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Does simultaneous bilateral total joint arthroplasty increase deep infection risk compared to staged surgeries? A meta-analysis

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SUMMARY

Background: Several studies have compared the incidence of periprosthetic joint infection (PJI) between simultaneous bilateral total joint arthroplasty (SBTJA) and staged bilateral total joint arthroplasty (StBTJA) patients following primary total joint arthroplasty. However, these studies lacked statistical power.

Aim: To determine by meta-analysis whether SBTJA increases deep infection risk compared to StBTJA.

Methods: All studies were retrieved from PubMed, Embase, Cochrane Library databases, Web of Science, PEDro, CINAHL, SPORTDiscus, and Scopus. A meta-analysis was conducted to compare PJI rate between SBTJA and StBTJA patients.

Findings: Overall, there were 16 studies with 36,765 patients who underwent SBTJA and 71,558 patients who underwent StBTJA. The pooled data showed that the PJI rate of SBTJA was lower than that of StBTJA (0.84% vs 1.57%; odds ratio (OR): 0.57; 95% confidence interval (CI): 0.49–0.66; heterogeneity, $I^2 = 0\%$; $P = 0.74$). In subgroup analysis, the pooled data revealed that there was no significant difference between SBTJA and StBTJA groups for PJI if the two groups had similar baseline demographics (four studies; OR: 0.55; 95% CI: 0.21–1.40; heterogeneity, $I^2 = 0\%$; $P = 0.77$). The pooled data showed that the PJI rate of SBTJA patients was comparable with that of StBTJA patients within a three-month staging interval (three studies; OR: 1.22; 95% CI: 0.38–3.88; heterogeneity, $I^2 = 0\%$; $P = 0.42$).

Conclusion: SBTJA does not increase the risk of subsequent PJI compared to StBTJA. Further studies are needed to provide higher quality evidence to evaluate the two modes of procedure.

Introduction

Total joint arthroplasty (TJA) is a safe and effective procedure for improving the quality of life and restoring function to patients with arthritis of the knee and hip [1]. In many patients, osteoarthritis affects the joints bilaterally, causing pain and deformity of both joints. These patients may be treated with simultaneous (SBTJA) or staged bilateral TJA (StBTJA).

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However, there is no evidence-based guideline regarding the optimal choice between SBTJA and StBTJA.

Periprosthetic joint infection (PJI) is a major complication of arthroplasty, which may be overwhelming to the patient. The infection itself and the treatment, consisting of sequential interventions and antibiotic administration, have an enormous psychosocial and economic impact [2]. Hence, it is critical that every effort is made to reduce the risk of PJI. Several studies have compared the incidence of PJI between SBTJA and StBTJA patients following primary TJA [3–6]. However, the existing studies lacked statistical power due to small sample size, selection bias by surgeons, different staging interval used in comparing PJI rates, and non-standardized definition of PJI.

Therefore, we conducted a systematic review and meta-analysis to answer the following question: does SBTJA increase deep infection risk compared to staged surgeries?

Methods

Search strategy

A literature search was performed using PubMed, Embase, Cochrane Library databases, Web of Science, PEDro, CINAHL, SPORTDiscus and Scopus between January 1990 and December 2017. The main key words were ('simultaneous' OR 'staged' OR 'unilateral' OR 'one-stage' OR 'two-stage'), AND ('periprosthetic joint infection' OR 'prosthesis-related infection' OR 'PJI' OR 'prosthetic' OR 'surgical site infection' OR 'SSI' OR 'deep infection' OR 'implant infection' OR 'knee infection' OR 'hip infection'), AND ('total knee arthroplasty' OR 'TKA' OR 'total knee replacement' OR 'TKR' OR 'total hip arthroplasty' OR 'THA' OR 'total hip replacement' OR 'THR'). Additional studies were added to the analysis by screening bibliographies of studies.

Eligibility criteria

To minimize any possible selection bias, the following criteria were established: (i) patients had to undergo primary total hip arthroplasty (THA) or total knee arthroplasty (TKA); (ii) studies that compared SBTJA with StBTJA regardless of whether unilateral TJA were included in the comparison; (iii) reported results included PJI; and (iv) data were presented to allow estimates of the odds ratio (OR) for PJI. We excluded: (i) studies published in non-English language; (ii) studies that were systematic reviews, book chapters, expert opinion pieces, narratives or level V evidence; (iii) studies that grouped StBTJA and unilateral TJA cases together; and (iv) studies that define PJI and superficial infection together.

