Systematic Review and Meta-Analysis

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Correlation between Body Mass Index and Periprosthetic Joint Infection following Total Joint Arthroplasty

A protocol for systematic review and meta analysis

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Abstract

Background: Despite rapid reports on the correlation between body mass index (BMI) and periprosthetic joint infection (PJI) after total joint arthroplasty, some have conducted regression tests or meta-analyses with controversial results. In this study, we systematically meta-analyzed relevant trials and carefully evaluated the correlation for verification.

Methods: Literature on the correlation between BMI and PJI following total joint arthroplasty was retrieved in PubMed, Embase and Cochrane Library due September 2019. Stata 13.0 software was adopted for data synthesis and analyses of publication bias and sensitivity. Random-effect models were used to summary the overall estimate of the multivariate adjusted odds ratio (OR)/hazard ratio/rate ratio with 95% confidence intervals (CIs).

Results: A total of 29 observational studies representing 3,204,887 patients were included. The meta-analysis revealed that the risk of postoperative PJI significantly increased by 1.51 times in the obese group (OR = 1.51; 95% CI = 1.30–1.74 for the obese group *vs.* the non-obese group), and by 3.27 times in the morbid obese group (OR = 3.27; 95% CI = 2.46–4.34 for the morbid obese group vs the non-morbid obese group). A significant association remained consistent, as indicated by subgroup analyses and sensitivity analyses.

Conclusion: Our findings demonstrate that postoperative PJI is positively correlated with BMI, with obese patients showing a greater risk of developing PJI than non-obese patients. Similarly, morbid obese patients present a higher risk of PJI than non-morbid obese patients. However, this conclusion needs to be corroborated by more prospective studies.

Abbreviations: BMI = body mass index, CI = confidence interval, OR = odds ratio, PJI = periprosthetic joint infection, TJA = total joint arthroplasty, TSA = total shoulder arthroplasty.

Keywords: Body mass index, periprosthetic joint infection, systematic review, total joint arthroplasty

Editor: Qinhong Zhang.

Supported by the Natural Science Foundation of China (81704101) from the Ministry of Science and Technology of the P.R. China, and the Natural Science Foundation of Guangdong (2015A030313353) and the Science and Technology Project of Guangdong (2013A032500009) from the Bureau of Science and Technology of Guangdong Province, P.R. China.

All data supporting our findings are contained in the manuscript.

All analyses were based on previous published studies, no ethical approval and patient consent were required thereby.

All authors agree to publish this study.

The authors have no conflicts of interest to disclose.

All data generated or analyzed during this study are included in this published article [and its supplementary information files].

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How to cite this article: Xu JL, Liang ZR, Xiong BL, Zou QZ, Lin TY, Yang P, Chen D, Zhang QW. Correlation between Body Mass Index and Periprosthetic Joint Infection following Total Joint Arthroplasty: a protocol for systematic review and meta analysis. Medicine 2020;99:24(e20549).

Received: 19 November 2019 / Received in final form: 10 April 2020 / Accepted: 4 May 2020

http://dx.doi.org/10.1097/MD.0000000000020549

1. Introduction

Total joint arthroplasty (TJA) is a successful and cost-effective elective surgical intervention that is widely used to treat disabling joint pain mainly caused by osteoarthritis. Periprosthetic joint infection (PJI) as 1 of the main complications following TJA has attracted more solicitous attentions from orthopedic surgeons. Though PJI affects 0.5% to 1.2% of primary total hip arthroplasties, it still remains a major complication that is associated with high morbidity and healthcare expenditure[1]–for example the mortality in elderly patients can reach 8% due to the infection following joint arthroplasties[2,3]. There is a pressing need to facilitate the prevention of PJIs and its risk factors.

Obesity as a high risk of osteoarthritis has a prevalence of over 60% in patients undergoing TJA[4,5]. Some studies have further graded the severity of obesity, showing that morbid obesity and super obesity are strongly associated with postoperative complications compared with milder forms[6,7].

Lately, though the correlation between body mass index (BMI) and PJI following TJA have been reported by many, they have yielded inconsistent results. This may attribute to the small sample size and univariate analyses unadjusted for confounders in some meta-analyses[8–10] despite their conclusion of an uncertain correlation. In this study, we retrieved the published studies on PJI after TJA, extracted high-relevant multi-factor data with adjustment for confounders for the subsequent systematic review and meta-analyses, and evaluated the significance of the BMI, aiming at paving the way for the prevention and treatment of this complication.

2. Methods

2.1. Search strategies

This study was executed in line with the guidelines of the Preferred Reporting Items for Systematic Reviews and Meta-Analyses[11] and reported based on the guidelines developed by the Meta-Analysis of Observational Studies in Epidemiology group[12]. Because all the analyses were performed on the basis of previous published studies, no ethical approval or informed consent was required. In the initial screening, 2 investigators (J-LX and B-LX) independently conducted the main search in the electronic databases of PubMed, Embase and Cochrane Library to retrieve eligible articles on the correlation between BMI and PJI after TJA from the inception of the databases to September 2019, without restrictions to languages, publication types or regions. The combined terms of medical subject headings and non- medical subject headings were searched as follows: "Arthroplasty, Replacement", "Arthroplasties, Replacement", "Joint Prosthesis Implantation", "Implantation, Joint Prosthesis", "Implantations, Joint Prosthesis", "Joint Prosthesis Implantations", "Prosthesis Implantation, Joint", "Prosthesis Implantations, Joint", "Replacement Arthroplasty", "Joint Replacement", "Joint Replacements", "Replacement, Joint", "Replacements, Joint", "Replacement Arthroplasties", "Total Joint Replacement", "Joint Replacement, Total", "Joint Replacements, Total", "Replacement, Total Joint", "Replacements, Total Joint", "Total Joint Replacements", "Prosthesis-Related Infections", "Prosthesis Related Infections", "Infections, Prosthesis-Related", "Prosthesis-Related Infection", "PJI", "periprosthetic joint infection", "prosthetic joint infections", "periprosthetic infections", "infection of joint", "joint infection", "Body Mass Index", "Index, Body Mass", "Quetelet Index", "Index, Quetelet", "Quetelet's Index", "Quetelets Index", "Obesity", "fat" and "Obese". A third investigator irrelevant to the initial procedure was consulted in case of any discrepancy.

2.2. Study selection criteria

Two independent investigators (J-LX and Z-RL) analyzed the initially selected articles to verify their relevance with the topic of BMI and PJI after TJA. The following items of inclusion criteria should be considered:

(1) participants were selected without limitations to regions, ages or social status;
(2) studies (except for reviews) had sufficient original data to describe the correlation between BMI and PJI after TJA;
(3) studies based on either case-control, cross-sectional, or retrospective or prospective design.
(4) Trials were excluded as with the following identifications: duplicate or overlapping data, animal experiments, conference abstracts, letters and review articles.

