Archives of Orthopaedic and Trauma Surgery (2019) 139:695–707
https://doi.org/10.1007/s00402-019-03121-x

KNEE REVISION SURGERY

Comparison of infection eradication rate of using articulating spacers containing bio-inert materials versus all-cement articulating spacers in revision of infected TKA: a systematic review and meta-analysis

Qiang Yu[1] · Mayao Luo[2] · Shaoyu Wu[2] · Anli Lai[2] · Yang Sun[2] · Qinyuan Hu[2] · Yi He[2] · Jing Tian[1]

Received: 17 May 2018 / Published online: 8 March 2019

Abstract

Purpose To assess the infection eradication rate when using two types of articulating spacers (prosthetic articulating spacers and all-cement articulating spacers) in two-stage revision of infected total knee arthroplasty (TKA).

Methods We comprehensively searched PubMed, Embase, and the Cochrane Library databases and performed a systematic review and meta-analysis of retrospective comparative studies assessing two types of articulating spacers. A quality assessment of the included studies was performed following the STROBE statement.

Results Thirty retrospective studies, including a total of 821 knees, were identified. The pooled infection control rates in stage I were as follows: 0.98 (95% confidence interval [CI], 0.97 to 1.00) and 0.98 (95% CI, 0.96 to 0.99) for the prosthetic articulating spacer group and all-cement articulating spacer group, respectively. The pooled postoperative reinfection rate was 0.05 (95% CI, 0.03 to 0.08) for the prosthetic spacer group and 0.03 (95% CI, 0.01 to 0.06) for the all-cement spacer group. Results of the subgroup analyses showed that the weight of the antibiotic cement, antibiotic type, mean period of spacers in situ, postoperative antibiotic treatment period, and postoperative antibiotic treatment approach had no effect on the reinfection rates ($p < 0.05$).

Conclusions Compared to all-cement articulating spacers, articulating spacers containing bio-inert materials have a similar infection control rate but a higher postoperative reinfection rate. Although the 95% CIs of reinfection rates in the two groups overlapped, our results indicate that articulating spacers containing bio-inert materials may be associated with higher reinfection rates and poorer clinical outcomes than all-cement articulating spacers.

Keywords Total knee arthroplasty · Total knee replacement · Revision TKA · Periprosthetic infection · Articulating spacer · Bio-inert material

Introduction

Infection in total knee arthroplasty (TKA) is a devastating complication for patients and surgeons alike. Two-stage revision arthroplasty and 6-week systemic antibiotic use have been the gold standard treatment in recent years, with an infection control rate of approximately 85–95% [1–5].

A two-stage revision procedure involves removal of the prosthesis and implantation of a temporary, antibiotic-impregnated cement spacer, including static spacers and articulating spacers [6]. However, static spacers may have some disadvantages, such as restricted mobility of the knee joint, high risk of thrombosis [7, 8], great difficulty in exposure at the time of second-stage reimplantation and a possibility of additional bone loss [9]. Attempts to overcome these problems led to the development of articulating spacers.

Currently, two types of articulating spacers are commonly used. The first type is made entirely of cement (all-cement spacers), and the second is made of antibiotic-loaded cement covered with bio-inert materials, such as plastic or metal (prosthetic spacers). Prosthetic spacers offer smoother articulating surfaces as well as better mobility in the interval

✉ Jing Tian
tianjing_ortho@163.com

[1] Department of Orthopaedics, Zhujiang Hospital, Southern Medical University, 253 Industrial Avenue, Haizhu, Guangzhou 510282, Guangdong, China

[2] The Second Clinical Medical School, Zhujiang Hospital, Southern Medical University, 253 Industrial Avenue, Haizhu, Guangzhou 510282, Guangdong, China

between the two procedures. They also have advantages of lower costs when reusing the original autoclaved femoral component. However, there are multiple concerns regarding the possibility of microorganisms adhering to either a metallic or plastic prosthesis [10], which may lead to a lower infection control rate and higher reinfection rate after revision. A limited number of studies have concentrated on the clinical results of the infection control rate and the reinfection rate between prosthetic spacers and all-cement spacers. Spivey et al. [11] compared four types of articulating spacers, including metal-on-polyethylene, cement-on-cement handmade, cement-on-cement prefabricated, and cement-on-cement moulded spacers. They examined the outcome scores, range of motion (ROM), reinfection rates, reimplantation rates, and complications. However, Spivey JC et al. did not evaluate the infection control rate or perform comprehensive subgroup analyses, which were performed in our study.

Infection eradication rates play an important role in influencing the surgeon's choice of spacer type. In this review, we compared articulating spacers containing bio-inert materials (metal or plastic) with all-cement articulating spacers with respect to the infection control rates at stage I and the postoperative reinfection rates after revision. The aim of this review was to analyse to what extent the infection eradication rates differ between the two types of articulating spacers. We hypothesized that the all-cement articulating spacer group would have higher infection eradication rates than the prosthetic spacer group because of the lack of foreign materials.

Materials and methods

This review meets the requirements of the Preferred Reporting Items for Systematic reviews and Meta-Analyses (PRISMA) statement [12]. The literature search strategy, inclusion and exclusion criteria, quality assessment, data extraction and methods of statistical analysis were in accordance with the statement requirements.

Search strategy

A comprehensive search of the PubMed, Embase, and Cochrane Library databases was performed in July 2017. The following MeSH terms and their combinations were searched in the [Title/Abstract]: "total knee arthroplasty", "TKA", "total knee replacement", "TKR", "periprosthetic infection", "PPI" and "spacer". When multiple reports describing the same population were published, the most recent and complete report was considered eligible for inclusion.

Inclusion and exclusion criteria

Two reviewers (Yu and Luo) independently screened the title and abstract of retrieved articles and selected the relevant studies for full-text review. Studies were included in this meta-analysis if they (1) were published in English between 2000 and July 1, 2017; (2) included the patients who underwent two-stage revision for the first time using antibiotic-loaded articulating cement spacers to treat a periprosthetic infection after TKA; (3) included patients using articulating cement spacers containing a bio-inert material or patients using all-cement articulating spacers; and (4) were independent from other studies to prevent double weighting. Studies that met the following criteria were excluded: (1) designed as a review; (2) employed special antibiotics carriers; (3) patients were reported in other manuscripts; and (4) detailed data were not extractable.

Quality assessment

Methodological quality was defined as confidence that the study design and reporting were free of bias. The latest version of the STROBE statement was used to assess the quality of the studies that were included [13]. Each included study was independently read and scored by two reviewers (He and Wu). Disagreements were discussed until a unanimous conclusion was reached.

Data extraction and statistical analysis

Two reviewers (Lai and Hu) independently extracted relevant data from included studies according to pre-developed forms. The following items were extracted from each study: authors and publication year, total number of knees, basic information of patients (i.e., country, mean age and gender), spacer type, weight and type of antibiotics in cement, mean period of spacers in situ, the length and type of postoperative antibiotic treatment, pathogens, the length of follow-up, infection control rate after the first stage and reinfection rate after the second stage, when available. The methods each included study performed to diagnose the infection in the first stage or after the second stage were also extracted.

Gender, mean ages and bacterial strains of the two groups were compared using a Chi square test performed by SPSS (Version 20.0, Chicago, IL, USA). The pooled infection control rates as well as the postoperative reinfection rates between two articulating spacer groups were analysed using R software (version 3.4.0). R software was also used for the subgroup analyses, including the weight of antibiotics in cement, the type of antibiotics in cement, the mean period of spacers in situ, the length

of postoperative antibiotic treatment and the approach of postoperative antibiotic treatment. Normality was assessed by Shapiro's test. Statistical heterogeneity between studies was assessed using the Q statistic (Chi-square test) and I^2 statistic. An I^2 test result greater than 50% indicated moderate-to-high heterogeneity, and a random-effects model was subsequently used. Otherwise, a fixed-effects model was used. Egger's test and funnel plots were used to screen for potential publication bias. A p value of 0.05 or lower was considered statistically significant, and all measures were reported with 95% confidence intervals (CIs).

