Relationship between body mass index and the risk of periprosthetic joint infection after primary total hip arthroplasty and total knee arthroplasty

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Background: Periprosthetic joint infection (PJI) is a disastrous complication after total hip arthroplasty (THA) and total knee arthroplasty (TKA). The relationship between body mass index (BMI) and the incidence of PJI remains controversial. To better understand the impact of increasing BMI on PJI, we conducted this study to investigate the dose-response relationship between BMI and the risk of PJI after primary THA or TKA.

Methods: A systematic search was conducted in PubMed, Embase, and Cochrane Library databases from inception to August 17, 2019. After study selection and data extraction, a dose-response meta-analysis was performed to investigate the relationship between BMI and PJI. Adjusted relative risks (RRs) with 95% confidence intervals (CIs) were pooled using fixed-effects or random-effects models.

Results: Eleven studies comprising 505,303 arthroplasties were included. The dose-response analysis showed a significant non-linear relationship between BMI and the risk of PJI ($P_{non-linearity}$ <0.001). Patients following THA (RR, 1.489; 95% CI, 1.343–1.651; P<0.001) were more likely to suffer from PJI than patients following TKA. Furthermore, American Society of Anesthesiologists (ASA) score ≥3 (RR, 2.287; 95% CI, 1.650–3.170; P<0.001), lung disease (RR, 1.484; 95% CI, 1.208–1.823; P<0.001) and diabetes (RR, 1.695; 95% CI, 1.071–2.685; P=0.024) were identified as risk factors for PJI, but male (RR, 1.649; 95% CI, 0.987–2.755; P=0.056) and hypertension (RR, 0.980; 95% CI, 0.502–1.916; P=0.954) were not recognized as risk factors for PJI.

Conclusions: The J-shaped non-linear relationship demonstrated that increased BMI was associated with an increased risk for PJI after primary THA or TKA. Patients following THA were more likely to suffer from PJI than patients following TKA. Also, patients with ASA score ≥3, lung disease and diabetes have a higher risk of PJI. Gender and hypertension did not influence the incidence of PJI.

Keywords: Body mass index (BMI); periprosthetic joint infection (PJI); risk factors; total hip arthroplasty (THA); total knee arthroplasty (TKA)

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Introduction

Total hip arthroplasty (THA) and total knee arthroplasty (TKA) are generally regarded as two of the most commonly done and highly successful surgical interventions performed annually to treat end-stage joint disease (1,2). Increasing levels of obesity and population aging, the volume of total joint arthroplasty (TJA) in the United States has increased steadily during the past several decades and is predicted to increase continuously (3,4). The demand for primary THA is projected to grow 71%, to 635,000 procedures, by 2030 and the demand for primary TKA is projected to grow 85%, to 1.26 million procedures, by 2030 in United States (5). A similar pattern of historical increase in the incidence of joint arthroplasty has been reported by many worldwide joint registries, such as New Zealand (6), United Kingdom (7) and Australia (8). With the increasing burden of joint replacement surgery, it is required to ensure that demand can be met and desired outcomes can be achieved.

Periprosthetic joint infection (PJI), also referred to as prosthetic joint infection, is defined as an infection involving the artificial joint prosthesis and adjacent tissue (9). It is a devastating complication of arthroplasty and causes pain, loss of function, systemic inflammatory, and even death, which will lead to a tremendous burden to patients and health-care systems worldwide. As the volume of TJA procedures constantly increasing in the United States using the Nationwide Inpatient Sample, the PJI incidence rate increased from 1.99% in 2001 to 2.18% in 2009 for THA, and from 2.05% in 2001 to 2.18% in 2009 for TKA, respectively (10). More significantly, PJI is the most common cause for revision TKA (25.2%), and is the third most common cause for revision THA (14.8%), following instability/dislocation (22.5%) and mechanical loosening (19.7%) (11,12). Recognition and optimization of any modifiable risk factors before joint arthroplasty are central to the reduction of the prevalence of PJI.

The PJI is attributed to multiple factors, including patient, surgical, and health-care factors. High body mass index (BMI), as a modifiable factor, has been recognized for its association with increased risk of PJI in many but not all previous studies (9,13,14). However, the relationship between BMI and the incidence of PJI remains controversial. After a review of 9,245 patients who underwent primary TJA, Pulido *et al.* found that morbid obesity (BMI >40 kg/m^2) was an independent predictor of infection (13). Berbari *et al.* reported that a low BMI of <25 kg/m^2 was associated with an increased risk of PJI in patients undergoing THA or TKA (15).

Meanwhile, Shohat *et al.* documented that the risk for PJI increases gradually throughout the full range of BMI, but no threshold exists (16). To better understand the impact of increasing BMI on PJI after TJA, we conducted this dose-response analysis to assess the dose-response relationship between BMI and the risk of PJI in patients undergoing primary THA or TKA.

Methods

The present study was conducted and reported following the guidelines for Meta-Analyses and Systematic reviews for Observational Studies and the PRISMA guidelines (17,18).