In case of any disagreement the results were discussed and unified by senior authors.

2.3. Data extraction

Data from the included studies were extracted and independently categorized by 2 authors (X-BL and Q-ZZ) using a predefined data extraction form. All disagreements were resolved by discussions. Design information, baseline population characteristics (mean age, sample size and country), surgical approaches, risk factors from all included studies were stratified into a standardized evidence table. All data were rechecked to ensure accuracy. Study selections were shown in a the Preferred Reporting Items for Systematic Reviews and Meta-Analyses flow diagram (Fig. 1).

2.4. Methodological quality assessment

The methodological quality of the included studies was evaluated by 2 independent reviewers (J-LX and T-YL) based on the items of modified Newcastle-Ottawa Scale[13], comprising patient selection, study group comparability and outcome assessment. The observational studies scored 0 to 9. Distinct opinions were discussed among the authors.

2.5. Statistical analysis

The meta-analysis and statistical analysis were performed using Stata 13.0 software (Stata Corp). The odds ratio (OR) and 95% confidence interval (CIs) were calculated. The *I*-square (I^2) test was adopted to evaluate the influence of heterogeneity on the output of the meta-analysis. I^2 values of 0%, 25%, 50%, and 75% represented no, low, medium and high heterogeneity, respectively. Heterogeneity was tested using Cochran *Q* statistic and the I^2 metric: a $I^2 > 25\%$ was the cutoff of significant heterogeneity, and a fixed-effect model was used when a $I^2 < 25\%$; otherwise, a random-effect model was preferred[14]. A *P* value of less than .05 was accepted as statistical significant. A sensitivity analysis[15] was conducted by excluding 1 study at a time to evaluate the quality and consistency of the results. Egger and Begg linear regression tests for publication bias were carried out. Subgroup analyses were performed according to different countries, study designs, operation methods and different grades of BMI.

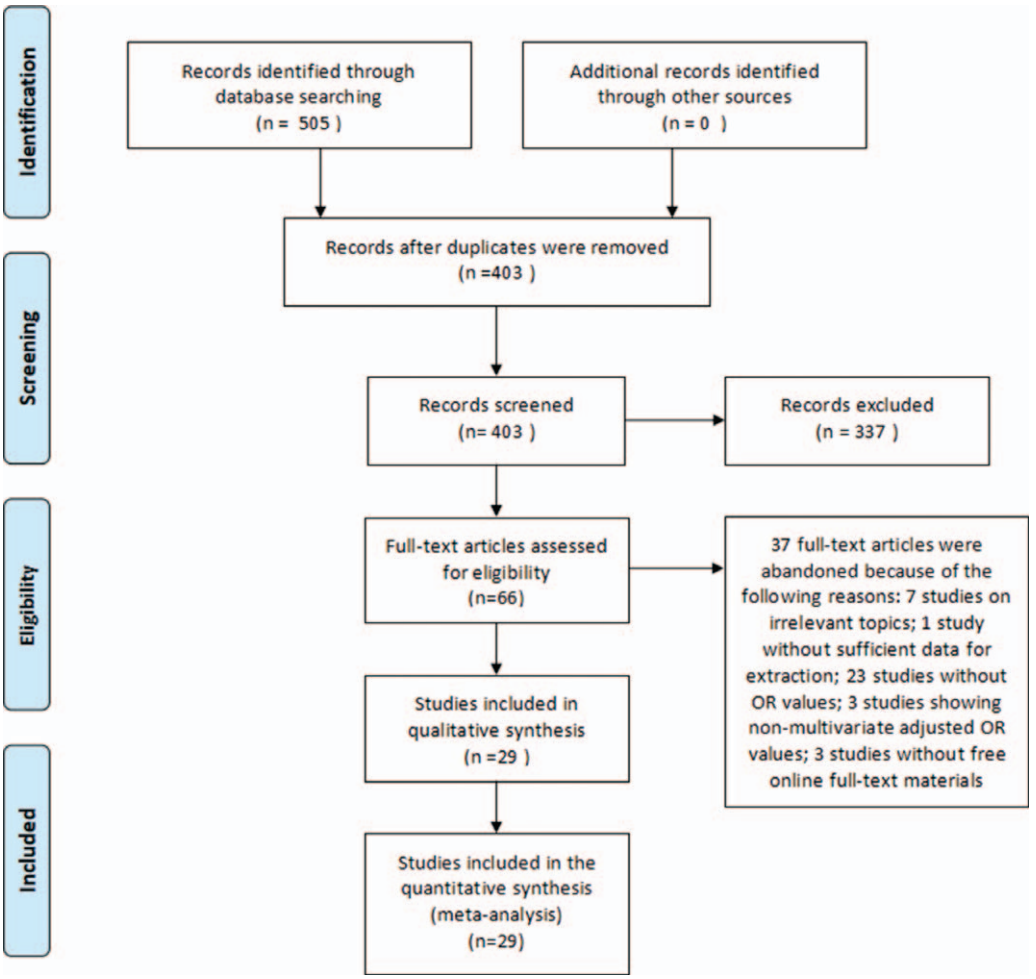

Figure 1. The flow diagram of literature search and selection.

3. Results

3.1. Study selection process

As a result, 505 references were initially retrieved, 403 were left after eliminating duplicate literature; and then 337 without high-relevant to our topic were discarded by reading titles and abstracts, and 66 studies remained. Finally, 37 full-text articles were abandoned because of the following reasons: 7 studies on irrelevant topics; 1 study without sufficient data for extraction; 23 studies without OR values; 3 studies showing non-multivariate adjusted OR values; 3 studies without free online full-text materials. Therefore, 29 observational studies representing 3,204,887 patients were included in the meta-analysis. The flow chart describing the selection process was shown in Fig. 1.

3.2. Study characteristics and methodological quality

The 29 included references encompassed retrospective cohort, retrospective case-control, prospective cohort, and prospective case-control studies, with the publication years differing from 2008 to 2019. Two were conducted in China (including 1 in Taiwan), 17 in the United States, 2 in New Zealand, Finland, and England and Wales, and 1 in Switzerland, Germany, Australia and Spain, respectively. In the selected clinical trials, the sample size varied between 236 and 871,058. The basic characteristics of these studies were summarized in Table 1. In addition, all studies were evaluated as high methodological quality in accordance with the the Newcastle-Ottawa Scale scores.