Study selection and data extraction

Two authors independently assessed the search results for inclusion in this systematic review by scanning titles/abstracts or the full text to ensure that they met the eligibility criteria. Disagreements between the two authors were resolved by consensus or through discussion with a third author. If any additional information on potential studies was needed, the corresponding author of the publication was contacted through e-mail.

All information relevant to the research question was extracted from the included articles including the study design, publication year, number of study subjects, demographic data, superficial infection, PJI, cumulative operation time, staging interval, allogeneic transfusion, and mean hospital length of stay (LOS). Two reviewers reviewed the information in each article and came to a consensus on all extracted information.

Study quality assessment

We used an adapted version of the Newcastle–Ottawa Scale (NOS) for assessing the quality of retrospective studies and prospective studies [7]. The NOS is used to assess the quality of non-randomized studies with respect to selection, comparability, and exposure/outcome. The maximum achievable score for included studies was nine stars. According to the Cochrane Bone, Joint and Muscle Trauma Group, the methodology assessment of each included study was made by the two reviewers who were blinded with respect to the journal, the authors, and the source institution [8]. If there was disagreement, it was discussed with a third orthopaedic surgeon. Studies rated less than six stars with NOS scores were excluded.

Statistical analysis

The mean difference (MD) for continuous data and odds ratio (OR) for dichotomous data with their corresponding 95% confidence intervals (CIs) were calculated for each study and pooled with random (DerSimonian–Laird method) or fixed (Mantel–Haenszel method)-effect models according to heterogeneity detected across studies. Based on the practice recommendation of the Cochrane Handbook, studies with zero events in both the intervention and the control groups were not included in the meta-analysis when ORs were calculated [9]. Heterogeneity was analysed by means of I^2-statistic and the χ^2-based Q-test. The cut-points were set at $I^2 > 50\%$ or $P < 0.1$ for the χ^2-test. Publication bias was assessed by a funnel plot, which is a scatter plot of treatment effect versus an assessment of study error; when all publications fall within a symmetric funnel there is a lower likelihood that publication bias exists, whereas if publications fall outside of the symmetric funnel, there is a higher risk of bias. Sensitivity analysis was conducted by removing one study at a time and comparing the resulting meta-analysis with the complete one.

A series of subgroup analyses based on baseline characteristic features (comparable or not) and staging intervals (more than three months or not) was conducted [10]. Studies were considered to have comparable baseline characteristic features if there was no significant difference in age, sex, body mass index (BMI; kg/m^2) and preoperative major comorbidities between the SBTJA and StBTJA groups.

We directly extracted and performed pooled analyses of the data. For the effect estimate, two-tailed $P < 0.05$ was considered statistically significant. All statistical analysis was performed with RevMan (Version 5.3.5 Copenhagen: The Nordic Cochrane Centre, The Cochrane Collaboration, 2014).

Results

Study selection and characteristics

A total of 892 articles were identified through our literature search using the keywords described in the Methods section. During the first round of screening, 255 duplicated articles

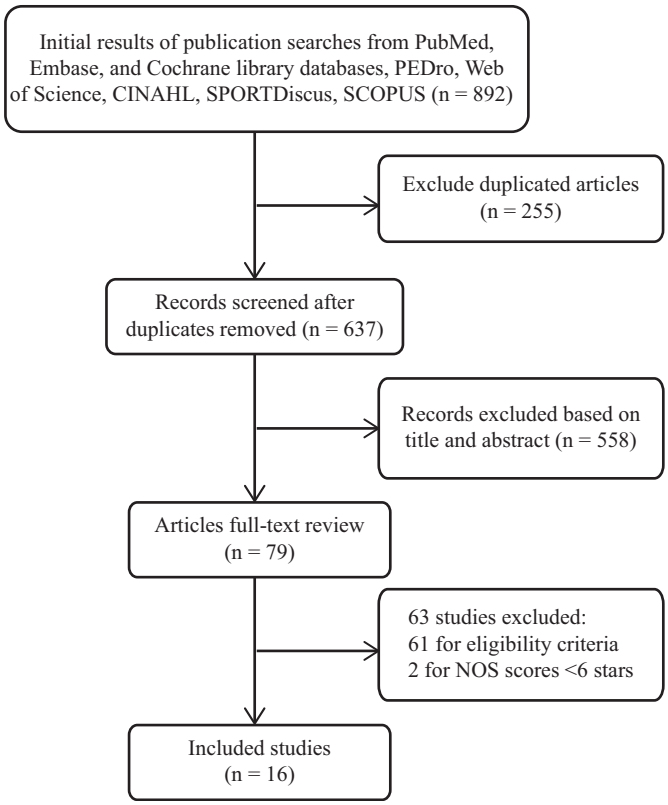

Figure 1. Study selection for the meta-analysis.