Search strategy

The systematic literature search without restrictions of language was performed in three databases (PubMed, Embase, Cochrane Library) from their inception to August 17, 2019. The following search terms were used: "total hip arthroplasty", "total knee arthroplasty", "body mass index", "periprosthetic joint infection" and their variants. Details of the search strategy are available in *Tables S1,S2,S3*. Also, the reference list of retrieved studies and relevant reviews were carefully checked for any potential inclusion.

Study selection

After the removal of duplicates, two authors (Junlong Zhong and Bin Wang) independently screened the titles and abstracts of potentially relevant studies, and full text of all relevant studies was obtained for systematic assessment against the inclusion criteria. Studies were eligible for inclusion if they met the following criteria: (I) a case-control study or a cohort study design; (II) patients undergoing primary THA or primary TKA; (III) overweight, obesity, and BMI were the exposures of interest; (IV) PJI was the outcome of interest [diagnostic criteria of PJI as reported by Parvizi *et al.* (19)]; and (V) investigated the association between BMI and PJI, and reported appropriate estimates such as the hazard ratio (HR), relative risk (RR) or odds ratio (OR) and the corresponding 95% confidence interval (CI). Case reports, editorials, letters, comments, reviews, conference abstracts, and studies that did not report sufficient data were excluded. If the same participants were overlapping reported, we retained only the most recent one or the most informative one to avoid duplication of

information.

Data extraction

Data were extracted independently by two authors (Junlong Zhong and Yufeng Chen) and were checked for accuracy by another author (Bin Wang). The following variables were extracted from each included studies: first author, year of publication, country, research databases, study period, study design, number of participants, participant's mean age, type of surgery, number of PJI, type of PJI, duration of follow-up, BMI categories (at least three BMI categories), number of participants in each category, adjusted HRs, RRs or ORs with the corresponding 95% CIs, and other interesting items. All the extracted data were entered into a predetermined Excel (Microsoft Corporation, USA) file.

Quality assessment of studies

The quality of the included studies was assessed using the Newcastle-Ottawa Scale (NOS), which included 8 items and allowed a maximum of nine stars (20). We assigned scores of 0 to 3, 4 to 6, and 7 to 9 for the low, moderate, and high quality of studies, respectively.

Statistical analysis

The ORs and HRs were directly considered as equivalent to the RRs because of the incidence of PJI is rare (21). The RRs were calculated assuming the minimum BMI category as the reference category. The median or mean BMI in each category was assigned to each corresponding adjusted RRs and 95% CIs. If the median or mean BMI per category was not reported in one study, we defined the midpoint of the upper and lower boundaries of each BMI category as the average. When the highest or lowest category was open-ended, we assumed that the width of the interval to be equal to the adjacent category. Beyond that, we considered mean BMI is 18 kg/m^2 for BMI ≤18.5 kg/m^2 and 41 kg/m^2 for BMI ≥40 kg/m^2. We used the method proposed by Greenland *et al.* and Orsini *et al.* to conduct a two-stage random-effects dose-response analysis, which required cases of PJI, doses of BMI and corresponding adjusted RRs and 95% CIs in at least three BMI categories (22,23). Furthermore, other potential risk factors for PJI were pooled using a random or fixed effects model as a secondary outcome.

The degree of heterogeneity among included studies was assessed using the Cochran's Q test and quantified by calculating the I^2 statistic (24,25). An $I^2 > 50\%$ or $P < 0.1$ indicated significant heterogeneity, and then a random-effects model was used; otherwise, a fixed-effects model was used. To perform sensitivity analysis, one study was omitted in each turn and the remaining studies were analyzed to explore the impact of the individual study on the overall risk of PJI. Publication bias was also evaluated using Begg's test and Egger's test (26,27). If any publication bias was detected, it was checked via the "trim and fill method" (28) for estimating the impact of these missing studies on overall effect size. A $P < 0.05$ was considered statistically significant. All statistical analyses were performed using Stata 14.0 (Stata Corporation, College Station, TX, USA).

Results

Study selection

The flow diagram of the study selection process is presented in *Figure 1*. A total of 630 records were identified through the aforementioned databases from their inception to August 17, 2019. After the exclusion of duplicates and irrelevant records based on titles and abstracts, the remaining 113 studies were further assessed for detailed full-text analysis. After reviewing the full text in detail, 24 studies met the inclusion criteria and were included in the qualitative synthesis. Thirteen studies that did not report available data for analysis were excluded from the quantitative meta-analysis. Finally, 11 studies were eligible for inclusion in the present analysis.