3.3. Overall meta-analysis

3.3.1. Obesity vs. non-obesity. Of the 29 included studies, 20 reported[16–18,20–25,27–31,35,38,40–42] the correlation between BMI (obesity *vs.* non-obesity) and PJI following TJA. The meta-analysis revealed that the risk of PJI after TJA significantly increased by 1.51 times in the obese group ($OR = 1.51$; 95% CI = 1.30–1.74), with high heterogeneity ($I^2 = 78.6\%$, $P = .000$; Fig. 2). Thus, subgroup analyses were conducted to investigate the underlying factors that could substantially affect the between-study heterogeneity.

3.3.2. Morbid obesity vs. non-morbid obesity. Data from 14 studies[16–19,22,26,29,35–38,40,41,44] on morbid obesity *vs.* non-morbid obesity were available for the meta-analysis. It was found that the risk of PJI after TJA significantly boosted by 3.27 times in the morbid obese group ($OR = 3.27$; 95% CI = 2.46–4.34), with medium heterogeneity($I^2 = 69.0\%$, $P = .000$; Fig. 3). Thus, subgroup analyses were conducted to investigate the potential factors that could substantially affect the between-study heterogeneity.

Table 1

Characteristics of the Included Studies.

Included studies	Study design	Country	Study characteristics	Study period	Factors	Operation type
George J 2017[16]	Retrospective cohort	The United States	57265 males, Unclear	2011–2015	Age, sex, ASA, functional status (independent vs partially/totally dependent), smoking, BMI, anesthesia (general vs others), congestive heart failure, chronic obstructive pulmonary disease, diabetes mellitus, disseminated cancer, dialysis, corticosteroid use, and recent weight loss	TKA
Lubbeke A 2016[17]	Retrospective cohort	Switzerland	3533 males, 18–96 y	1996–2013	Age, sex, ASA scores (ASA 1–2 vs 3–4), presence of diabetes, smoking status, etiology of osteoarthritis (primary vs secondary), site of arthroplasty, use of antibiotic-laden cement, and length of operation	THA/TKA
Wagner ER 2016[18]	Prospective cohort	The United States	8354 males, 11–103 y	1985–2012	Age, sex, primary diagnosis, and surgical indication	THA
Baier C 2019[19]	Retrospective cohort	Germany	784 males, 62–75 y	2007–2010	Postoperative bleeding/hematoma, postoperative wound healing disorder, Ahlback's disease, duration of surgery $>$ 180 min, preexisting phenprocoumon therapy, Adiposity $>$ 40 kg/m^2, chronic skin disease, regular smoking, postoperative stay at a certain ward (ward A), male gender, revision following primary, surgery (but not due to surgical surface infection), antibiotic therapy pre-or postoperatively, postoperative blood transfusion	TKA
Jamsen E 2010[20]	Retrospective cohort	Finland	1863 males, 35–97 yr	2002–2006	Sex, diagnosis, and ASA risk scores	TKA
Salt E 2017[21]	Retrospective case-control	The United States	1081 males, 59.8±10.2 yr	2007–2009	Gender, race, replacement surgery location, follow-up (days), cancer, lupus, immunodeficiency condition, HIV/AIDS, diabetes, obesity, gout, perioperative prednisone use, perioperative immunosuppressive medication use, and diagnosis of RA or OA	THA/TKA/TSA
Dowsey MM 2009[22]	Prospective cohort	Australia	449 males, 65–77 yr	1998–2005	Cardiovascular disease, diabetes mellitus, respiratory, smoking, obese, morbidly obese, RA, transfusion, drain tube, antibiotic cement, gender (male), age	TKA
Althoff A 2017[23]	Retrospective cohort	The United States	Unclear	2005–2012	Age, male gender, time of procedure, obesity, low BMI, tobacco use, alcohol abuse, inflammatory arthritis, depression, hypercoagulable disorder, diabetes mellitus, hyperlipidemia, hypertension, peripheral vascular disease, congestive heart failure, coronary artery disease, chronic kidney disease, lung disease, liver disease, current hemodialysis use, hypothyroidism, preoperative anemia	TAA
Bozic KJ 2012[24]	Retrospective case-control	The United States	Unclear	1998–2007	Age, sex, race, census region, public assistance (indicated by Medicare premiums and deductibles that were subsidized by the state because of the patient's financial status), and all other baseline comorbidities	THA
Bozic KJ 2012[25]	Retrospective case-control	The United States	Unclear	1998–2007	Age, gender, race, census region, receipt of public assistance (identified by Medicare buy status for patients whose Medicare premiums and deductibles were subsidized by the state as a result of their financial status), and all other baseline comorbidities	TKA
Pulido L 2008[26]	Retrospective cohort	The United States	3882 males, 14–97 yr	2001–2006	BMI, ASA, simultaneous bilateral surgery, TKA, allogenic blood transfusion, postoperative atrial fibrillation, postoperative myocardial infarction, postoperative urinary infection, longer hospital stay	THA/TKA
Tornero E 2015[27]	Retrospective cohort	Spain	700 males, 64–77 yr	2010–2013	Demographics (age and gender), comorbidities (having or not having one of the following entities: hypertension, diabetes mellitus, malignancy, liver disease, lung disease, or chronic renal failure), BMI, drug allergies, preoperative performance status (measured by the American Association of Anesthesiology (ASA) classification), laterality, type of implant (TKA or THA), duration of surgery, duration (in days) of hospitalization, preoperative and postoperative (day 4) hemoglobin value, and the need for red blood cell transfusion	THA/TKA

(*continued*)

Table 1

(continued).