were excluded. During the second round of screening, 558 articles were excluded after reviewing the titles and abstracts. During the third round of full-text screening, 61 articles were excluded based on eligibility criteria. Another two articles were excluded for NOS scores of less than six stars [11,12]. After all three rounds of screening, 16 articles were included for further evaluation and were eventually included in the combined analysis (Figure 1).

Table I demonstrates the study characteristics. Among the 16 studies, one was a prospective cohort study, nine were retrospective cohort studies, and six reported on national data or registry data. The studies involved a total of 108,323 patients, of which 36,765 patients underwent SBTJA and 71,558 patients underwent StBTJA. As shown in Table I, the NOS scores of the 16 included studies varied from six to eight stars.

Overall analysis

As shown in Figure 2, the 16 included studies compared the risk of infection between the SBTJA (36,765 patients) and StBTJA groups (71,558 patients). The overall incidence of PJI was 1.32% (1430/108,323). The incidence of PJI was 0.84% (307/36,765) in the SBTJA group compared with 1.57% (1123/71,558) in the StBTJA group. No significant heterogeneity was observed between studies ($I^2 = 0\%$; $P = 0.74$); therefore, a fixed-effects model was used to pool the results. The pooled data showed lower PJI rates in SBTJA versus StBTJA (OR: 0.57; 95% CI: 0.49–0.66). With regard to superficial infection (five studies; 6928 patients in SBTJA and 3765 patients in StBTJA group), SBTJA patients were also less likely to develop infection when compared with StBTJA cases (OR: 0.36; 95% CI: 0.22–0.59; heterogeneity, $I^2 = 0\%$; $P = 0.59$).

Eight studies (14,494 patients in SBTJA group and 11,624 patients in StBTJA group) provided data on mean and standard deviation of age; the pooled data showed that SBTJA patients were younger than StBTJA cases (MD: −2.84; 95% CI: −5.25 to −0.43; heterogeneity, $I^2 = 99\%$; $P < 0.001$) (Table II). Seven studies (11,777 patients in SBTJA and 32,774 patients in StBTJA group) provided data on allogeneic transfusion, and SBTJA patients were more likely to need allogeneic transfusion compared with StBTJA patients (OR: 2.91; 95% CI: 2.42–3.50;

Table I
Characteristics of the included studies

First author [reference]	Country	Study type	NOS	SBTJA			StBTJA		
				No.	% Male	Age (years)	No.	% Male	Age (years)
Bohm [24]	Canada	ND	7	6349	41	NR	25,253	39	NR
Bolognesi [25]	USA	ND	6	8307	22	73.3	3788	39	74.1
Courtney [26]	USA	RC	6	103	37	59.4	131	23	64.2
Hadley [4]	USA	RC	7	371	30	63.9	67	36	63.1
Houdek [3]	USA	RC	8	94	57	52.2	94	57	52.1
Hutchinson [5]	Australia	PC	7	438	56	67.0	125	38	65.0
Liu [27]	China	RC	6	64	5	66.7	24	0	68.6
Meehan [16]	USA	RC	8	11,445	46	67.2	23,715	39	67.7
Namba [28]	USA	ND	7	324	NR	NR	8475	NR	NR
Poultsides [1]	USA	RC	8	2825	38	65.2	1151	32	69.5
Ritter [29]	USA	RC	6	2050	44	69.9	152	23	69.2
Seol [30]	Korea	RC	7	759	6	68.3	315	8	66.0
Sobh [17]	USA	RC	6	225	48	61.0	337	38	68.0
Spicer [31]	Canada	Registry	7	373	29	69.1	966	34	69.6
Stefano [32]	USA	Registry	6	1230	42	66.0	2123	34	67.0
Triantafyllopoulos [2]	USA	RC	7	1808	51	56.3	4842	41	63.8
Total	–	–	–	36,765	37	64.7	71,558	32	66.3

NOS, Newcastle–Ottawa Scale; SBTJA, simultaneous bilateral total joint arthroplasty; StBTJA, staged bilateral total joint arthroplasty; ND, national database; NR, not reported; RC, retrospective cohort; PC, prospective cohort.