Results

Search result and quality assessment

We completed the literature search on July 1, 2017. A flow chart of the search strategy is shown in Fig. 1. Thirty studies [9, 10, 14–41] with a total of 821 knees were eventually identified and included in the final analysis. Agreement between the two reviewers was 96% for study selection and 90% for the quality assessment of the included studies. We evaluated the methodological quality of all included studies using the STROBE statement, and the results were confirmed by mutual consensus. The STROBE scores of the

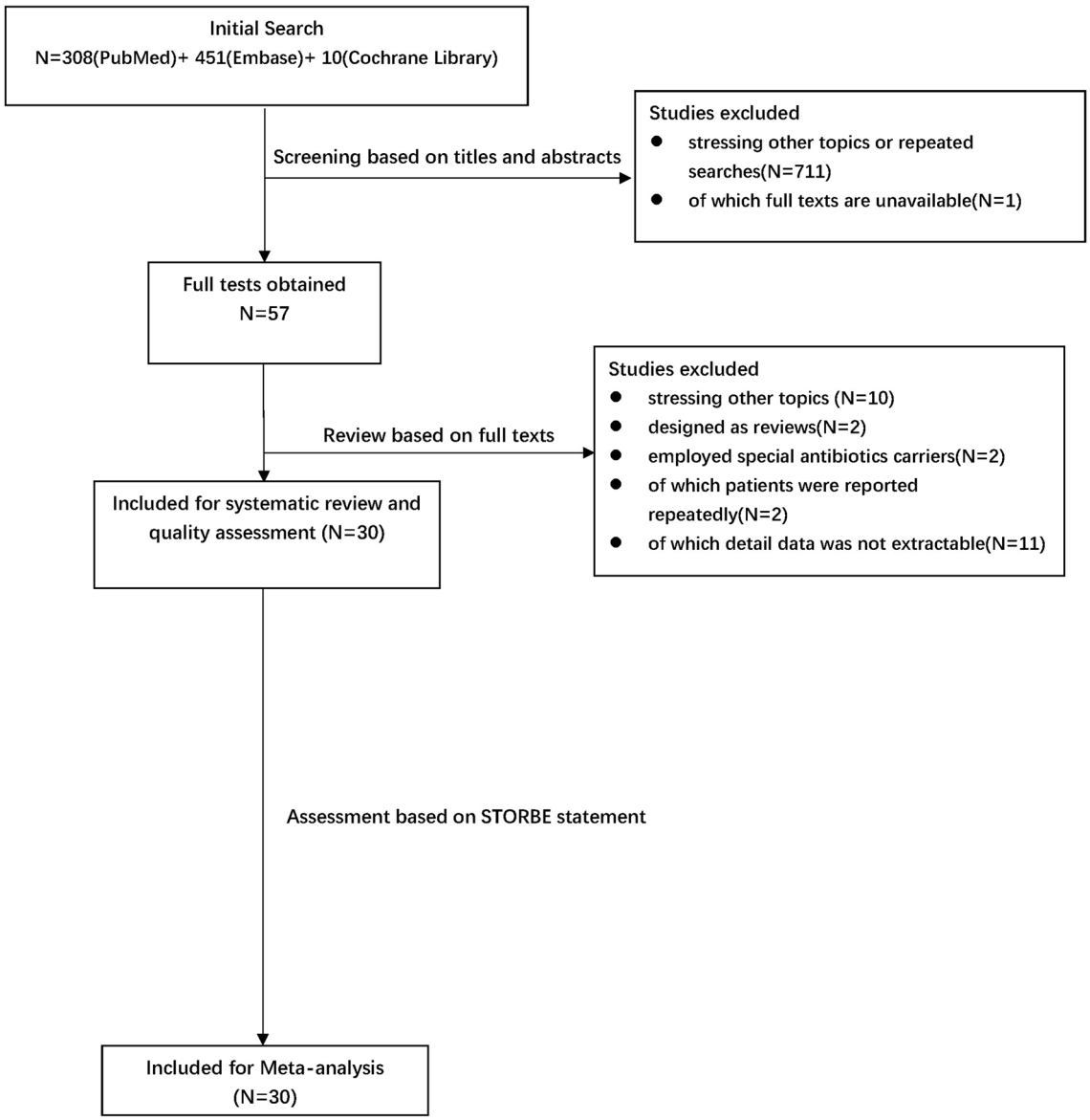

Fig. 1 Flowchart of the literature search

included studies ranged from 12 to 18 points, with an average of 15 points. The results of the quality assessment are provided in Table 1.

Characteristics of eligible studies

The characteristics of the included studies are summarized in Table 1. Among these 30 retrospective studies, all-cement articulating spacers were used in 15 studies [10, 16, 20–23, 25, 28, 34–36, 38–41], and prosthetic articulating spacers were used in 14 studies. One study performed by Kalore et al. [29] compared all-cement spacers with prosthetic spacers. Prosthetic articulating spacers mainly include two subtypes based on their components: one containing autoclaved original components (AOC) and the other containing new components (NC).

The characteristics of the participants in the prosthetic spacer group and all-cement spacer group are shown in Table 2. Significant differences were found using the Chi-square test in gender composition ($\chi^2 = 71.52$, $p < 0.00001$), the proportion of Gram-negative bacterial infection ($\chi^2 = 5.97$, $p = 0.018$) and the proportion of fungal infection ($\chi^2 = 10.44$, $p = 0.001$) between the two groups. These results suggest a potential bias that may influence the results. Other

Table 1 Information of the included studies

Authors	Country	Knees	Infection type	Spacer type	Mean age (y)	Mean follow-up (Mo)	Score
Classen et al. [18]	Germany	23	NI	AOC	66	47	17
Kim et al. [30]	Korea	20	NI	AOC	61.5	22.3	16
Lee and Choi [32]	Korea	20	Chronic	AOC	64.8	64.8	14
Choi et al. [17]	USA	14	NI	AOC/NC	64	43	16
Anderson et al. [14]	USA	25	Chronic	AOC	64	54	15
Huang et al. [26]	Taiwan	21	NI	AOC	68.7	52.2	14
Hofmann et al. [24]	USA	50	Chronic	AOC	67	74	18
Cuckler [19]	England	44	Chronic	AOC	68	64.8	15
Emerson et al. [9]	USA	22	NI	AOC	65.1	45.6	14
Lee et al. [31]	Korea	20	Chronic	AOC	71	29	18
Jämsen et al. [27]	Finland	24	NI	AOC	68	25	17
Brunnekreef et al. [15]	Netherlands	26	NI	NC	58	12	16
Meek et al. [33]	Canada	47	NI	NC	N	41	18
Qiu et al. [37]	China	10	NI	AOC/NC	63	50	16
Kalore et al. [29]	USA	16	Chronic	NC	67.3	73	18
		22		ACAS	61.1	32	
		15		AOC	63.6	19	
Castelli et al. [16]	Italy	50	NI	ACAS	68	84	17
Jia et al. [28]	China	21	NI	ACAS	64.4	32.2	16
Garg et al. [22]	India	36	Chronic	ACAS	63	62	12
Van Thiel et al. [40]	USA	60	NI	ACAS	66	35	14
Shen et al. [38]	China	17	NI	ACAS	67	31	15
Park et al. [34]	Korea	16	NI	ACAS	60.2	29	17
Villanueva-Martínez et al. [41]	Spain	30	NI	ACAS	71	18	15
Hsu et al. [25]	China	21	NI	ACAS	NA	58	15
Freeman et al. [21]	USA	48	NI	ACAS	64.9	62.2	16
Pascale and Pascale [35]	Italy	14	NI	ACAS	68	12	14
Pitto et al. [36]	New Zealand	21	NI	ACAS	67	24	15
Durbhakula et al. [20]	USA	24	NI	ACAS	72	33	15
Ocguder et al. [10]	Turkey	17	NI	ACAS	63	20	16
Ha et al. [23]	Korea	12	Chronic	ACAS	65.1	NA	14
Su et al. [39]	Taiwan	15	NI	ACAS	72	47.5	14
Total		821					