Included studies	Study design	Country	Study characteristics	Study period	Factors	Operation type
Triantafyllopoulos GK 2018[28]	Retrospective cohort	The United States	20497 males, 64.44±12.49 yr	1999-2013	Age, gender, coronary artery disease, coagulopathy, diabetes, hypertension, obesity, pulmonary disease, pulmonary hypertension, renal disease, and sleep apnea	THA
Meller MM 2016[29]	Retrospective cohort	The United States	219133 males, ≥65 yr	2011–2013	Patient demographics, morbidity, and institutional factors	TKA
Lenguerrand E 2018[30]	Prospective cohort	England and Wales	250997 males, average 68 yr	2003–2013	Age, sex, ASA grade, and BMI	THA
Lenguerrand E 2019[31]	Prospective cohort	England and Wales	292963 males, 63–76 yr	2003–2014	Age, sex, ASA grade, and BMI	TKA
Morris BJ 2014[32]	Prospective cohort	The United States	Unclear, 18–93 yr	2004–2011	Age, sex, smoking,diabetes, RA, BMI, and history of prior failed hemiarthroplasty or TSA	RSA
Bozic KJ 2014[33]	Retrospective case-control	The United States	323 males, > 65 yr	1990–2011	Age, gender, and race	TKA
Meller MM 2016[34]	Retrospective cohort	The United States	147989 males, > 65 yr	2010–2014	Age, sex, race, resident census region, economic status using state Medicaid buy-in as a proxy, and overall health status as captured by the CCI.	THA
Scully W 2019[35]	Retrospective cohort	The United States	42265 males, Unclear	2011–2015	Age, sex, race, ASA, functional status (independent *vs.* partially/totally dependent), smoking status, anesthesia (general versus others), congestive heart failure, chronic obstructive pulmonary disease, diabetes mellitus, on dialysis, disseminated cancer, corticosteroid use, and recent weight loss	THA
Smith OJ 2018[36]	Retrospective cohort	New Zealand	42957 males, Unclear	2000–2014	Gender, diagnosis of RA, BMI, ASA grade, theater, approach, articulation, sector, primary surgeon	THA
Maoz G 2014[37]	Retrospective cohort	The United States	1685 males, Unclear	2009–2011	Age, gender, Nonsame-day surgery, diabetes complications, revision surgery, ASA score, Hemiarthroplasty, BMI, operating time, staphylococcus aureus colonization, caseload, active tobacco use, use of blood product	THA
Jamsen E 2012[38]	Retrospective cohort	Finland	2593 males, 26.4–97.1 yr	2002–2008	Age, sex, ASA risk score, arthroplasty site (hip or knee), BMI, and diabetic status	THA/TKA
Namba NS 2013[39]	Retrospective cohort	The United States	20797 males, 67.4±9.6 yr	2001–2009	Age, gender, race, diabetes, BMI, ASA score, diagnosis, hospital/surgeon characteristics, hospital volume, procedure characteristics, exposure, infection prophylaxis	TKA
Gupta A 2015[40]	Prospective case-control	The United States	330 males, 26–95 yr	2001–2006	Sex and age	THA/TKA
Jung P 2017[41]	Retrospective cohort	New Zealand	Unclear, averaged 70 yr	2013–2015	Age, gender, ASA, BMI	THA/TKA
Kuo FC 2019[42]	Retrospective cohort	China Taiwan	46 males, Unclear	2005–2013	BMI, diabetes, allograft use, extended postoperative prophylactic antibiotics	TKA
Xu C 2018[43]	Retrospective case-control	China	432 males, Unclear	2008–2015	CCI, smoking status, alcohol use, diabetes, inflammatory arthritis, liver disease, renal disease, cardiovascular disease, coronary artery disease, chronic pulmonary disease, blood transfusion, operating time and length of stay.	THA/TKA
Wyles CC 2019[44]	Retrospective cohort	The United States	13343 males, 65.2±11.4 yr	2004–2017	Cefazolin usage, BMI, Arthroplasty, ASA score	THA/TKA

THA = total hip arthroplasty, TKA = total knee arthroplasty, TAA = total ankle arthroplasty, RSA = reverse shoulder arthroplasty, TSA = total shoulder arthroplasty, ASA = the American Society of Anesthesiologists, RA = rheumatoid arthritis, BMI = body mass index, CCI = Charlson Comorbidity Index score.

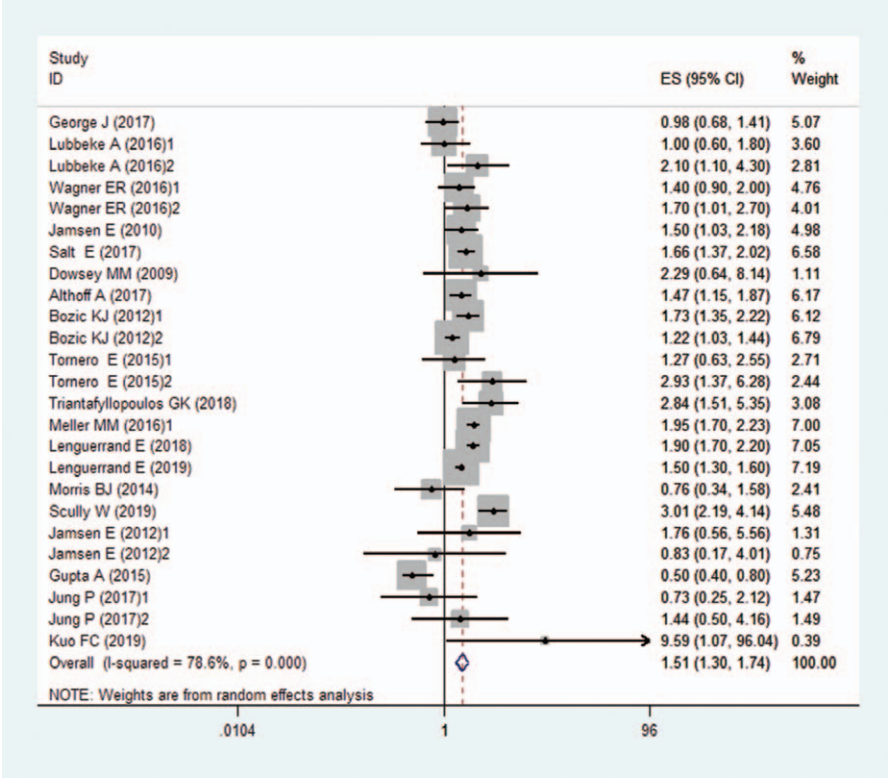

Figure 2. The meta-analysis results of the correlation between BMI (obesity vs non-obesity) and PJI following TJA. BMI = body mass index, PJI = periprosthetic joint infection, TJA = total joint arthroplasty.