Study characteristics

The characteristics of the included studies are shown in *Table 1*. A total of 11 observational studies (including 10 cohort studies and 1 case-control study) were included in the present analysis (16,29-38). These 11 studies were published between 2008 and 2018, and were predominantly from North America (n=4), followed by Europe (n=3), Oceania (n=2) and Asia (n=2). Regarding the site of arthroplasty, one study (29) and three studies (30-32) only reported outcomes in knee and hip, respectively, while seven studies (16,33-38) reported outcomes in both sites. Of the seven studies, two studies (33,38) reported outcomes in knee and hip separately, and five studies (16,34-37) reported combining data of both sites. A total of 505,303 participants undergoing primary THA or TKA, which involved 4,148

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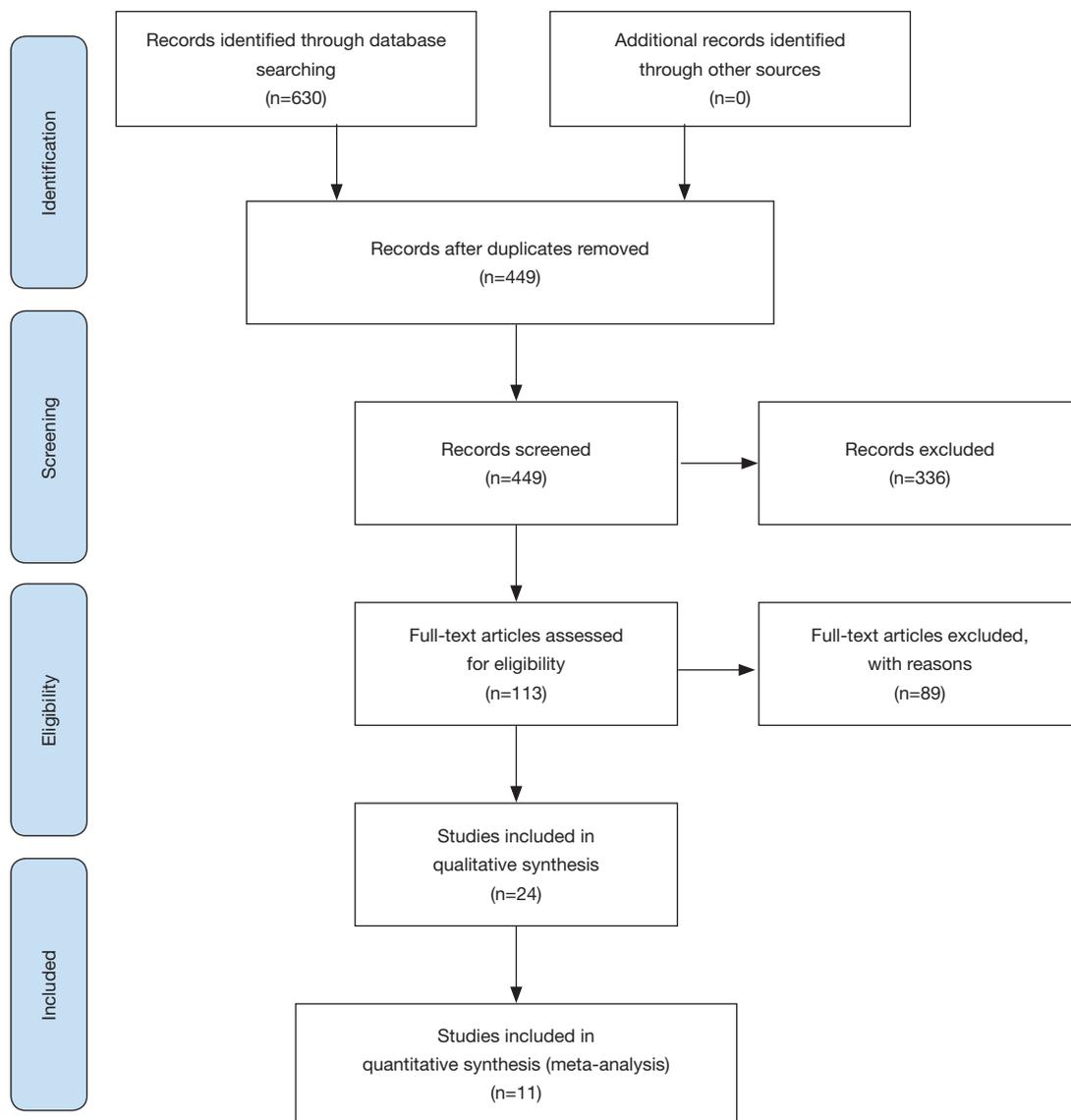
Figure 1 Flow diagram of the study selection process.

cases of PJI, were included among these 11 studies. The average age of the participants in each study varied from 56.5 to 71.5 years. The detailed score of NOS of each study is summarized in *Table 2*. The average score of the NOS was 6.9, and the score for each study was 6 or above, indicating that all included studies were of moderate or high quality.

Primary outcome: dose-response analysis

A total of 11 studies were included for dose-response analysis. We observed a significant non-linear dose-response relationship between BMI and the risk of PJI

in patients undergoing primary THA or TKA ($P_{non-linearity}$ <0.001). *Figure 2* showed the impact of BMI as a continuous variable on the risk of PJI. The J-shaped dose-response curve indicated that the increase of BMI accompanied with an accelerated increase of postoperative PJI rate in patients undergoing primary THA or TKA, especially when the BMI was greater than 24 kg/m^2 (reaching the upper limit of normal BMI).