The column "score" indicates the quality assessment of each study according to the STROBE statement

NI not identified, *AOC* autoclaved original components, *NC* new components, *ACAS* all-cement articulating spacer, *NA* data not available

Table 2 Characteristics of participants

	Group A	Group B	*P* value
Patients	416	393	
Knees	424	397	
Mean age (mean ± SD)	66.24 ± 3.27	64.62 ± 2.39	NS
Gender			
Female	220	242	< 0.01
Male	127	151	
UA	69	0	
Pathogens			
Gram-positive	195	185	NS
S. aureus	108	93	NS
S. epidermidis	59	74	NS
Streptococcus	28	18	NS
Gram-negative	30	13	0.018
Fungus	11	0	0.001
Unknown	58	41	NS
Drug-resistant	52	37	NS
Multiple	12	17	NS

Group A: the all-cement spacers group; Group B: the prosthetic spacers group; UA: information unavailable; NS: no significance

characteristics, including mean age, Gram-positive bacterial infection, drug-resistant pathogens and multiple pathogens, were not found to be significantly different between the two groups ($p > 0.05$).

Antibiotic treatment information was collected from all of the studies, if available, and the results are shown in Table 3.

Infection diagnosis information was also obtained from the included studies, and the results are shown in Table 4. The results suggest that all included studies differ as to how the infection was detected, which may potentially increase the risk of the bias.

Pooled infection control rate in stage I

Data from 15 studies were pooled to assess the infection control rate of the all-cement articulating spacer group. Among these studies, five studies [21–23, 34, 35] reported the highest infection control rate of 100%, while Kalore et al. [29] reported the lowest infection control rate of 91%. The pooled infection control rate was 0.98 (95% CI, 0.96 to 0.99, $I^2 = 31\%$), as shown in Fig. 2. For the prosthetic articulating spacer group, data from 13 studies [9, 14, 17–19, 24, 26, 27, 29–32, 37] showed a pooled infection control rate of 0.98 (95% CI, 0.97 to 1.00, $I^2 = 49\%$), as shown in Fig. 3. Eight studies [9, 14, 17, 18, 26, 27, 30, 31] reported the highest infection control rate of 100%, while Kalore et al. [29] reported the lowest rate of 87%. The results indicate that the infection control rate at stage I was not different between the prosthetic articulating spacer and all-cement spacer groups.

Pooled postoperative reinfection rate

The reinfection rates after knee arthroplasty were collected from 29 studies. In all 15 studies [10, 16, 20–23, 25, 28, 34–36, 38–41] that assessed reinfection rates of all-cement articulating spacers, nine studies [19–21, 26, 33, 34, 36, 37, 39] reported no reinfection, while Van Thiel et [40] and Ocguder et al. [10] reported high reinfection rates of 12%. The pooled postoperative reinfection rate was 0.03 (95% CI, 0.01 to 0.06, $I^2 = 28\%$), as shown in Fig. 4. Among the 14 studies that reported on groups with prosthetic spacers [9, 14, 15, 17–19, 24, 26, 27, 30–33, 37], three studies [15, 19, 37] reported no reinfection, while Choi et al. [17] reported high reinfection rates of 40%. The pooled reinfection rate was 0.05 (95% CI, 0.03 to 0.08, $I^2 = 44\%$), as shown in Fig. 5. In addition, the pooled reinfection rate of the prosthetic spacer group was higher than that of the all-cement group, although a similar 95% CI was noted.

Subgroup analysis outcomes

Considering that different antibiotic therapies may affect the reinfection rate. Subgroup analyses were conducted to determine whether the weight of antibiotic cement, type of antibiotic, mean length of the spacers in situ period, postoperative antibiotic treatment period, and postoperative antibiotic treatment approach of all included studies influenced the reinfection rate. The data are shown in Table 5. Subgroup analyses showed no significant differences between the two groups.

Assessment of publication bias

Begg's funnel plot and Egger's test were performed to assess the publication bias of the articles in this meta-analysis. The shapes of the funnel plot did not reveal notable asymmetry (Fig. 6), and all *p* values from the Egger's tests were greater than 0.05, which provided statistical evidence of funnel plot symmetry. Thus, these results suggest that publication bias was not evident in this meta-analysis.

Discussion

Infected TKA remains one of the greatest challenges for orthopaedic surgeons. The purpose of the present study was to analyse the differences in the infection control rate and reinfection rate when using different types of articulating spacers to treat infected TKA.

The most important finding of the present study was that articulating spacers containing bio-inert materials resulted in a higher postoperative reinfection rate than all-cement articulating spacers, although the two types of articulating

Table 3 Antibiotic treatment information

Authors	Spacer type	Antibiotics in cement		Mean period of spacers in situ (weeks)	Postoperative antibiotic treatment	
		Weight	Type		Period (weeks)	Approach
Classen et al. [18]	AOC	0.8 g/40 g	S	26	6	Intravenous/oral
Kim et al. [30]	AOC	5 g/40 g	D	13.2	10	Intravenous/oral
Lee and Choi [32]	AOC	3.4 g/40 g	D	20	6	Intravenous/oral
Choi et al. [17]	AOC/NC	3.4 g/40 g	D	24	6	Intravenous
Anderson et al. [14]	AOC/NC	5.6 g/40 g	D	11	6	Intravenous
Huang et al. [26]	AOC	1 g/40 g	S	20.7	6	Intravenous
Hofmann et al. [24]	AOC	4.8 g/40 g	S	12	6	Intravenous
Cuckler [19]	AOC	4.8 g/40 g	S	18 weeks–2 years	6	Intravenous
Emerson et al. [9]	AOC	5.6 g/40 g	D	6–12	6	parenteral
Lee et al. [31]	AOC	NA	T	25	4 ~ 6	Intravenous
Jämsen et al. [27]	AOC	NA	NA	24.3	5	Intravenous/oral
Brunnekreef et al. [15]	NC	NA	NA	19	6	Intravenous/oral
Qiu et al. [37]	AOC	1 g/40 g	S	12	4	Intravenous
Meek et al. [33]	NC	NA	NA	NA	6	Intravenous
Kalore et al. [29]	NC	2.5 g/40 g	D	10.8	6	Intravenous
	AOC	2.5 g/40 g	D	23.2	6	Intravenous
	ACAS	2.5 g/40 g	D	19.6	6	Intravenous
Castelli et al. [16]	ACAS	1.1 g/40 g	S/D	16	6	NA
Jia et al. [28]	ACAS	4 g/40 g	D	11.5	4.9	NA
Garg et al. [22]	ACAS	2.4 g/40 g	T	18 m	10–12	NA
Van Thiel et al.[40]	ACAS	4 g/40 g	S/D	10.7	NA	Intravenous
Shen et al. [38]	ACAS	3.5 g/40 g	D	31.2	6	Intravenous
Park et al. [34]	ACAS	7.5 g/40 g	T	13.2	6	Intravenous/oral
Villanueva-Martínez et al. [41]	ACAS	3 g/40 g	S/D	14	4–6	Intravenous
Hsu et al. [25]	ACAS	1.2-2 g/40 g	S/D	13.7	8.4	NA
Freeman et al. [21]	ACAS	1.7–3.4 g/40 g	D	12	6	Intravenous
Pascale and Pascale [35]	ACAS	4–5 g/40 g	NA	9	6	Intravenous
Pitto et al. [36]	ACAS	0.8–1.8 g/40 g	S	12	6	Intravenous
Durbhakula et al. [20]	ACAS	3.4 g/40 g	D	12	6	Intravenous
Ocguder et al. [10]	ACAS	NA	S	16.8	6.8	Parenteral/oral
Ha et al. [23]	ACAS	4–4.8 g/40 g	S	9	4 ~ 8	Intravenous/oral
Su et al. [39]	ACAS	2 g/40 g	S	14	6.1	Intravenous/oral