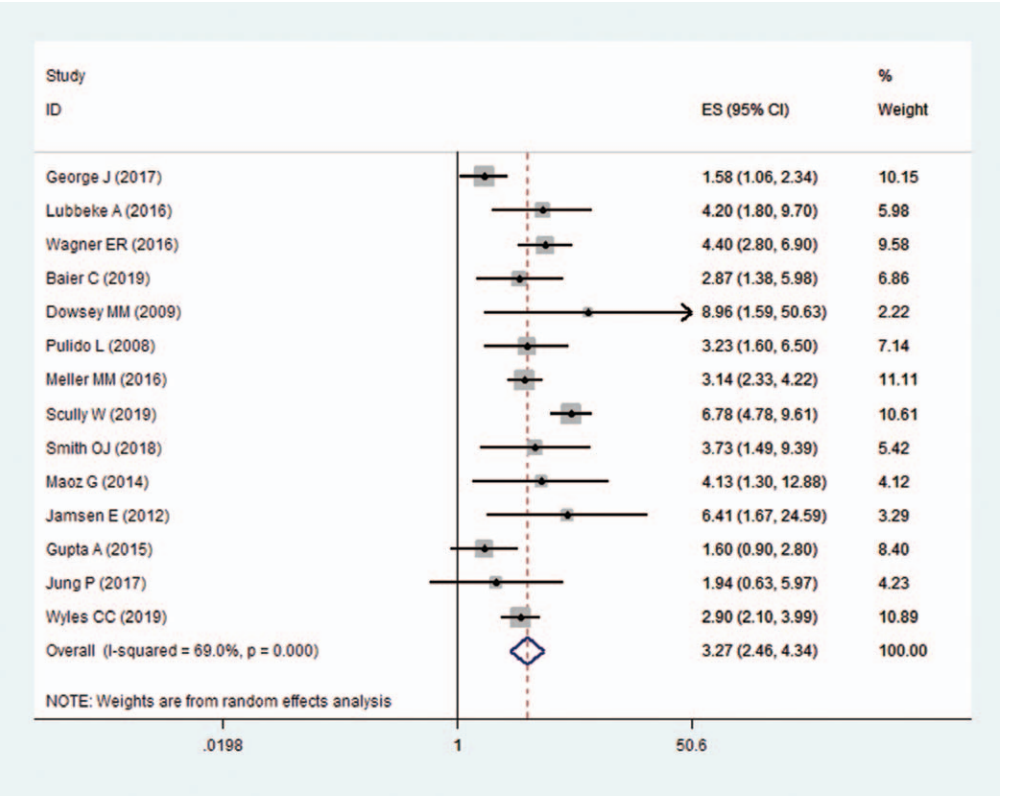

Figure 3. The meta-analysis of the correlation between BMI (morbid obesity vs. non-morbid obesity) and PJI after TJA. BMI = body mass index, PJI = periprosthetic joint infection, TJA = total joint arthroplasty.

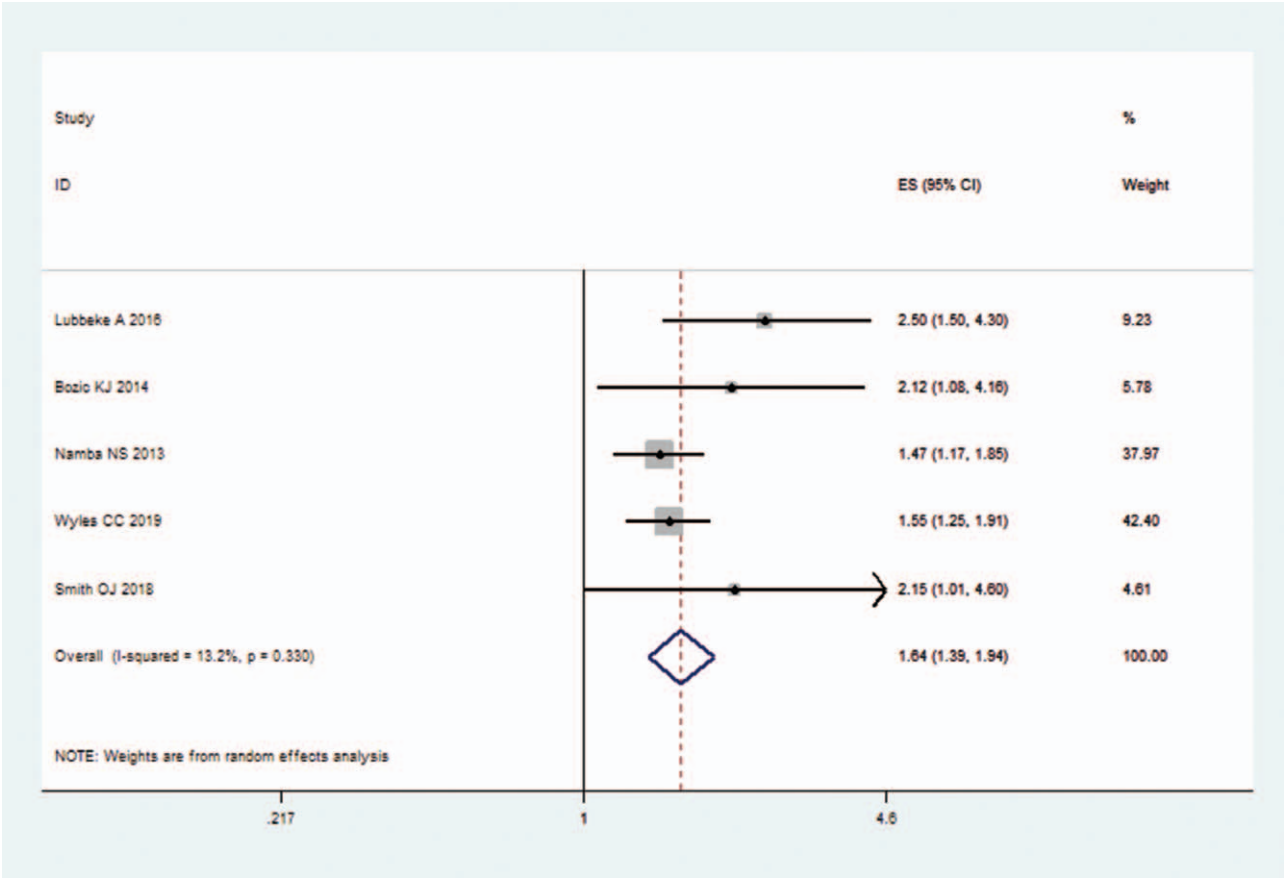

Figure 4. The meta-analysis of the correlation between BMI (BMI ≥ 35 kg/m^2 vs. BMI < 35 kg/m^2) and PJI after TJA. BMI = body mass index, PJI = periprosthetic joint infection, TJA = total joint arthroplasty.

3.3.3. BM≥ 35kg/m^{2}vs. BMI < 35kg/m^2. Data from 5 studies[17,33,36,39,44] on BMI ≥ 35 kg/m^2 vs BMI < 35 kg/m^2 were available for the meta-analysis. The analysis revealed that the risk of PJI after TJA significantly rose by 1.64 times in patients with BMI ≥ 35 kg/m^2 (OR = 1.64; 95% CI = 1.39–1.94), with low heterogeneity (I^2 = 13.2%, P = .330; Fig. 4).