Secondary outcomes

Furthermore, we conducted a meta-analysis to identify

Table 1 Characteristics of the included studies

Study [year]	Country	Databases	Study period	Average age (years)	No. of arthroplasties	Surgery	No. of PJI	BMI category, kg/m²	Adjusted RR (95% CI)	Study design
George et al. [2018]	United States	American College of Surgeons National Surgical Quality Improvement Project	2011.1.1–2015.12.31	66.6	150,934	Primary TKA	About 451	18.5–25	1	Retrospective cohort
								25–30	0.85 (0.58–1.26)	
								30–40	0.98 (0.68–1.41)	
								≥40	1.58 (1.06–2.34)	
Smith et al. [2018]	New Zealand	New Zealand Joint Registry data	2000–2014	–	91585	Primary THA	137	<35	1	Retrospective cohort
								35–40	2.15 (1.01–4.60)	
								>40	3.73 (1.49–9.39)	
Shohat et al. [2018]	Israel	The Rothman Institute at Thomas Jefferson University	2006–2015	64	18,173	Primary THA and TKA	100	≤18.49	1.8 (0.23–13.9)	Retrospective cohort
								18.5–24.9	1	
								25–29.9	0.72 (0.38–1.36)	
								30–34.9	1.06 (0.57–1.96)	
								35–39.9	1.08 (0.52–2.23)	
								≥40	3.09 (1.46–6.54)	
Jung et al. [2017]§	New Zealand	New Zealand Surgical Site Infection Improvement Programme	2013.7–2015.9	70	10,690	Primary THA	82	<25	1	Retrospective cohort
								25–30	1.12 (0.52–2.43)	
								30–35	1.65 (0.75–3.62)	
								35–40	3.03 (1.31–7.00)	
								>40	5.62 (2.26–14.0)	
Jung et al. [2017]§	New Zealand	New Zealand Surgical Site Infection Improvement Programme	2013.7–2015.9	70	9,481	Primary TKA	44	<25	1	Retrospective cohort
								25–30	0.31 (0.09–1.09)	
								30–35	0.73 (0.25–2.12)	
								35–40	1.44 (0.50–4.16)	
								>40	1.94 (0.63–5.97)	
Lübbeke et al. [2016]	Switzerland	Geneva University Hospitals and Faculty of Medicine, University of Geneva	1996.3–2013.12	70	9,061	Primary THA and TKA	111	<25	1	Prospective cohort
								25–29.9	1 (0.6–1.7)	
								30–34.9	1 (0.6–1.8)	
								35–39.9	2.1 (1.1–4.3)	
								≥40	4.2 (1.8–9.7)	
Bohl et al. [2016]	United States	American College of Surgeons National Surgical Quality Improvement Program database	2005–2013	–	117,935	Primary THA and TKA	1,163	<25	1	Retrospective cohort
								25–30	1.1 (0.9–1.4)	
								≥30	1.9 (1.5–2.3)	

Table 1 (*continued*)

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Table 1 (*continued*)

Study [year]	Country	Databases	Study period	Average age (years)	No. of arthroplasties	Surgery	No. of PJI	BMI category, kg/m^2	Adjusted RR (95% CI)	Study design
Tornero et al. [2015]	Spain	Hospital Clinic of Barcelona	2010.3–2013.2	71.5	1,786	Primary THA and TKA	45	<30	1	Retrospective cohort
								30–35	1.266 (0.628–2.554)	
								≥35	2.932 (1.370–6.275)	
Wu et al. [2014]	China	Shanghai Ninth People's Hospital	2000.1–2012.12	63.6	297	Primary THA and TKA	45	<18.5	1.55 (0.12–20.16)	Case-control
								18.5–28	1	
								≥28	2.77 (1.20–6.40)	
Wallace et al. [2014]¶	United Kingdom	Clinical Practice Research Datalink	1995.1.1–2011.8.11	69.4	31,817	Primary THA	704	<18.5	1.03 (0.48–2.19)	Retrospective cohort
								18.5–25	1	
								25–30	1.34 (1.09–1.64)	
								30–35	1.52 (1.21–1.90)	
								>35	2.18 (1.67–2.86)	
Wallace et al. [2014]¶	United Kingdom	Clinical Practice Research Datalink	1995.1.1–2011.8.11	69.4	32,485	Primary TKA	1,100	<18.5	0.97 (0.36–2.67)	Retrospective cohort
								18.5–25	1	
								25–30	0.98 (0.81–1.19)	
								30–35	1.23 (1.01–1.50)	
								>35	1.39 (1.11–1.72)	
Namba et al. [2012]	United States	Kaiser Permanente Total Joint Replacement Registry	2001.4.1–2009.12.30	65.5	30,815	Primary THA	155	<18.5	2.88 (0.89–9.23)	Retrospective cohort
								18.5–30	1	
								30–35	1.56 (1.03–2.37)	
								≥35	2.37 (1.55–3.61)	
Grant et al. [2008]	United States	Veteran Affairs Medical Center in Durham	–	56.5	244	Primary THA	11	<30	1	Retrospective cohort
								30–39	0.54 (0.08–3.6)	
								≥40	5.2 (0.45–60.9)	

§, the results of THA and TKA are reported separately in this study; ¶, the results of THA and TKA are reported separately in this study. THA, total hip arthroplasty; TKA, total knee arthroplasty; PJI, periprosthetic joint infection; BMI, body mass index; RR, relative risk; CI, confidence interval.