AOC autoclaved original components, *NC* new components, *ACAS* all-cement articulating spacers, *NA* data not available, *S* single type of antibiotic was employed, *D* two types of antibiotics were employed, *T* three types of antibiotics were employed; intravenous/oral, combined application of intravenous antibiotics and oral antibiotics

spacers had similar infection control rates in stage I. Based on several previous studies, we believe that such results are associated with the pathogenesis of biofilm formation in periprosthetic infections. Biofilms are formed when individual planktonic bacteria adhere to a surface and begin to produce an extracellular polymeric slime matrix composed of polysaccharides, DNA and proteins [42]. Once formed, these matrices can resist antibiotics and the host immune system through various mechanisms [43]. Bacteria on the biofilm surface are continuously detached to become free-floating bacteria, and the free-floating bacteria can also reattach to the biofilm and become loosely bound, forming a cycle between free-floating bacteria and anchored bacteria [28] and leading to long-term periprosthetic infection or a high reinfection rate. Metallic or plastic surfaces of the devices are more prone to bacterial adherence and biofilm formation [43]. Therefore, prosthetic spacers with metal or polyethylene surfaces have higher risks of bacterial colonization than all-cement spacers, as they provide a site for biofilm adherence. In addition, because of the presence of metallic and plastic components, the prosthetic spacers have a relatively smaller cement area for antibiotic release than all-cement spacers, which may lead to unsatisfactory antibacterial effects. Studies have shown that antibiotic elution

Table 4 The methods each included study performed to diagnose the infection

Authors	Diagnosis of periprosthetic infection	Diagnosis of infection in stage I	Diagnosis of postoperative reinfection after stage II
Classen et al. [18]	JAC	JAC; BT	JAC
Kim et al. [30]	IB; JAC; BT	IB; JAC; BT	IB; JAC; BT
Lee and Choi [32]	IB; JAC; BT	JAC; BT	JAC; BT
Choi et al. [17]	IB; JAC; BT	IB; JAC; BT	IB; JAC; BT
Anderson et al. [14]	JAC; BT	BT	JAC; BT
Huang et al. [26]	IB; JAC; BT	IB; JAC; BT	IB; JAC; BT
Hofmann et al. [24]	IB; JAC; BT	IB; BT	IB; JAC; BT
Cuckler [19]	JAC; BT	BT	NM
Emerson et al. [9]	IB; JAC; BT	BT	IB; JAC; BT
Lee et al. [31]	IB; JAC; BT	IB; BT	IB; JAC; BT
Jämsen et al. [27]	IB; JAC; BT	NM	NM
Brunnekreef et al. [15]	IB; JAC; BT	NM	NM
Meek et al. [33]	IB; JAC; BT	BT	IB; JAC; BT
Qiu et al. [37]	JAC; BT	BT	JAC; BT
Kalore et al. [29]	NM	BT	BT
Castelli et al. [16]	IB; JAC; BT	BT	IB; JAC; BT
Jia et al. [28]	IB; JAC; BT	JAC; BT	IB; JAC; BT
Garg et al. [22]	IB; JAC; BT	BT	NM
Van Thiel et al. [40]	IB; JAC	CO	JAC
Shen et al. [38]	IB; JAC; BT	IB; BT	NM
Park et al. [34]	NM	IB; BT	BT
Villanueva-Martínez et al. [41]	IB	IB	NM
Hsu et al. [25]	NM	BT	JAC
Freeman et al. [21]	IB; JAC; BT	JAC; BT	IB; JAC; BT
Pascale and Pascale [35]	JAC; BT	JAC	NM
Pitto et al. [36]	IB; JAC; BT	IB; JAC	IB; JAC; BT
Durbhakula et al. [20]	IB; JAC; BT	IB; JAC; BT	IB; JAC; BT
Ocguder et al. [10]	IB; JAC; BT	BT	IB; JAC; BT
Ha et al. [23]	IB; JAC	BT	BT
Su et al. [39]	IB	BT	CO

JAC joint aspirates cultures, *BT* blood test, *IB* intraoperative biopsy, *NM* not clearly mentioned, *CO* clinical observation

from polymethylmethacrylate (PMMA) is directly dependent on the surface area of the implant and the absolute amount of antibiotics in the cement [44]. With respect to the postoperative reinfection rates, however, the confidence intervals were similar. Nevertheless, the results indicate a potentially higher risk of postoperative reinfection when using the articulating spacers containing bio-inert materials than when using all-cement spacers. Additional studies are needed to strengthen this conclusion.

Spivey et al. [11] recently published a meta-analysis comparing 4 types of articulating spacers that included 34 retrospective studies. Their results showed that there was no significant difference in the postoperative reinfection rate among all types of articulating spacers. Compared to their meta-analysis, our study established a series of more specific inclusion and exclusion criteria, which are mentioned above, to guarantee high rigour and low heterogeneity among the screened studies. Additionally, in our meta-analysis, subgroup analyses were performed to evaluate the risk factors for postoperative reinfection (as shown in Table 5), and the results indicated that the different reinfection rates between the two groups were mainly caused by the type of articulating spacer. This result strengthened the reliability of our statistical outcomes and conclusions.

Choosing optimal spacers during certain stages has always been a focus as well as a difficult decision for two-stage revision of infected TKA because patient function must be balanced with infection eradication. Multiple factors should be considered when choosing a spacer in clinical practice. An ideal articulating spacer should offer a high infection control rate, permit sufficient motion, minimize exposure issues at secondary reimplantation,