3.3.4. BMI ≥ 50kg/m^{2}vs. BMI 40–50kg/m^2. Data from 2 studies[29,34] on BMI ≥ 50 kg/m^2*vs.* BMI 40–50 kg/m^2 were available for the meta-analysis. It was found that the risk of PJI after TJA significantly increased by 1.68 times in patients with BMI ≥ 50 kg/m^2 (OR = 1.68; 95%CI = 1.25–2.24), with nonsignificant heterogeneity (I^2 = 0%, P = .532; Fig. 5).

3.3.5. Other BMI comparisons. One study[23] reported a comparison between BMI < 19 kg/m^2 and BMI ≥ 19 kg/m^2 (OR = 2.67; 95% CI = 1.07–6.67, P = .019). Another[18] reported a comparison between BMI ≥ 25 kg/m^2 and BMI < 25 kg/m^2 (OR = 1.09; 95% CI = 1.07–1.12, P < .001). One[43] showed a comparison between BMI ≥ 28 kg/m^2*vs.* BMI < 28 kg/m^2 (OR = 2.48; 95% CI = 1.66–3.69, P < .05). And 1 study[34] exhibited a comparison between BMI ≥ 50 kg/m^2*vs.* BMI < 25 kg/m^2 (OR = 1.22; 95% CI = 0.58–2.55, P < .05).

3.4. Subgroup analyses

3.4.1. Subgroup analysis of studies on obesity vs. non-obesity. Subgroup analyses of studies on obesity vs non-obesity were conducted, and the results were summarized in Table 2. When the studies were stratified by BMI, the subgroup analysis showed inconsistencies in the results of comparisons between different BMI intervals. This could attribute to the lack of eligible studies. When the studies were stratified by other factors, the subgroup analysis showed that significant correlations were basically consistent.

3.4.2. Subgroup analysis of studies on morbid obesity vs. non-morbid obesity. The subgroup analysis was conducted, with results listed in Table 3. A statistically significance was observed in the retrospective cohort and prospective cohort studies, but not in prospective case-control studies. When the studies were stratified by the other factors, the subgroup analysis showed that significant correlations remained consistent.

3.5. Sensitivity analyses

The sensitivity analysis was performed to assess whether individual studies would affect the overall results. We evaluated the effect of each study on the methodological quality through the sequential exclusion of single studies. The results showed that there was a nonsignificant difference in the stability of the results (Fig. 6), which validated the rationality and reliability of our analysis.

3.6. Evaluation of publication bias

Egger and Begg analyses of publication bias showed that publication bias did not exist in our meta-analysis (P = .854). (Figs. 7 and 8).

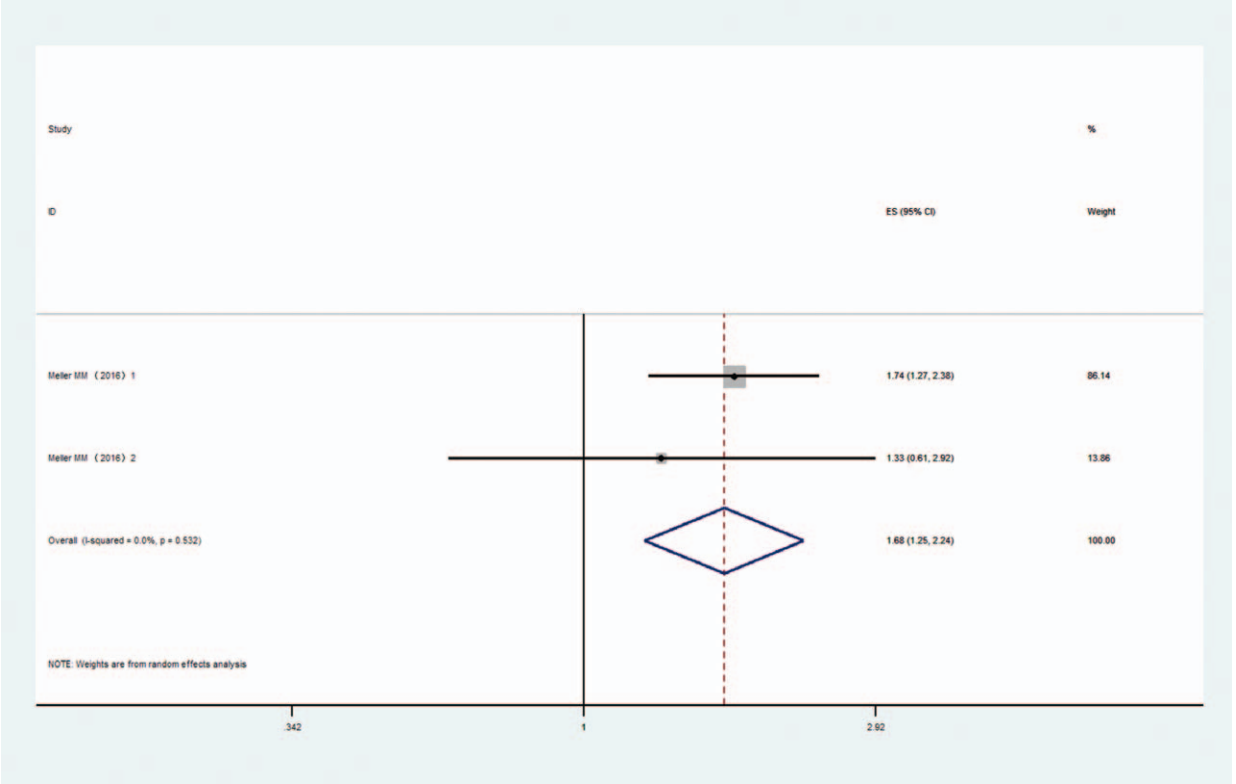

Figure 5. Meta-analysis results of the correlation between BMI (BMI≥50 kg/m^2 vs BMI <50 kg/m^2) and PJI after total joint arthroplasty. BMI = body mass index, PJI = periprosthetic joint infection.

Table 2

Results of subgroup analyses of studies on obesity *vs.* non-obesity.