Table 2 Quality assessment of included studies according to NOS

Study	Selection	Comparability	Outcome/exposure	Total score
George *et al*. [2018]	****	*	*	6
Smith *et al*. [2018]	****	*	**	7
Shohat *et al*. [2018]	****	*	**	7
Jung *et al*. [2017]	****	*	**	7
Lübbeke *et al*. [2016]	****	*	**	7
Bohl *et al*. [2016]	****	*	*	6
Tornero *et al*. [2015]	****	*	**	7
Wu *et al*. [2014]	****	**	*	7
Wallace *et al*. [2014]	****	*	**	7
Namba *et al*. [2012]	****	*	***	8
Grant *et al*. [2008]	****	*	**	7

Each asterisk (*) indicates 1 score. NOS, Newcastle-Ottawa Scale.
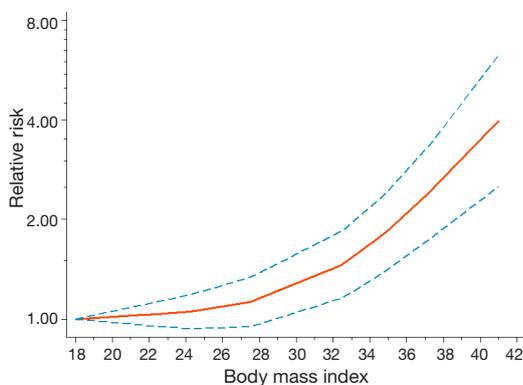
Figure 2 Non-linear dose-response relationship between BMI (kg/m^2) and the risk of PJI in patients undergoing primary THA or TKA. The red solid line represents the pooled RRs, and the blue dashed line represents corresponding 95% CIs. The RR is plotted on the log scale. BMI, body mass index; PJI, periprosthetic joint infection; THA, total hip arthroplasty; TKA, total knee arthroplasty; RRs, relative risks; CIs, confidence intervals.

other risk factors for PJI, including gender (male *vs.* female), American Society of Anesthesiologists (ASA) score (ASA score ≥3 *vs.* ASA score <3), surgical site (TKA *vs.* THA), and comorbidities (including lung disease, diabetes and hypertension).

Five studies (30,31,33,36,37) including a total of 144,321 participants (PJI =559, and non-PJI =143,762) reported gender as a potential risk factor for PJI. The pooled result showed no significant difference in the risk of PJI between the male patient (RR, 1.649; 95% CI, 0.987–2.755; P=0.056) and the female patient. There was significant heterogeneity among these studies (I^2=84.7%, P$_{heterogeneity}$<0.001).

Three studies (30,31,33) including a total of 55,165 participants (PJI =225, and non-PJI =54,940) reported ASA score as a potential risk factor for PJI. The pooled result showed that the higher ASA score (ASA score ≥3) was positively associated with the higher incidence of PJI (RR, 2.287; 95% CI, 1.650–3.170; P<0.001). No significant heterogeneity was found among these studies (I^2=0, P$_{heterogeneity}$=0.815).

Two studies (35,37) including a total of 118,232 participants (PJI =1,208, and non-PJI =117,024) reported surgical site (TKA *vs.* THA) as a potential risk factor for PJI. The pooled result showed that the patients following THA were more likely to suffer from PJI than the patients following TKA (RR, 1.489; 95% CI, 1.343–1.651; P<0.001). No significant heterogeneity was found among these studies (I^2=26.2, P$_{heterogeneity}$=0.244).

As for the comorbidities, the pooled result revealed that the patients suffered from lung disease (RR, 1.484; 95% CI, 1.208–1.823; P<0.001) or diabetes (RR, 1.695; 95% CI, 1.071–2.685; P=0.024) were significantly associated with the increased incidence of PJI, while the patients who suffered from hypertension (RR, 0.980; 95% CI, 0.502–1.916; P=0.954) were not significantly associated with the increased incidence of PJI. The results of heterogeneity

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Table 3 The pooled effect of risk factors associated with PJI

Risk factors	No. studies	Test of relationship		Test of heterogeneity	
		RR (95% CI)	P value	I^2, %	P value
Male *vs.* female	5	1.649 (0.987, 2.755)	0.056	84.7	<0.001
ASA score (≥3 *vs.* <3)	3	2.287 (1.650, 3.170)	<0.001	0	0.815
THA *vs.* TKA	2	1.489 (1.343, 1.651)	<0.001	26.2	0.244
Lung disease	3	1.484 (1.208, 1.823)	<0.001	23.5	0.271
Diabetes	3	1.695 (1.071, 2.685)	0.024	66.9	0.049
Hypertension	2	0.980 (0.502, 1.916)	0.954	50.5	0.155

PJI, periprosthetic joint infection; ASA, American Society of Anesthesiologists; THA, total hip arthroplasty; TKA, total knee arthroplasty; RR, relative risk; CI, confidence interval.