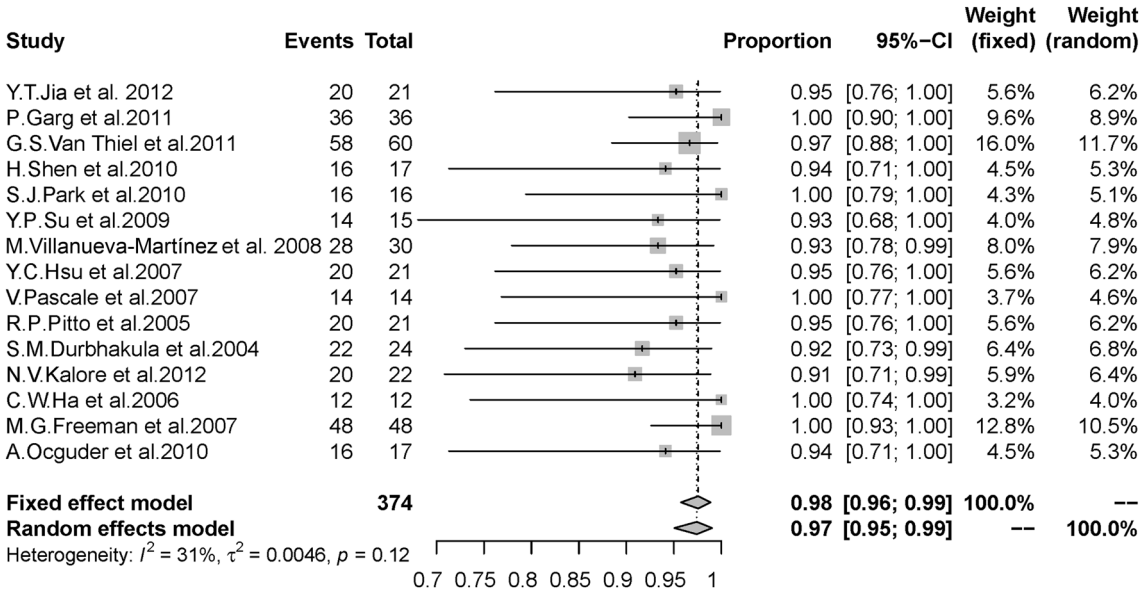

Fig. 2 Forest plot showing the pooled infection control rate of all-cement articulating spacers

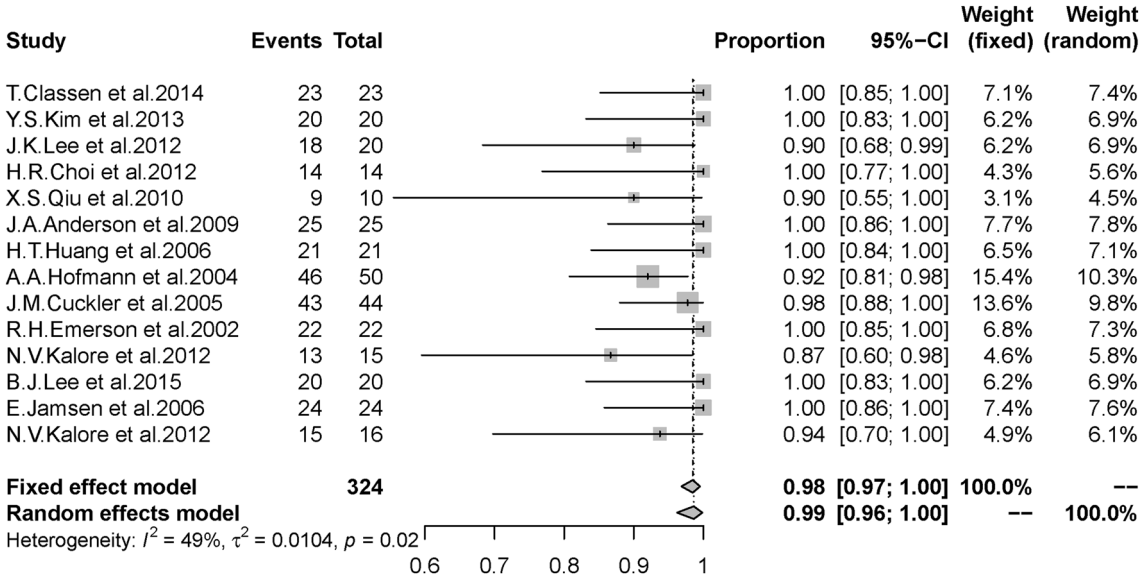

Fig. 3 Forest plot showing the pooled infection control rate of prosthetic articulating spacers

and minimize dislocation, fracture, wound complications, and bone loss [29]. Considering these factors, articulating spacers appear to be better options than static spacers. Controversy exists regarding which type of articulating spacer is superior for ROM. Spivey et al. [11] found that metal-on-polyethylene spacers exhibited a significantly increased interim ROM compared to other articulating spacers ($p < 0.003$). This result differed from the studies by Kalore et al. [29] and Jämsen et al. [27], which found no difference in ROM among articulating spacers. Nevertheless, given that ROM is influenced by several factors, such as the surgeon's skills, patient compliance, early rehabilitation, and especially preoperative ROM [38], the differing results were not entirely surprising. As mentioned above, all-cement spacers have a larger area for antibiotic elution that may play a role in reducing the reinfection rate, but potential wear debris from the cement-on-cement surface of spacers is a concern. Evans [44] suggested that cement-on-cement articulation has a high coefficient of friction that subsequently leads to increased wear debris

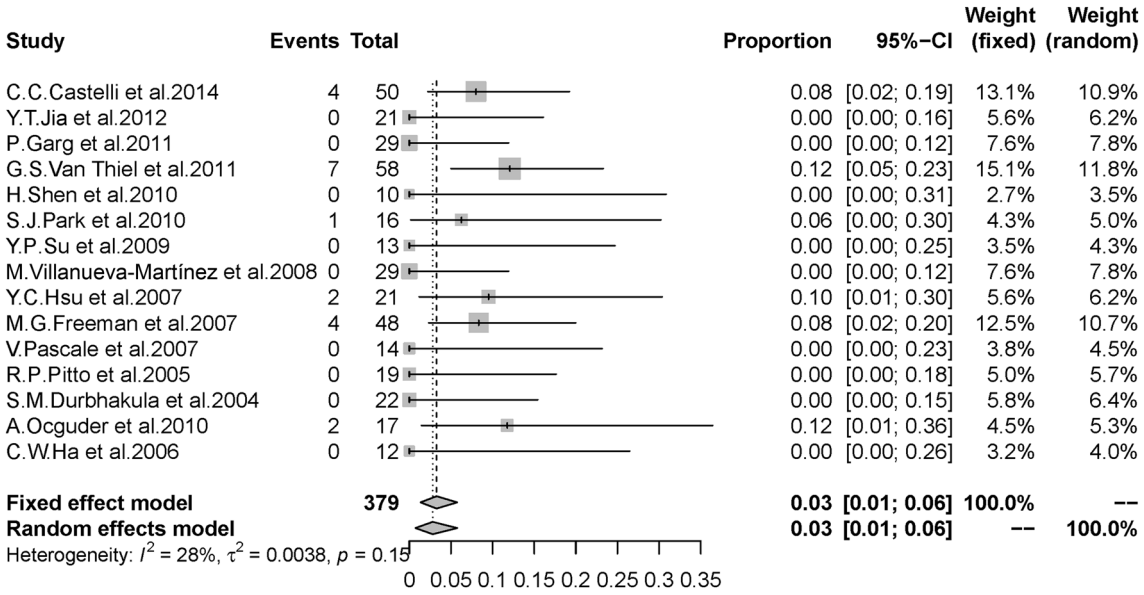

Fig. 4 Forest plot showing the pooled postoperative reinfection rate of all-cement articulating spacers