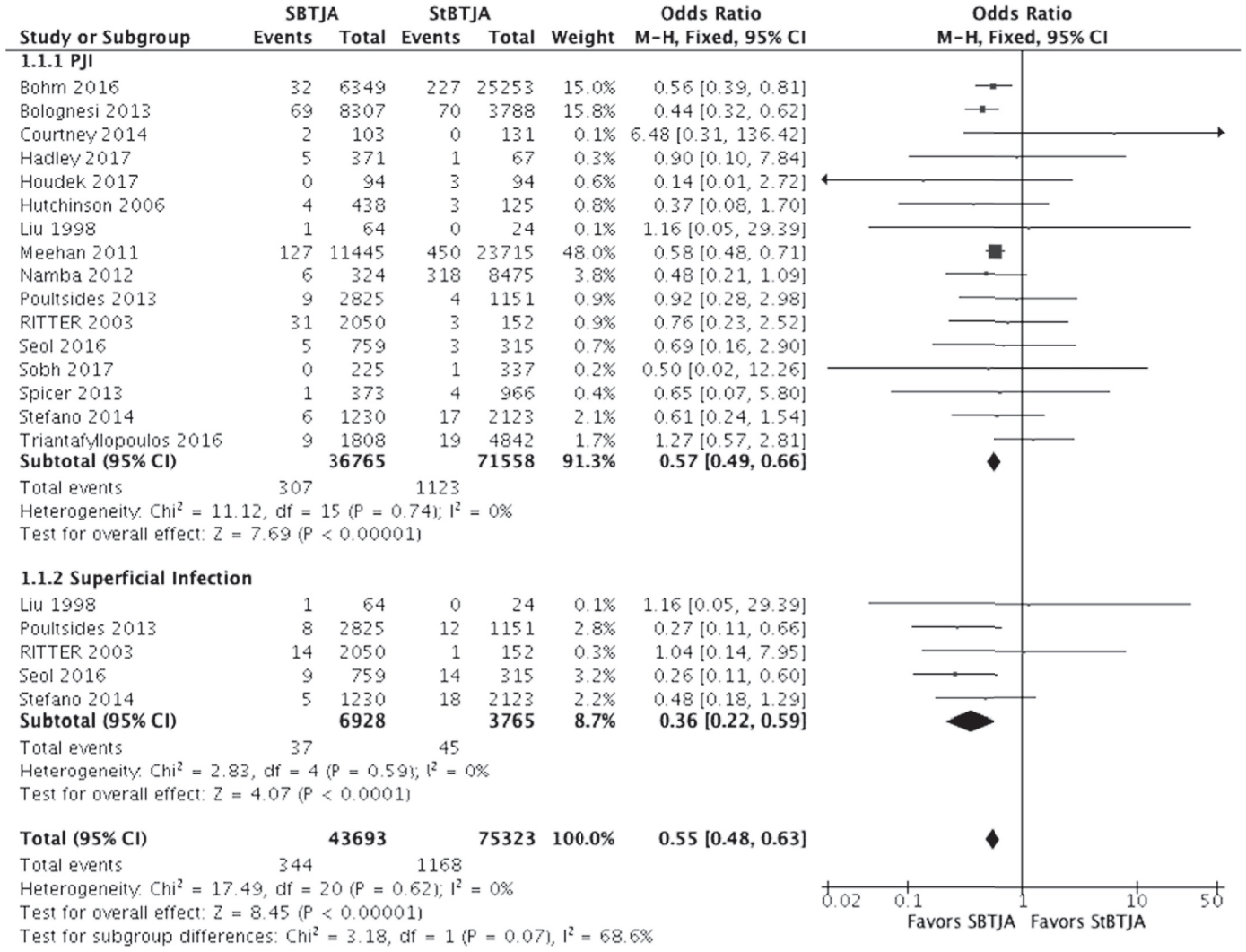

Figure 2. Forest plot demonstrating the odds ratio and 95% confidence interval (CI) for periprosthetic joint infection (PJI) and superficial infection. SBTJA, simultaneous bilateral total joint arthroplasty; StBTJA, staged bilateral total joint arthroplasty.

heterogeneity, $I^2 = 81\%$; $P < 0.001$). The cumulative operative time (three studies; 2983 patients in SBTJA and 1269 patients in StBTJA group) and LOS (six studies; 5932 patients in SBTJA and 7429 patients in StBTJA group) of SBTJA were shorter than those of StBTJA (cumulative operative time: MD: −40.63; 95% CI: −76.38 to −4.88; heterogeneity, $I^2 = 98\%$; $P < 0.001$; cumulative LOS: MD: −4.82; 95% CI: −6.36 to −3.29; heterogeneity, $I^2 = 100\%$; $P < 0.001$).