Table 4 Sensitivity analysis

Study Omitted	RR	95% CI
George *et al.* [2018]	1.602	1.420–1.808
Smith *et al.* [2018]	1.555	1.403–1.724
Shohat *et al.* [2018]	1.584	1.415–1.773
Jung *et al.* [2017] (THA)[§]	1.571	1.408–1.754
Jung *et al.* [2017] (TKA)[§]	1.567	1.409–1.743
Lübbeke *et al.* [2016]	1.599	1.430–1.789
Bohl *et al.* [2016]	1.556	1.385–1.748
Tornero *et al.* [2015]	1.591	1.425–1.777
Wu *et al.* [2014]	1.563	1.405–1.739
Wallace et al. [2014] (THA)[¶]	1.616	1.425–1.833
Wallace *et al.* [2014] (TKA)[¶]	1.622	1.504–1.749
Namba *et al.* [2012]	1.528	1.386–1.684
Grant *et al.* [2008]	1.581	1.418–1.763
Combined	1.579	1.421–1.755

[§], this study reported the results of THA and TKA separately; [¶], this study reported the results of THA and TKA separately. THA, total hip arthroplasty; TKA, total knee arthroplasty; RR, relative risk; CI, confidence interval.

analysis were shown in *Table 3*.

Sensitivity analysis and publication bias

To evaluate the influence of each study on the combined effect, we conducted a sensitivity analysis. Exclusion of any individual study, we observed no significant change of the relationship between obesity (compared with non-obesity) and risk of PJI (*Table 4*). The Begg's test and Egger's test (P_{Begg}=0.300; P_{Egger}=0.099) showed that there was no significant publication bias in the present study.

Discussion

Causes of PJI are multifactorial and can be broadly classified into patient-related factors, surgery-related factors, and hospital-related factors. In the present study, we identified a significant non-linear relationship between BMI and the risk of PJI in patients undergoing primary THA or TKA. Also, our study revealed that higher ASA score (ASA score ≥3), lung disease, and diabetes were significant risk factors for PJI, and the patients following THA were more likely to suffer from PJI than the patients following TKA. However, we did not observe significant associations between hypertension and gender and the risk of PJI.

In the present study, we evaluated patient-related risk factors for PJI, including gender, BMI, ASA score, and some comorbidities. We found that the RR of PJI increased with the increase of BMI, and dramatically increased in obese patients. As documented in previous literature, the increased risks of PJI in patients with higher BMI are mainly attributed to thicker adipose tissue layer (large potential dead space that enhanced the risk of hematoma), additional comorbidities (such as diabetes mellitus, lung disease), longer operative time, and even increased allogeneic blood transfusions (39,40). Also, obese patients have impaired tissue antibiotic penetration, and an under-dosing of tissue concentrations leads to an increased risk of infection (41). Furthermore, some studies suggested

that obesity is a pro-inflammatory state associated with a low-grade inflammatory response, and may affect the postoperative immune response and increase the risk of surgical site infection (SSI) (42,43). Previous studies reported that males had a significantly increased risk for PJI than females for both TKA and THA, which may be attributed to some potential confounding variables, such as smoking and alcohol consumption (31,44). After controlling for possible confounders, our results revealed that male was not an independent risk factor for PJI in patients following primary THA or TKA with high heterogeneity (RR, 1.649; P=0.056; I^2=84.8%; $P_{heterogeneity}$<0.001). Meanwhile, our results revealed that patients with diabetes, lung disease or higher ASA score (ASA score ≥3) had an increased risk of PJI, but hypertension was not a risk factor for PJI. It is reported that patients with diabetes, especially those with insulin-dependent diabetes, exhibited significantly increased odds of postoperative infection, due to hyperglycemia may impair the immune system and provide a favorable environment for certain bacterial reproduction (45,46). Pathogenic bacteria located in lung lesions, mainly including pneumonia and chronic bronchitis, can spread through blood circulation or lymphatic circulation to the surgical site and become a potential source of PJI. The higher ASA score for patients indicates the poor physical condition and serious multiple comorbidities, such as obesity, cardiopulmonary diseases, immune diseases and metabolic diseases, which may contribute to increasing overall infection risk (47). Unfortunately, other patient-related risk factors for PJI after primary THA and TKA, such as age, smoking, alcohol consumption and other basic diseases, were not analyzed due to insufficient data in the present study.