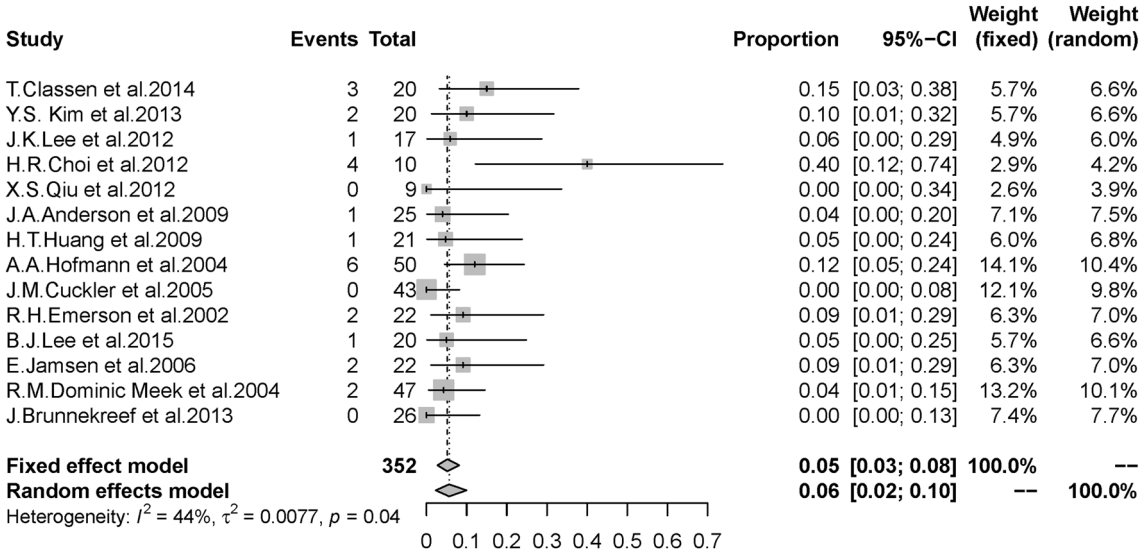

Fig. 5 Forest plot showing the pooled postoperative reinfection rate of prosthetic articulating spacers

and fragmentation. However, some studies have shown no significant difference between all-cement spacers and metal-on-polyethylene spacers in the wear at the interface [45]. Another concern is that the subluxation of articulating spacers may be associated with poor outcome scores after stage II. Lanting et al. [46] quantified, through his retrospective studies of 72 cases, the amount of subluxation with an articulating spacer and investigated its relationship to outcome following second-stage revision. And the results showed that knees that subluxated more than one standard deviation from the mean in the sagittal plane had lower Knee Society Function Scores ($p = 0.045$). In addition, there are various ways to make articulating spacers. All-cement spacers can be prepared intraoperatively using moulds or can be handmade or prefabricated. Prefabricated spacers have the advantages of reduced time in the operating room and few intraoperative complications. However, because these spacers are not made according to the exact specifications of the patient's knee, the risk of loosening is a concern. The spacers made by moulds cost less but require surgeons to have relatively strong operating skills and may also require long operation times.

Table 5 Subgroup analysis of reinfection rates according to different antibiotic treatments

Group	Number of studies	Knees	Reinfection rates		I^2 (%)	χ^2	*P* value
			Pooled rates	95% CI			
Antibiotic cement weight (g)							
≤ 3.5	15	371	0.04	[0.02;0.07]	43	0.54	0.47
> 3.5	11	301	0.03	[0.004;0.047]	34		
Antibiotic type							
Single	9	203	0.03	[0.02;0.07]	45	1.5	0.22
Multiple	14	371	0.05	[0.01;0.10]	60		
Mean period of spacers in situ (weeks)							
≤ 14	16	399	0.04	[0.02;0.07]	22	0.35	0.57
> 14	12	285	0.05	[0.01;0.10]	55		
Postoperative antibiotic treatment period							
< 6	6	113	0.01	[0.00;0.05]	0	2.95	0.09
≥ 6	23	541	0.05	[0.03;0.07]	32		
Postoperative antibiotic treatment approach							
Intravenous	17	500	0.05	[0.03;0.07]	46	1.05	0.31
Intravenous/oral	9	162	0.03	[0.00;0.07]	0		

The present meta-analysis has the following limitations that must be considered. The main limitation is that all the included studies were retrospective, and the differences between two groups concerning gender distribution, the incidence of Gram-negative bacterial infection and the incidence of fungal infection (as shown in Table 2) tended to increase the risk of bias. Therefore, when larger studies are available, further correction and matching should be conducted, such as omitting some of the included studies to equalize gender proportion prior to reanalysis. What's more, different ways of infection detection were performed in different studies (as shown in Table 4), which may be a potential bias, because a definite diagnosis of infection plays the key role in the results of infection control rates in stage I or postoperative reinfection rate after stage II. Hoell et al. [47] points out that CRP in serum, white blood counts and cultures of synovial fluid are routinely used to detect the periprosthetic infection, but the sensitivities of these parameters do vary from 12 to 100% and in 4% CRP in serum is even negative. Hence a standard diagnosis procedure is needed to be made and followed in the future to make the data more reliable. Furthermore, articles not published in English were excluded in the screening process, which may have resulted in the exclusion of some high-quality studies. In addition, there was no standardization in perioperative treatment, operation technique and assessment of patient health. Finally, the mean follow-up period of the included studies varied to some extent, which may influence the data on reinfection rates. Hoffman et al. [48] reported no recurrences of infection in their study in 1955 (with a mean follow-up of 30 months), but they found that 6 out of 50 patients suffered recurrences in their study in 2005 (with a mean follow-up of 73 months) [24].

Conclusion

This meta-analysis indicates that prosthetic articulating spacers have a similar infection control rate in stage I, but a higher postoperative reinfection rate than all-cement articulating spacers. In general, despite the overlapping confidence intervals for reinfection rates between the two groups and the limitations that may prevent us from reaching definitive conclusions, our study still indicates a higher reinfection risk when using spacers containing bio-inert materials than when using all-cement spacers. This study offers helpful information for future clinical comparative studies. Given the inherent limitations of the included studies, further large-volume, well-designed RCTs with extensive follow-up are needed to confirm and update the findings of this analysis.