Subgroup analysis

Separate subgroup analyses were performed with respect to baseline characteristic features and staging intervals. Having regard to baseline characteristic features (age, sex, BMI, comorbidities), four studies had similar baseline between SBTJA and StBTJA groups, whereas nine studies had different baselines between the two groups. The other three studies were not included in this subgroup analysis due to unavailable baseline data. The analysis of the four studies with comparable baseline demographics suggested that there were no significant differences between SBTJA and StBTJA groups for PJI (OR: 0.55; 95% CI: 0.21–1.40; heterogeneity, $I^2 = 0\%$; $P = 0.77$) (Figure 3), whereas the 12 studies with different baselines showed that STBJA had lower PJI rates than StBJTA (OR: 0.57; 95% CI: 0.49–0.66; heterogeneity, $I^2 = 15\%$; $P = 0.31$).

Twelve studies provided data on staging intervals, and these studies were stratified based on three-month intervals. The results indicated that there was no significant difference in PJI between SBTJA and StBTJA patients with staging intervals less than three months (OR: 1.22; 95% CI: 0.38–3.88; heterogeneity, $I^2 = 0\%$; $P = 0.42$) (Figure 4). However, the PJI rate of the SBTJA group was lower than that of the StBTJA group when staging intervals were longer than three months (OR: 0.57; 95% CI: 0.49–0.66; heterogeneity, $I^2 = 0\%$; $P = 0.44$).

Publication bias and sensitivity analysis

The funnel plot of the included studies for PJI indicates symmetry, suggesting no heterogeneity, and therefore publication bias is unlikely (Figure 5). The sensitivity analysis showed no significant changes when each of the studies included were removed sequentially.

Table II
Comparison of periprosthetic joint infection and other parameters between SBTJA and StBTJA

Variables	No. of studies	No. of patients (SBTJA/StBTJA)	Overall effect		Heterogeneity	
			P-value	MD/OR (95% CI)	I^2	*P*-value
Periprosthetic joint infection	16	36,765/71,558	<0.001	0.57 (0.49, 0.66)	0%	0.740
Superficial infection	5	6928/3765	<0.001	0.36 (0.22, 0.59)	0%	0.590
Age	8	14,494/11,624	0.020	−2.84 (−5.25, −0.43)	99%	<0.001
Transfusion rate	7	11,777/32,774	<0.001	2.91 (2.42, 3.50)	81%	<0.001
Operative time	3	2983/1269	0.030	−40.63 (−76.38, −4.88)	98%	<0.001
Length of stay	6	5932/7429	<0.001	−4.82 (−6.36, −3.29)	100%	<0.001

SBTJA, simultaneous bilateral total joint arthroplasty; StBTJA, staged bilateral total joint arthroplasty; MD, mean difference; OR, odds ratio; CI, confidence interval.