Some potential confounding variables, such as surgery-related factors and hospital-related factors, were not analyzed due to lack of available data in this study. To recognize the influence of these related factors comprehensively, we had a discussion about that based on published literature and data concerned. Among the surgery-related factors, anesthetic management, operative procedure, operative time, drain usage and blood transfusion were possibly associated with PJI following TJA. A retrospective study found that patients receiving primary THA or TKA under general anesthesia were associated with a higher risk of PJI compared with epidural or spinal anesthesia (48). Prolonged operative time was also associated with a higher risk of PJI following TJA, which may result from increased potential wound contamination, increased soft tissue damage, increased

blood loss, and even perioperative transfusion. The risk of PJI significantly increased in primary THA in which operative time lasted for 120 minutes or more (49). Also, Kurtz *et al.* reported that TKA operative time lasted more than 210 minutes was associated with an increased risk of infection in comparison with those less than 120 minutes (50), and Namba *et al.* found that each 15-minute increase in operative time was associated with a 9% increased risk of PJI following TKA (51). Significantly, postoperative wound drainage reduced the incidence of hematoma formation and subsequently decreased the risk of infection after TJA. However, persistent wound drainage more than 48 hours has been identified as a risk factor for PJI (52). Patel *et al.* reported that every additional day of prolonged wound drainage increased the risk of wound infection by 42% in THA and by 29% in TKA (53). In addition, although the use of blood products during the perioperative period is a valuable means for the treatment of anemia, the immunomodulating response of allogeneic blood transfusion may be the cause of the increased risk of PJI (54). The impact of surgical approach or prosthesis selection on infection is needed to be confirmed in further research.

Furthermore, the incidence of PJI following TJA was decreasing with the surgeon's or hospital's arthroplasty volume increased. Generally, increased arthroplasty volume has been associated with decreased length of stay, resulting in decreased exposure to nosocomial organisms (13). It is also possible that the medical staff in a high-volume institution had more experience in recognizing the early signs and symptoms of developing infection and in taking efficient measures to prevent infection (55,56). In previous studies, it was reported that laminar flow ventilation in the operating room was identified as a risk factor for PJI (30,57). It may be that improper positioning of surgical personnel and lower intraoperative tissue temperatures in the surgical wound increased the risk of infection (58).

Some limitations of this study should be highlighted. First, most of the included studies were observational and retrospective and therefore limited the ability to control for confounding variables, which may have a certain impact on the credibility of the results. Second, the race of patients, primary disease, surgical indication, and follow-up duration varied among these studies, which might result in substantial heterogeneity. Third, due to the limited number of studies available, it was impossible to estimate the effects of all potential risk factors (such as basic diseases, surgery-related factors and hospital-related factors) and to perform

valuable subgroup analysis. Further high-quality studies are warranted to comprehensively clarify the risk factors for PJI after primary THA and TKA.

Conclusions

In conclusion, the J-shaped non-linear relationship between BMI and the risk of PJI demonstrated that increased BMI was associated with an increased risk for PJI in patients undergoing primary THA or TKA. Patients following THA were more likely to suffer from PJI than patients following TKA. Besides, ASA score ≥3, lung disease and diabetes were identified as significant risk factors for PJI, but gender and hypertension were not recognized as risk factors for PJI. Further research is warranted to confirm these findings and to develop effective prevention.

Acknowledgments

Footnote

Conflicts of Interest: All authors have completed the ICMJE uniform disclosure form (available at http://dx.doi.org/10.21037/atm.2020.03.112). The authors have no conflicts of interest to declare.

Ethical Statement: The authors are accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved.

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Supplementary

Table S1 Detailed search strategy in PubMed

Search	Query	Results
#1	"arthroplasty, replacement"[MeSH Terms]	51,108
#2	"total joint arthroplasty"[Title/Abstract]	2,737
#3	TJA[Title/Abstract]	735
#4	"total joint replacement"[Title/Abstract]	1,803
#5	TJR[Title/Abstract]	262
#6	#1 OR #2 OR #3 OR #4 OR #5	53,275
#7	"arthroplasty, replacement, knee"[MeSH Terms]	21,966
#8	"total knee arthroplasty"[Title/Abstract]	17,155
#9	TKA[Title/Abstract]	9,855
#10	"total knee replacement"[Title/Abstract]	5,236
#11	TKR[Title/Abstract]	1,928
#12	#7 OR #8 OR #9 OR #10 OR #11	29,532
#13	"arthroplasty, replacement, hip"[MeSH Terms]	25,177
#14	"total hip arthroplasty"[Title/Abstract]	17,105
#15	THA[Title/Abstract]	9,737
#16	"total hip replacement"[Title/Abstract]	8,000
#17	THR[Title/Abstract]	24,396
#18	#13 OR #14 OR #15 OR #16 OR #17	59,917
#19	#6 OR #12 OR #18	93,795
#20	"surgical wound infection"[MeSH Terms]	34,996
#21	"surgical site infections"[Title/Abstract]	4,711
#22	"surgical site infection"[Title/Abstract]	6,732
#23	SSI[Title/Abstract]	6,059
#24	"periprosthetic joint infections"[Title/Abstract]	329
#25	"periprosthetic joint infection"[Title/Abstract]	1,288
#26	PJI[Title/Abstract]	1,330
#27	#20 OR #21 OR #22 OR #23 OR #24 OR #25 OR #26	43,409
#28	"body mass index"[MeSH Terms]	119,194
#29	"body mass index"[Title/Abstract]	170,596
#30	BMI[Title/Abstract]	133,374
#31	obesity[Title/Abstract]	231,257
#32	overweight[Title/Abstract]	64,379
#33	#28 OR #29 OR #30 OR #31 OR #32	432,598
#34	#19 AND #27 AND #33	235

Source: PubMed; Searched on: August 17, 2019; Results: 235. TJA, total joint arthroplasty; TJR, total joint replacement; TKA, total knee arthroplasty; TKR, total knee replacement; THA, total hip arthroplasty; THR, total hip replacement; SSI, surgical site infection; PJI, periprosthetic joint infection; BMI, body mass index.