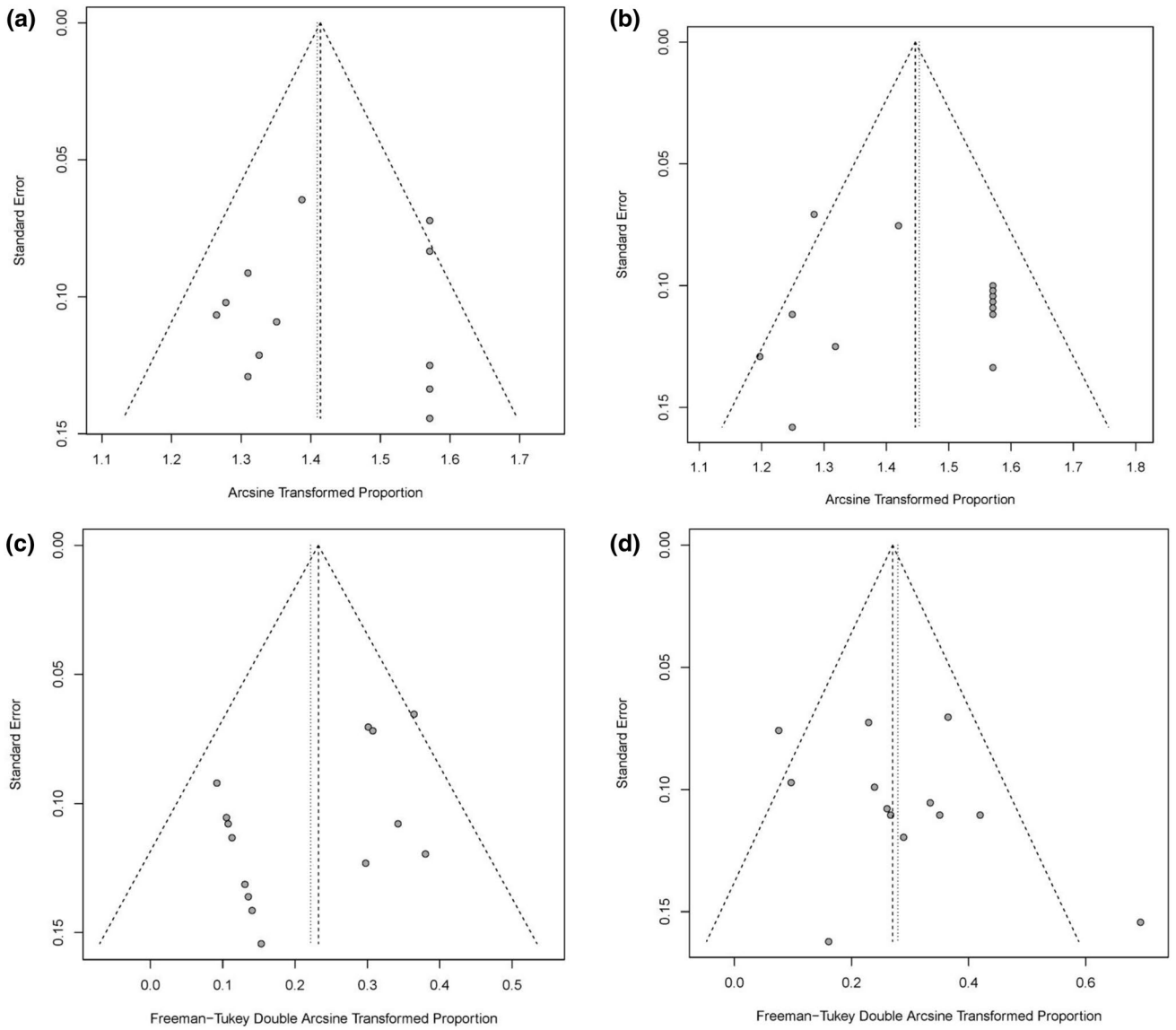

Fig. 6 Funnel plots showing the publication bias of the meta-analysis: **a** infection control rate of all-cement articulating spacers; **b** infection control rate of prosthetic articulating spacers; **c** postoperative reinfection rate of all-cement articulating spacers; **d** postoperative reinfection rate of prosthetic articulating spacers

Acknowledgements We acknowledge Professor Jing Tian for selecting the topic and offering valuable suggestions. His instruction was a great help for the completion of our study.

Funding There is no funding source.

Compliance with ethical standards

Conflict of interest The authors declare that there are no conflicts of interest.

Ethical approval This article does not contain any studies with human participants or animals performed by any of the authors.

References

1. Lee YS, Chen AF (2018) Two-stage reimplantation in infected total knee arthroplasty. Knee Surg Rel Res 30(2):107–114. https://doi.org/10.5792/ksrr.17.095
2. George J, Miller EM, Curtis GL, Klika AK, Barsoum WK, Mont MA, Higuera CA (2018) Success of two-stage reimplantation in patients requiring an interim spacer exchange. J Arthroplasty 33(7 s):S228–Ss232. https://doi.org/10.1016/j.arth.2018.03.038
3. Charette RS, Melnic CM (2018) Two-stage revision arthroplasty for the treatment of prosthetic joint infection. Current reviews in musculoskeletal medicine 11(3):332–340. https://doi.org/10.1007/s12178-018-9495-y
4. Chang MJ, Song MK, Shin JH, Yoon C, Chang CB, Kang SB (2018) Two-stage approach to total knee arthroplasty using

colistin-loaded articulating cement spacer for vancomycin-resistant Pseudomonas aeruginosa infection in an arthritic knee. Eur J Orthopaedic Surg Traumatol. https://doi.org/10.1007/s00590-018-2268-x
5. Anagnostakos K, Fink B (2018) Antibiotic-loaded cement spacers—lessons learned from the past 20 years. Expert Rev Med Dev 15(3):231–245. https://doi.org/10.1080/17434440.2018.1435270
6. Lu J, Han J, Zhang C, Yang Y, Yao Z (2017) Infection after total knee arthroplasty and its gold standard surgical treatment: Spacers used in two-stage revision arthroplasty. Intractable Rare Dis Res 6(4):256–261. https://doi.org/10.5582/irdr.2017.01049
7. Ding H, Yao J, Chang W, Liu F (2017) Comparison of the efficacy of static versus articular spacers in two-stage revision surgery for the treatment of infection following total knee arthroplasty: a meta-analysis. J Orthop Surg Res 12(1):151. https://doi.org/10.1186/s13018-017-0644-6
8. Massin P, Delory T, Lhotellier L, Pasquier G, Roche O, Cazenave A, Estellat C, Jenny JY (2016) Infection recurrence factors in one- and two-stage total knee prosthesis exchanges. Knee Surg, Sports Traumatol, Arthrosc 24(10):3131–3139. https://doi.org/10.1007/s00167-015-3884-1
9. Emerson RH Jr, Muncie M, Tarbox TR, Higgins LL (2002) Comparison of a static with a mobile spacer in total knee infection. Clin Orthop Relat Res (404):132–138
10. Ocguder A, Firat A, Tecimel O, Solak S, Bozkurt M (2010) Two-stage total infected knee arthroplasty treatment with articulating cement spacer. Arch Orthop Trauma Surg 130(6):719–725. https://doi.org/10.1007/s00402-010-1054-y
11. Spivey JC, Guild GN, Scuderi GR (2017) Use of articulating spacer technique in revision total knee arthroplasty complicated by sepsis: a systematic meta-analysis. Orthopedics 40(4):212–220. https://doi.org/10.3928/01477447-20170208-06
12. Moher D, Liberati A, Tetzlaff J, Altman DG, Group P (2009) Preferred reporting items for systematic reviews and meta-analyses: the PRISMA statement. J Clin Epidemiol 62(10):1006–1012. https://doi.org/10.1016/j.jclinepi.2009.06.005
13. von Elm E, Altman DG, Egger M, Pocock SJ, Gotzsche PC, Vandenbroucke JP, Initiative S (2007) Strengthening the reporting of observational studies in epidemiology (STROBE) statement: guidelines for reporting observational studies. BMJ 335(7624):806–808. https://doi.org/10.1136/bmj.39335.541782.AD
14. Anderson JA, Sculco PK, Heitkemper S, Mayman DJ, Bostrom MP, Sculco TP (2009) An articulating spacer to treat and mobilize patients with infected total knee arthroplasty. J Arthroplast 24(4):631–635. https://doi.org/10.1016/j.arth.2008.04.003
15. Brunnekreef J, Hannink G, Malefijt Mde W (2013) Recovery of knee mobility after a static or mobile spacer in total knee infection. Acta Orthop Belg 79(1):83–89
16. Castelli C, Gotti V, Ferrari R (2014) Two-stage treatment of infected total knee arthroplasty: two to thirteen year experience using an articulating preformed spacer. Int Orthop 38(2):405–412. https://doi.org/10.1007/s00264-013-2241-6
17. Choi HR, Malchau H, Bedair H (2012) Are prosthetic spacers safe to use in 2-stage treatment for infected total knee arthroplasty? J Arthroplast 27(8):1474–1479.e1471. https://doi.org/10.1016/j.arth.2012.02.023
18. Classen T, von Knoch M, Wernsmann M, Landgraeber S, Loer F, Jager M (2014) Functional interest of an articulating spacer in two-stage infected total knee arthroplasty revision. Orthop Traumatol Surg Res 100(4):409–412. https://doi.org/10.1016/j.otsr.2014.01.010
19. Cuckler JM (2005) The infected total knee: management options. J Arthroplast 20(4 Suppl 2):33–36
20. Durbhakula SM, Czajka J, Fuchs MD, Uhl RL (2004) Antibiotic-loaded articulating cement spacer in the 2-stage exchange of infected total knee arthroplasty. J Arthroplast 19(6):768–774
21. Freeman MG, Fehring TK, Odum SM, Fehring K, Griffin WL, Mason JB (2007) Functional advantage of articulating versus static spacers in 2-stage revision for total knee arthroplasty infection. J Arthroplast 22(8):1116–1121. https://doi.org/10.1016/j.arth.2007.04.009
22. Garg P, Ranjan R, Bandyopadhyay U, Chouksey S, Mitra S, Gupta SK (2011) Antibiotic-impregnated articulating cement spacer for infected total knee arthroplasty. Indian J Orthop 45(6):535–540. https://doi.org/10.4103/0019-5413.87126
23. Ha CW (2006) A technique for intraoperative construction of antibiotic spacers. Clin Orthop Relat Res 445:204–209. https://doi.org/10.1097/01.blo.0000201161.52196.c5
24. Hofmann AA, Goldberg T, Tanner AM, Kurtin SM (2005) Treatment of infected total knee arthroplasty using an articulating spacer: 2- to 12-year experience. Clin Orthop Relat Res (430):125–131
25. Hsu YC, Cheng HC, Ng TP, Chiu KY (2007) Antibiotic-loaded cement articulating spacer for 2-stage reimplantation in infected total knee arthroplasty: a simple and economic method. J Arthroplasty 22(7):1060–1066. https://doi.org/10.1016/j.arth.2007.04.028
26. Huang HT, Su JY, Chen SK (2006) The results of articulating spacer technique for infected total knee arthroplasty. J Arthroplasty 21(8):1163–1168. https://doi.org/10.1016/j.arth.2006.01.028
27. Jämsen E, Sheng P, Halonen P, Lehto MU, Moilanen T, Pajamäki J, Puolakka T, Konttinen YT (2006) Spacer prostheses in two-stage revision of infected knee arthroplasty. Int Orthop 30(4):257–261. https://doi.org/10.1007/s00264-006-0102-2
28. Jia YT, Zhang Y, Ding C, Zhang N, Zhang DL, Sun ZH, Tian MQ, Liu J (2012) Antibiotic-loaded articulating cement spacers in two-stage revision for infected total knee arthroplasty: individual antibiotic treatment and early results of 21 cases. Chin J Traumatol 15(4):212–221
29. Kalore NV, Maheshwari A, Sharma A, Cheng E, Gioe TJ (2012) Is there a preferred articulating spacer technique for infected knee arthroplasty? A preliminary study. Clin Orthop Relat Res 470(1):228–235. https://doi.org/10.1007/s11999-011-2037-1
30. Kim YS, Bae KC, Cho CH, Lee KJ, Sohn ES, Kim BS (2013) Two-stage revision using a modified articulating spacer in infected total knee arthroplasty. Knee Surg Rel Res 25(4):180–185. https://doi.org/10.5792/ksrr.2013.25.4.180
31. Lee BJ, Kyung HS, Yoon SD (2015) Two-stage revision for infected total knee arthroplasty: based on autoclaving the recycled femoral component and intraoperative molding using antibiotic-impregnated cement on the tibial side. Clin Orthop Surg 7(3):310–317. https://doi.org/10.4055/cios.2015.7.3.310
32. Lee JK, Choi CH (2012) Two-stage reimplantation in infected total knee arthroplasty using a re-sterilized tibial polyethylene insert and femoral component. J Arthroplasty 27(9):1701–1706.e1701. https://doi.org/10.1016/j.arth.2012.03.013
33. Meek RM, Dunlop D, Garbuz DS, McGraw R, Greidanus NV, Masri BA (2004) Patient satisfaction and functional status after aseptic versus septic revision total knee arthroplasty using the PROSTALAC articulating spacer. J Arthroplasty 19(7):874–879
34. Park SJ, Song EK, Seon JK, Yoon TR, Park GH (2010) Comparison of static and mobile antibiotic-impregnated cement spacers for the treatment of infected total knee arthroplasty. Int Orthop 34(8):1181–1186. https://doi.org/10.1007/s00264-009-0907-x
35. Pascale V, Pascale W (2007) Custom-made articulating spacer in two-stage revision total knee arthroplasty. An early follow-up of 14 cases of at least 1 year after surgery. HSS J: Musculoskelet