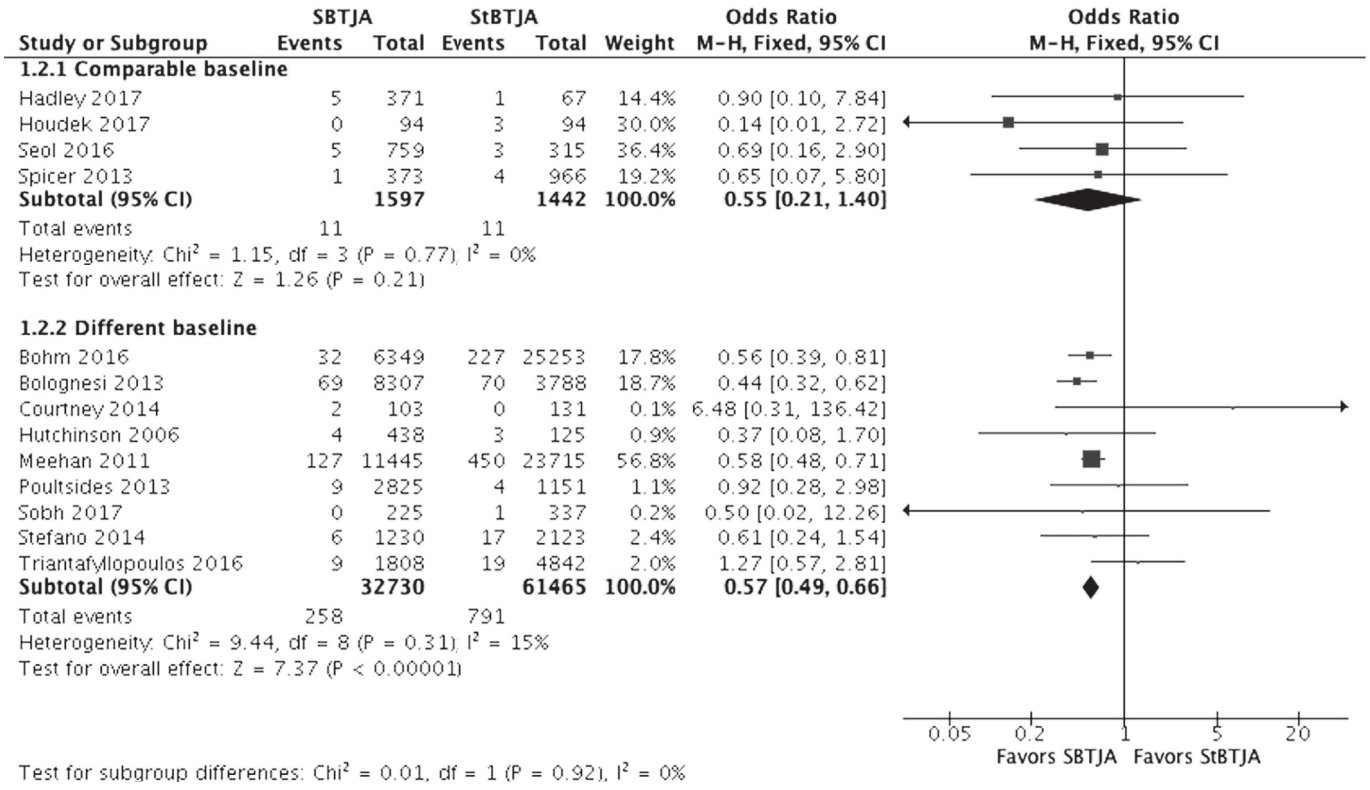

Figure 3. Forest plot demonstrating the odds ratio and 95% confidence interval (CI) for subgroup analysis of baseline characteristic features. SBTJA, simultaneous bilateral total joint arthroplasty; StBTJA, staged bilateral total joint arthroplasty.

Discussion

The most important finding of the present study was that SBTJA does not increase the risk of subsequent PJI compared to StBTJA. In this study, we further conducted subgroup analysis to take into account the impact of selection bias by surgeons and staging intervals on the difference between SBTJA and StBTJA groups for PJI rates.

Overall, our pooled data indicated that the SBTJA group had a lower infection rate than the StBTJA group. The rationale may be that surgeons likely choose younger and healthier patients for SBTJA, as younger age and fewer comorbidities are associated with a decreased risk of infection [2,13,14]. In the present study, the pooled data of studies with comparable baseline characteristics showed that there was no significant difference in infection rate between the two groups, which directly supports the aforementioned theory. StBTJA patients who underwent staged surgeries within a three-month interval may also be younger and healthier compared to StBTJA patients who had a longer staging interval. In the subgroup analysis, there was no significant difference in PJI between StBTJA within three-month staging interval and SBTJA. This may be explained by the fact that StBTJA patients within three-month staging interval may be comparable with SBTJA patients in terms of physical status, which again supports the existence of selection bias. In addition, surgeons are more likely to perform staged surgery for patients experiencing inflammatory or post-traumatic arthritis, conditions that have a significantly higher risk of developing infection than in patients with simple degenerative arthritis [2].