Table S2 Detailed search strategy in Embase

Search	Query	Results
#1	"replacement arthroplasty"/exp	35,825
#2	"total joint arthroplasty":ab,ti	2,992
#3	TJA:ab,ti	851
#4	"total joint replacement":ab,ti	2,299
#5	TJR:ab,ti	442
#6	#1 OR #2 OR #3 OR #4 OR #5	39,176
#7	"total knee arthroplasty"/exp	25,772
#8	"total knee arthroplasty":ab,ti	19,335
#9	TKA:ab,ti	11,378
#10	"total knee replacement":ab,ti	6,765
#11	TKR:ab,ti	3,006
#12	#7 OR #8 OR #9 OR #10 OR #11	33,430
#13	"total hip replacement"/exp	1,499
#14	"total hip arthroplasty":ab,ti	19,378
#15	THA:ab,ti	12,252
#16	"total hip replacement":ab,ti	9,995
#17	THR:ab,ti	30,021
#18	#13 OR #14 OR #15 OR #16	32,831
#19	#6 OR #12 OR #18	72,298
#20	"surgical infection"/exp	45,581
#21	"surgical site infections":ab,ti	6,761
#22	"surgical site infection":ab,ti	9,172
#23	SSI:ab,ti	9,239
#24	"periprosthetic joint infections":ab,ti	324
#25	"periprosthetic joint infection":ab,ti	1,192
#26	PJI:ab,ti	1,429
#27	#20 OR #21 OR #22 OR #23 OR #24 OR #25 OR #26	53,078
#28	"body mass"/exp	394,049
#29	"body mass index":ab,ti	244,519
#30	BMI:ab,ti	283,025
#31	obesity:ab,ti	327,920
#32	overweight:ab,ti	95,934
#33	#28 OR #29 OR #30 OR #31 OR #32	741,746
#34	#19 AND #27 AND #33	374

Source: Embase; Searched on: August 17, 2019; Results: 374. TJA, total joint arthroplasty; TJR, total joint replacement; TKA, total knee arthroplasty; TKR, total knee replacement; THA, total hip arthroplasty; THR, total hip replacement; SSI, surgical site infection; PJI, periprosthetic joint infection; BMI, body mass index.

Table S3 Detailed search strategy in Cochrane Library

Search	Query	Results
#1	MeSH descriptor: [arthroplasty, replacement] explode all trees	4,074
#2	"total joint arthroplasty":ti,ab,kw	2,717
#3	TJA:ti,ab,kw	47
#4	"total joint replacement":ti,ab,kw	2,434
#5	TJR:ti,ab,kw	32
#6	#1 OR #2 OR #3 OR #4 OR #5	5,980
#7	MeSH descriptor: [arthroplasty, replacement, knee] explode all trees	2,315
#8	"total knee arthroplasty":ti,ab,kw	5,534
#9	TKA:ti,ab,kw	2,383
#10	"total knee replacement":ti,ab,kw	4,229
#11	TKR:ti,ab,kw	537
#12	#7 OR #8 OR #9 OR #10 OR #11	6,804
#13	MeSH descriptor: [arthroplasty, replacement, hip] explode all trees	1,755
#14	"total hip arthroplasty":ti,ab,kw	3,818
#15	THA:ti,ab,kw	1,356
#16	"total hip replacement":ti,ab,kw	3,591
#17	THR:ti,ab,kw	639
#18	#13 OR #14 OR #15 OR #16 OR #17	6,118
#19	#6 OR #12 OR #18	12,093
#20	MeSH descriptor: [surgical wound infection] explode all trees	3,213
#21	"surgical site infections":ti,ab,kw	3,406
#22	"surgical site infection":ti,ab,kw	3,407
#23	SSI:ti,ab,kw	1,123
#24	"periprosthetic joint infections":ti,ab,kw	106
#25	"periprosthetic joint infection":ti,ab,kw	106
#26	PJI:ti,ab,kw	67
#27	#20 OR #21 OR #22 OR #23 OR #24 OR #25 OR #26	6,203
#28	MeSH descriptor: [body mass index] explode all trees	9,681
#29	"body mass index":ti,ab,kw	37,831
#30	BMI:ti,ab,kw	34,105
#31	obesity:ti,ab,kw	36,942
#32	overweight:ti,ab,kw	14,180
#33	#28 OR #29 OR #30 OR #31 OR #32	76,845
#34	#19 AND #27 AND #33	21

Source: Cochrane Library; Searched on: August 17, 2019; Results: 21. TJA, total joint arthroplasty; TJR, total joint replacement; TKA, total knee arthroplasty; TKR, total knee replacement; THA, total hip arthroplasty; THR, total hip replacement; SSI, surgical site infection; PJI, periprosthetic joint infection; BMI, body mass index.