J Hosp Spec Surg 3(2):159–163. https://doi.org/10.1007/s11420-007-9048-1
36. Pitto RP, Castelli CC, Ferrari R, Munro J (2005) Pre-formed articulating knee spacer in two-stage revision for the infected total knee arthroplasty. Int Orthop 29(5):305–308. https://doi.org/10.1007/s00264-005-0670-6
37. Qiu XS, Sun X, Chen DY, Xu ZH, Jiang Q (2010) Application of an articulating spacer in two-stage revision for severe infection after total knee arthroplasty. Orthop Surg 2(4):299–304. https://doi.org/10.1111/j.1757-7861.2010.00103.x
38. Shen H, Zhang X, Jiang Y, Wang Q, Chen Y, Wang Q, Shao J (2010) Intraoperatively-made cement-on-cement antibiotic-loaded articulating spacer for infected total knee arthroplasty. Knee 17(6):407–411. https://doi.org/10.1016/j.knee.2009.11.007
39. Su YP, Lee OK, Chen WM, Chen TH (2009) A facile technique to make articulating spacers for infected total knee arthroplasty. J Chin Med Assoc: JCMA 72(3):138–145. https://doi.org/10.1016/s1726-4901(09)70039-5
40. Van Thiel GS, Berend KR, Klein GR, Gordon AC, Lombardi AV, Della Valle CJ (2011) Intraoperative molds to create an articulating spacer for the infected knee arthroplasty. Clin Orthop Relat Res 469(4):994–1001. https://doi.org/10.1007/s11999-010-1644-6
41. Villanueva-Martínez M, Ríos-Luna A, Pereiro J, Fahandez-Saddi H, Villamor A (2008) Hand-made articulating spacers in two-stage revision for infected total knee arthroplasty: good outcome in 30 patients. Acta Orthop 79(5):674–682. https://doi.org/10.1080/17453670810016704
42. McConoughey SJ, Howlin R, Granger JF, Manring MM, Calhoun JH, Shirtliff M, Kathju S, Stoodley P (2014) Biofilms in periprosthetic orthopedic infections. Future Microbiol 9(8):987–1007. https://doi.org/10.2217/fmb.14.64
43. Antony S, Farran Y (2016) Prosthetic joint and orthopedic device related infections. The role of biofilm in the pathogenesis and treatment. Infect Disord Drug Targets 16(1):22–27
44. Evans RP (2004) Successful treatment of total hip and knee infection with articulating antibiotic components: a modified treatment method. Clin Orthop Relat Res (427):37–46
45. Villa T, Carnelli D (2007) Experimental evaluation of the biomechanical performances of a PMMA-based knee spacer. Knee 14(2):145–153. https://doi.org/10.1016/j.knee.2006.11.010
46. Lanting BA, Lau A, Teeter MG, Howard JL (2017) Outcome following subluxation of mobile articulating spacers in two-stage revision total knee arthroplasty. Arch Orthop Trauma Surg 137(3):375–380. https://doi.org/10.1007/s00402-017-2630-1
47. Hoell S, Moeller A, Gosheger G, Hardes J, Dieckmann R, Schulz D (2016) Two-stage revision arthroplasty for periprosthetic joint infections: What is the value of cultures and white cell count in synovial fluid and CRP in serum before second stage reimplantation? Arch Orthop Trauma Surg 136(4):447–452. https://doi.org/10.1007/s00402-015-2404-6
48. Hofmann AA, Kane KR, Tkach TK, Plaster RL, Camargo MP (1995) Treatment of infected total knee arthroplasty using an articulating spacer. Clin Orthop Relat Res (321):45–54