The present study showed that there was a significant difference between the two procedures in cumulative operative

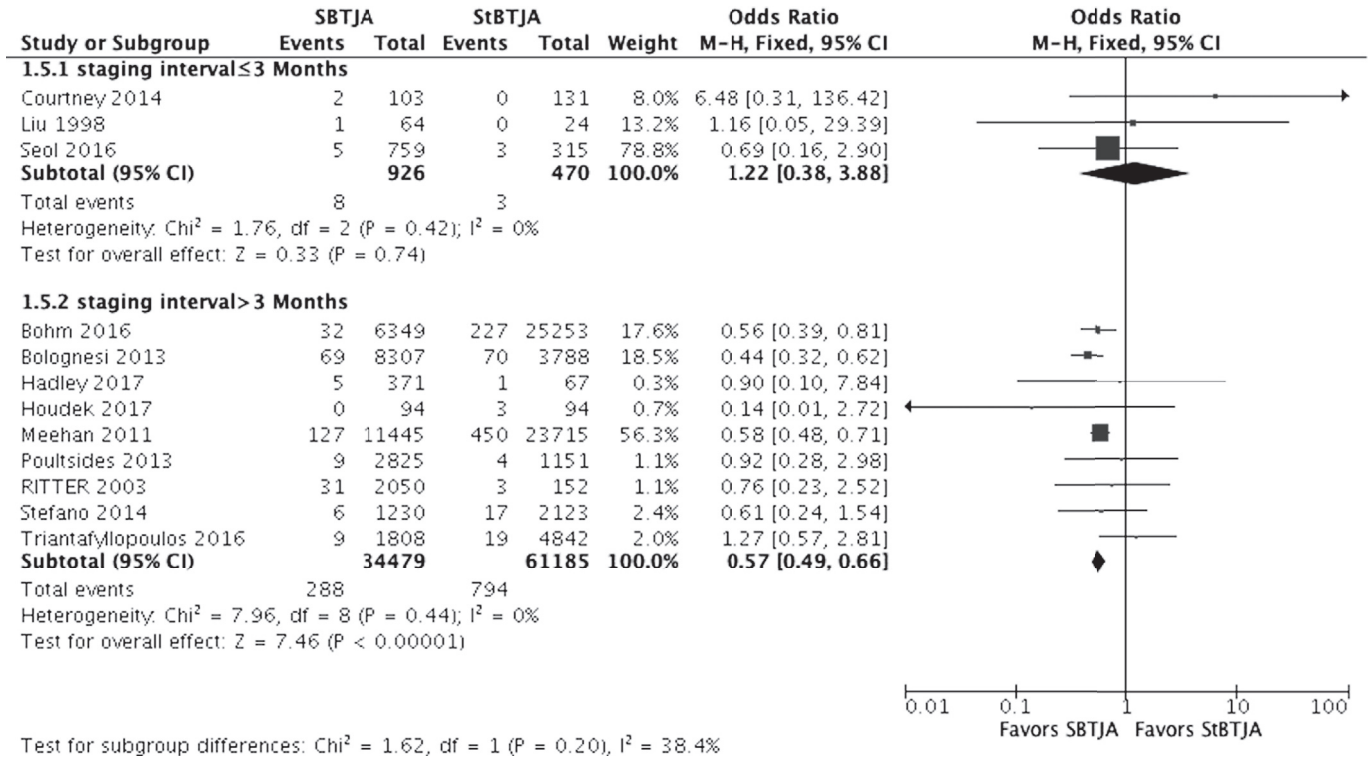

Figure 4. Forest plot demonstrating the odds ratio and 95% confidence interval (CI) for subgroup analysis of staging interval. PJI, periprosthetic joint infection; SBTJA, simultaneous bilateral total joint arthroplasty; StBTJA, staged bilateral total joint arthroplasty.

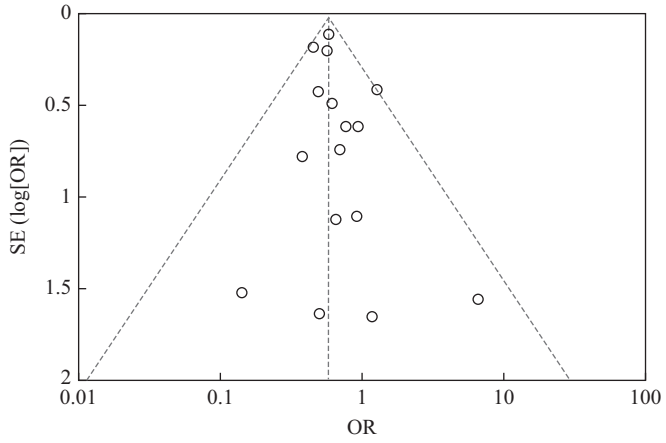

Figure 5. Funnel plot assessing heterogeneity of included studies. The symmetry of the plot demonstrates absence of publication bias and heterogeneity. SE, standard error; OR, odds ratio.

time and LOS, both predisposing factors in the development of PJI [15]. The SBTJA group had shorter surgical time and LOS for each procedure, which may partially account for the lower rates of PJI. Poultsides *et al.* reported that longer LOS was an independent risk factor for development of PJI even after adjusting for other variables [1]. It is possible that with a longer LOS, patients were more likely to be exposed to nosocomial and virulent pathogens that could result in PJI.