Total	Studies, *N*	Participants, *N*	*OR* (95% *CI*)	*P*	*P* of heterogeneity	I^2 (%)
	20	2650632	1.51 (1.30–1.74)	.000	.000	78.6
BMI						
BMI:≥30kg/m^2 vs <25kg/m^2	7	2,329,415	1.57 (1.35–1.84)	.000	.000	76.5
BMI: 30–35kg/m^2 vs <25kg/m^2	4	56,194	1.22 (0.91–1.65)	.185	.525	0
BMI: 35–40kg/m^2 vs <25kg/m^2	5	56,872	1.17 (0.56–2.42)	.681	.000	83.5
BMI: 30–40kg/m^2 vs <25kg/m^2	1	93,598	3.01 (2.19–4.14)	.000	NA	NA
BMI:≥30kg/m^2 vs <30kg/m^2	5	167,637	1.61 (1.23–2.10)	.000	.011	69.3
BMI: 30–35kg/m^2 vs <30kg/m^2	1	1,896	1.27 (0.63–2.56)	.510	NA	NA
BMI: 30–40kg/m^2 vs <30kg/m^2	1	1,214	2.29 (0.64–8.17)	.202	NA	NA
BMI: ≥35kg/m^2*vs.* <30kg/m^2	1	1,896	2.93 (1.37–6.27)	.006	NA	NA
Geographical region						
America	12	1,303,956	1.45 (1.15–1.83)	.000	.000	87.9
Europe	9	1,323,048	1.62 (1.37–1.91)	.000	.056	47.2
Australia	3	23,392	1.27 (0.66–2.42)	.476	.385	0
Asian	1	236	9.59 (1.01–90.86)	.049	NA	NA
Study design						
Retrospective cohort	15	1,180,082	1.67 (1.34–2.08)	.000	.000	65.6
Prospective cohort	6	1,321,552	1.59 (1.32–1.91)	.000	.028	60.1
Retrospective case-control	3	126,142	1.50 (1.19–1.89)	.001	.019	74.6
Prospective case-control	1	678	0.50 (0.35–0.71)	.000	NA	NA
Effect type						
OR	12	287,920	1.27 (0.91–1.77)	.157	.000	83.8
RR	4	1,311,324	1.61 (1.30–2.01)	.000	.009	73.8
HR	8	1,051,388	1.72 (1.38–2.14)	.000	.001	70.4
Operation method						
TKA	6	1,788,110	1.47 (1.20–1.81)	.000	.000	78.7
THA/TKA	9	40,994	1.20 (0.75–1.95)	.447	.000	72.8
THA	6	812,038	1.97 (1.01–2.41)	.000	.000	59.9
THA/TKA/TSA	1	2,212	1.66 (1.37–2.02)	.000	NA	NA
TAA	1	6,977	1.47 (1.15–1.87)	.002	NA	NA
RSA	1	301	0.76 (0.35–1.64)	.484	NA	NA

CI = confidence interval, NA = not available, OR = odds ratio, RR = rate ratio, HR = hazard ratio, THA = total hip arthroplasty, TKA = total knee arthroplasty, TAA = total ankle arthroplasty, RSA = reverse shoulder arthroplasty, TSA = total shoulder arthroplasty, BMI = body mass index.

Table 3

Subgroup analysis of studies on morbid obesity vs non-morbid obesity.

Total	Studies, *N*	Participants, *N*	*OR* (95% *CI*)	*P*	*P* of heterogeneity	I^2 (%)
	14	1303322	3.27 (2.46–4.34)	.000	.000	69.0
BMI						
BMI:≥40kg/m^2 vs <25kg/m^2	7	285,404	3.20 (1.82–5.62)	.000	.000	84.8
BMI:≥40kg/m^2 vs <30kg/m^2	1	1,214	8.96 (1.59–50.56)	.013	NA	NA
BMI:≥40kg/m^2 vs <35kg/m^2	1	91,585	3.73 (1.49–9.36)	.005	NA	NA
BMI:≥40kg/m^2 vs <40kg/m^2	3	15,356	3.21 (2.02–5.10)	.000	.871	0
BMI:≥45kg/m^2 vs <25kg/m^2	1	871,058	3.14 (2.33–4.23)	.000	NA	NA
BMI:≥45kg/m^2*vs.* <35kg/m^2	1	22,705	2.90 (2.10–4.00)	.000	NA	NA
Geographical region						
America	8	1169664	3.10 (2.15–4.48)	.000	.000	81.7
Europe	3	18,681	3.71 (2.22–6.19)	.000	.552	0
Australia	3	114,977	3.41 (1.69–6.86)	.001	.333	9.1
Study design						
Retrospective cohort	11	1,283,656	3.30 (2.41–4.53)	.000	.000	69.5
Prospective cohort	2	18,988	4.60 (2.98–7.12)	.000	.436	0
Prospective case-control	1	678	1.60 (0.91–2.82)	.105	NA	NA
Effect type						
OR	8	376,613	3.21 (1.81–5.70)	.000	.000	82
RR	2	12,733	4.18 (2.12–8.23)	.000	.982	0
HR	4	913,976	3.22 (2.67–3.89)	.000	.499	0
Operation method						
TKA	4	1,025,645	2.63 (1.59–4.34)	.000	.022	68.8
THA/TKA	6	71,048	2.75 (2.00–3.77)	.000	.246	25.0
THA	4	206,629	5.41 (4.09–7.14)	.000	.356	7.5

CI = confidence interval, NA = not available, OR = odds ratio, RR = rate ratio, HR = hazard ratio, THA = total hip arthroplasty, TKA = total knee arthroplasty, TAA = total ankle arthroplasty, RSA = reverse shoulder arthroplasty, TSA = total shoulder arthroplasty, BMI = body mass index.

4. Discussion

In this study, we have conducted a meta-analysis of 29 selected studies to corroborate the correlation between BMI and PJI following TJA. To ensure a reliable conclusion, previous published studies on this topic have been retrieved, reviewed and summarized to achieve those with high compliance and high quality, so as to resolve the controversy over this inconsistent correlation. Overall, our results revealed that the risk of PJI after TJA significantly increased by 1.51 times in the obese group ($OR = 1.51$; 95% CI = 1.30–1.74 for obesity *vs.* non-obesity), the risk of PJI after TJA rose by 3.27 times in the morbid obese group ($OR = 3.27$; 95% CI = 2.46–4.34 for morbid obesity *vs.* non-morbid obesity), the risk boosted by 1.64 times in patients with BMI ≥ 35 kg/m^2 ($OR = 1.64$; 95% CI = 1.39–1.94 for BMI≥35 kg/m^2 vs BMI<35 kg/m^2), and by 1.68 times in those with BMI≥50 kg/m^2 ($OR = 1.68$;95%CI = 1.25–2.24 for BMI≥50 kg/m^2 vs BMI 40–50 kg/m^2). A significant

