide useful insights, the lack of standardized cut-off values limits their utility in clinical research. Standardized scores such as the Mini Nutritional Assessment and the Rainey-MacDonald Nutritional Index incorporate measures such as anthropometry, activity levels, cognitive states, self-reported health, and nutritional perception to gauge malnutrition [34]. Prevalent markers for malnutrition in the current research are a lymphocyte count $< 1500/mm^3$, albumin < 3.5 g/dl, transferrin < 200 mg/dl, and zinc levels < 95 μg/dl. While our meta-analysis highlights the significant association between malnutrition and increased rates of postoperative SSIs and PJIs following TJA, it is important to consider the role of nutritional interventions in mitigating these risks. Several studies have investigated the impact of preoperative nutritional supplementation on postoperative outcomes in TJA patients [35]. These findings support the potential benefits of targeted nutritional interventions in this patient population. In the context of our current study, the strong association between malnutrition and postoperative infections underscores the importance of identifying and addressing malnutrition preoperatively.

The consensus in the clinical community recommends the use of protein-enriched supplemental drinks and increased caloric intake as part of the preoperative regimen. These interventions are designed to elevate the levels of essential amino acids and micronutrients in the bloodstream, thus bolstering the immune response and wound healing capabilities. These supplements often contain a balanced profile of essential amino acids, including branched-chain amino acids (BCAAs), which are critical for muscle preservation and immune system function. Some formulations also include micronutrients

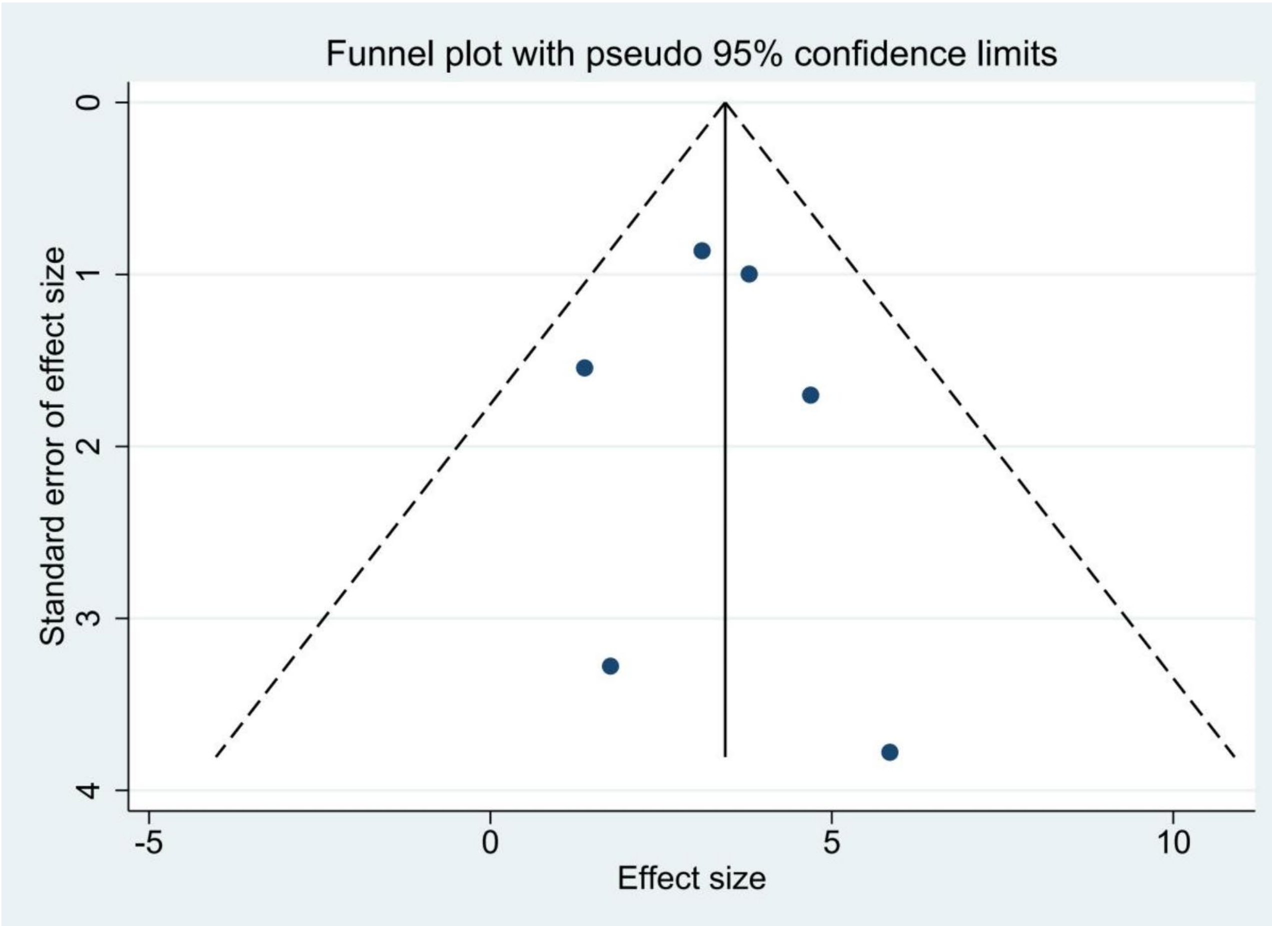

Fig. 4 Funnel plot for assessing publication bias in all included studies

such as zinc and vitamin C, which are pivotal in collagen synthesis and immune function [34, 36]. A carefully calibrated increase in caloric intake is advised to sustain the body's energy requirements during the stressful postoperative phase. This usually involves not just an increase in calories but a focus on the quality of those calories. High-quality fats (such as omega-3 fatty acids) and low-glycemic-index carbohydrates are often recommended to avoid any adverse metabolic effects.

This study faces several limitations that restrict its generalizability and interpretive scope. Primarily, the small sample size and lack of demographic diversity compromise the applicability of the findings to the broader population. Second, the absence of random participant selection introduces potential selection bias, weakening the study's external validity. Furthermore, the short duration of the follow-up period limits insights into long-term outcomes, particularly concerning the efficacy of preoperative nutritional interventions. Last, the study's reliance on self-reported data for nutritional intake raises questions about the accuracy and reliability of such information, as there is a potential for underreporting or overreporting. While our study combined THA and TKA into a single cohort to achieve sufficient statistical power, future research should also consider separate analyses for THA and TKA to better understand the specific effects of malnutrition on each procedure.

Conclusions

In conclusion, our meta-analysis demonstrates that malnutrition is significantly associated with increased rates of SSIs and PJIs following TJA. The findings strongly advocate for the implementation of preoperative optimization strategies targeted at malnourished patients to minimize these postoperative complications. Surgeons and internists should conduct thorough nutritional assessments, implement structured nutritional interventions, and collaborate with a multidisciplinary team to develop and monitor these plans. Additionally, patient education on the importance of adequate nutrition before and after surgery, along with close postoperative monitoring, can further enhance outcomes. These practical recommendations aim to reduce the risk of postoperative complications in malnourished patients undergoing TJA.

Further research is necessary to confirm these results and refine intervention approaches.

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All contributors are listed as author in the present study.

Author contributions
Yuxin Chen: Design, collection and analysis of data, literature review, writing the original draft. Wenzhu Chen: Responsible for the overall design, supervision, manuscript writing and revision, and provides interpretation and discussion of the final results. All authors read and approved the final manuscript.

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Data availability
No datasets were generated or analysed during the current study.

Declarations

Competing interests
The authors declare that there is no conflict of interest.

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