Several studies have reported that there were no significant differences between SBTJA patients and unilateral TJA patients for infection rate, but StBTJA patients had higher risks than those two groups [16–18]. They surmised that the risk of PJI is not the number of joints replaced, but the number of times that a patient undergoing TJA enters an operating room, which is likely the main source of infection. Therefore, patients who undergo staged surgery experience approximately twice the risk of a single procedure. We also conducted an analysis to compare the infection rate of unilateral TJA with that of SBTJA, and the pooled data showed that there was no difference between the two groups (Supplementary Figure 1), which supports this hypothesis. However, studies comparing SBTJA and unilateral TJA involve two very different patient populations, so the results are potentially biased and should be interpreted with caution [13].

As reflects surgeon choice and patient preference, a significant number of bilateral surgeries are performed by higher-volume surgeons and in high-volume arthroplasty centres worldwide, factors that are associated with lower rates of PJI, compared to low-volume surgeons and low-volume hospitals [19]. In addition, follow-up time bias may exist in some of the included studies, as patients who underwent StBTJA were monitored for double the number of days of follow-up cumulatively, compared with SBTJA patients [13].

However, postoperative infection is multi-factorial. Whereas many of the above findings reflect congruence between known risk factors of PJI and the pooled results, the analysis found other results that contradict expectations based on current understanding. First, previous studies determined that allogeneic transfusion rate is an independent risk factor in developing PJI, by increasing infection risk by transmitting infectious agents and modulating the immune system; however, the pooled data indicated that SBTJA patients were more likely

to have allogeneic transfusions compared to StBTJA patients, but had equivalent or lower rates of PJI [20]. Second, the literature reports that more than one-third of patients experiencing bilateral arthritis may not undergo the second stage operation for a variety of reasons including unsatisfactory function, unmet expectations, complications, or death after the first side [21]. In most retrospective studies, especially studies comprising national database or registry data, these patients were misclassified as simply having undergone unilateral TJA. This misclassification bias should influence reported complication rates, allowing the StBTJA group to appear to have a lower overall rate of major complications including infection rate [2]. However, the analysis showed that StBTJA had equivalent or higher rates of PJI and superficial infection.

In the literature there are two types of simultaneous operation in bilateral total joint arthroplasty (BTJA): sequential and concurrent [11,12]. Sequential procedures are defined as one operating team performing both surgeries one side following the other, whereas concurrent procedures occur when two operating teams perform the TKAs or THAs with a direct anterior approach at the same time. However, we were unable to investigate the difference between the two subgroups, as most of the studies we reviewed did not differentiate between them. Although some authors argued that concurrent BTJA patients are more vulnerable to PJI than sequential BTJA due to the increased number of personnel in the operating room, most authors conclude that sequential BTJA would have higher odds for developing PJI due to prolonged operative time and lack of redraping and rescrubbing [12,22,23]. Moreover, two separate sets of instruments and materials are usually used in concurrent BTJA, yet surgeons may not change instruments in sequential procedures. Luscombe *et al*. and Yoon *et al*. proposed that the absence of an increased postoperative infection rate in the STBJA group could be attributed to the use of two separate sets of instruments and materials [22,23].

Some limitations should be recognized in this meta-analysis. First, most of the included studies were retrospective studies, which are prone to aforementioned biases that can affect the validity of the results. However, it would be difficult to carry out a truly controlled randomized trial that compared SBTJA with StBTJA due to cost and ethical issues. Second, it is generally acknowledged that PJI is multi-factorial, yet most of the included studies provided unadjusted results that were used directly in the meta-analysis. However, we conducted a variety of subgroup analyses to explore these potential confounders. Third, there was clear publication bias in some results. However, we used random effect modelling to eliminate its high heterogeneity. Finally, both national-database and single-centre studies were included. However, the sensitivity analysis showed no significant changes when each of the studies included were removed sequentially.

In conclusion, SBTJA does not increase the risk of postoperative PJI compared with StBTJA. Further studies are needed to provide higher quality evidence to evaluate the two modes of procedure.

Conflict of interest statement
None declared.

Funding sources
None.

Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.jhin.2018.08.019.

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