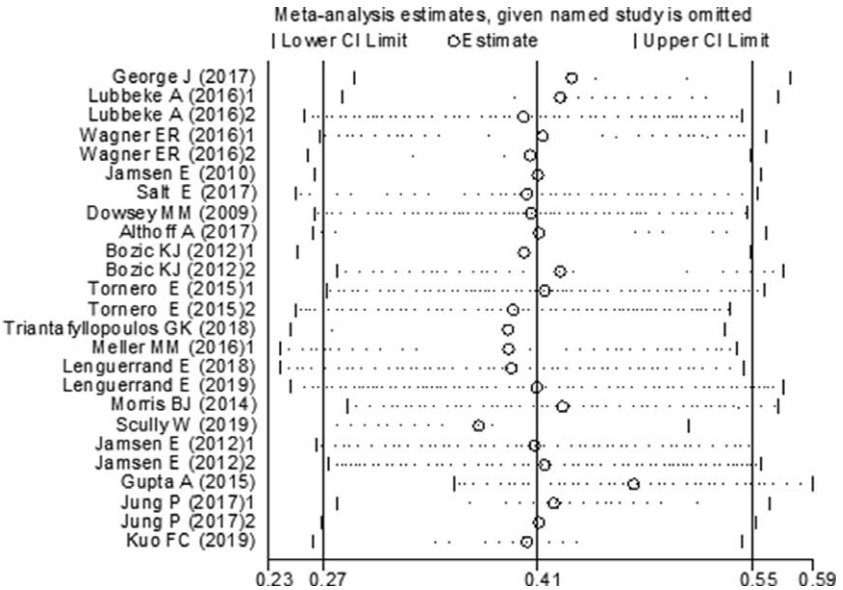

Figure 6. The influence analysis of included studies.

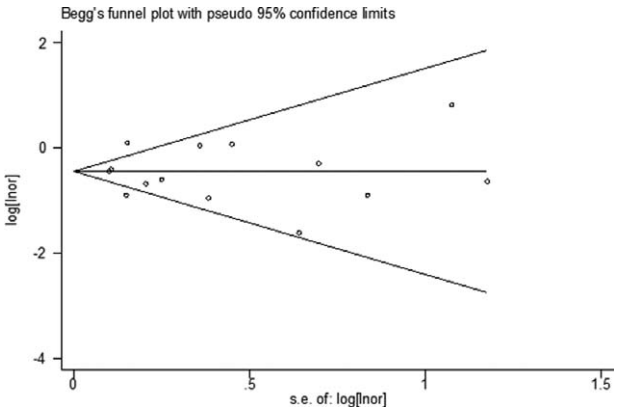

Figure 7. Egger funnel plot.

association remained consistent, as indicated by subgroup analyses. In addition, Egger and Begg analyses merely showed no publication bias. The sensitivity analysis revealed that there was a nonsignificant difference in the stability of the results, further verifying the rationality and reliability of our analysis.

TJA as a successful, cost-effective and selective surgical treatment has been universally used to treat joint pain mainly caused by osteoarthritis. Some patients experience complications and 1 of the most severe complications is PJI[45]. The identification of individuals at high risks of PJI can facilitate the development of preventive strategies with optimized detection of PJI. Though the correlation between BMI and PJI after TJA has been rapidly reported, their results still remain divergent and even controversial[16–44]. Our results suggest that the 1.51-fold risk of PJI after TJA in obese patients is consistent with previous studies[8–10]. By analyzing studies on obesity *vs.* non-obesity, we have found differences between various BMI stratification levels. In general, the growing risk of PJI is BMI-dependent. However, some comparisons have shown nonsignificant differences. This may attribute to the insufficient inclusion of eligible studies after BMI stratification. The 3.27-fold risk of PJI after TJA in the morbid obese group is consistent with the meta-analysis reported by Ma et al.[9]. However, his study has not adjusted for confounders despite few included studies. With regard to the subgroup analysis of studies on morbid obesity *vs.* non-morbid obesity, the correlations remain consistent when the studies are stratified by different BMI intervals. We have even compared a seldom reported BMI interval at 35 kg/m^2 in previous studies, and the present analysis reveals a 1.64-fold risk of PJI after TJA in patients with BMI≥35 kg/m^2. Furthermore, the risk can significantly increase by 1.68 times when the indice rises to over 50 kg/m^2 (as shown in the subgroup analysis of studies on BMI≥50 kg/m^2 vs BMI 40–50 kg/m^2). However, due to the insufficient included studies in this part, more large sample studies are needed for verification.

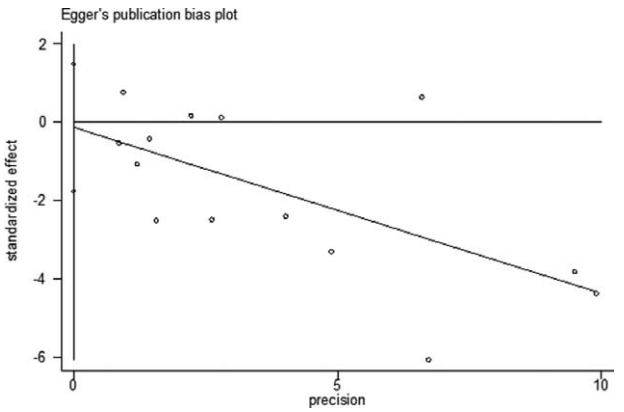

Figure 8. Begg funnel plot.

As the passages have expounded, 2 significant advantages of our study are clear. First, as the previously calculated correlation between BMI and PJI following TJA is uncertain, this meta-analysis assesses such a potential correlation through a thorough systematic study with rigorous analytical methods. Second, only multi-factor adjustment studies are included to exclude the influence from other confounders on the results. Third, the rationality and reliability of our meta-analysis have been prudently and significantly improved in that the overall comprehensive estimation is based on a large sample size. In addition, sufficient sensitivity analyses have been carried out to ensure the reliability of this study.

The current meta-analysis has the following limitations which must be considered before our results can be accepted. First, there are significant heterogeneities across the included studies, and a subgroup analysis can not fully trace each underlying source of heterogeneity. Second, retrospective and prospective studies are included in this meta-analysis. Thus, the heterogeneous design may limit their comparability and eventually the interpretability of the current meta-analysis. Third, this study only includes references in English. Therefore, we may have lost data from those in other languages.

5. Conclusion

In summary, our meta-analysis suggests that PJI after TJA is correlated with BMI, and that means obese patients have higher risks of developing PJI than non-obese individuals. Similarly, morbid obese patients show higher risks of such infections than non-morbid obese patients. This conclusion needs to be verified by more prospective studies. A significant association remains consistent, as indicated by subgroup analyses and sensitivity analyses.

Author contributions

LX conceived the study idea. J-LX, Z-RL and B-LX retrieved and screened literature. Q-ZZ and T-YL conducted data extraction and the evaluation of methodological quality. J-LX and P Y performed statistical analyses and interpretation of corresponding results. J-LX drafted the initial manuscript. D C modified the initial manuscript. D C and Q-WZ had primary responsibility for the final content. All authors made critical comments for the initial manuscript.

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