Spacers

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Published online in Wiley Online Library (wileyonlinelibrary.com). DOI 10.1002/jor.22555

 J Orthop Res 32:S120–S129, 2014.

Question 1: Is there a functional difference in the use of non-articulating or articulating spacers for the treatment of periprosthetic joint infection (PJI) in the knee, between two-stage exchange arthroplasty?

Consensus
Articulating spacers provide better function than non-articulating spacers for the patient in between the stages of total knee arthroplasty (TKA). An articulating spacer is especially preferred for patients who are likely to have a spacer in place for longer than 3 months.

Delegate Vote
Agree: 89%, Disagree: 6%, Abstain: 5% (Strong Consensus)

Justification
The current available peer-reviewed literature reveals an overall of 46 original articles (excluding case reports, review articles, and technical reports) including 4 level 2, 8 level 3, and 34 level 4 studies related to the use of spacers.

The majority of these studies have evaluated the mid-term functional outcome of patients after reimplantation and compared articulating with non-articulating spacers. A few studies that evaluated patient function between the stages for resection arthroplasty and reimplantation detected a superior outcome for patients receiving articulating spacers compared to those with non-articulating spacers.[1–46]

Question 2: Is there a functional difference in the use of non-articulating or articulating spacers for treatment of PJI in the knee at minimum 2 years after reimplantation?

Consensus
There is a non-significant trend in range of motion improvement with articulating compared to non-articulating spacers, but the panel believes that this is still of value to the patient

Delegate Vote
Agree: 82%, Disagree: 12%, Abstain: 6% (Strong Consensus)

Justification
A review of the current available peer-reviewed literature reveals an overall number of 46 original articles (excluding case reports, review articles, and technical reports) including 4 level 2, 8 level 3, and 34 level 4 studies related to the use of spacers.[1–46]

The majority of these studies have evaluated the mid-term functional outcome of patients after reimplantation and compared articulating with non-articulating spacers. The majority of studies have demonstrated a higher range of motion at mid-term follow-up for patients receiving articulating spacers compared to patients with non-articulating spacers. The average reported flexion angle for all reported patients receiving articulating spacers (1,195 cases) after an average follow-up of 44.3 months was 96.4° (range 63–115°; standard deviation (SD) = 10.8), whereas in all reported patients of the non-articulating group (474 cases) an average flexion angle of 91.2° (range 73.8–106°; SD = 8.7) was reported after an average follow-up of 52 months.

Question 3: Is there a functional difference in the use of non-articulating or articulating spacers for the treatment of PJI in the hip between the stages of two-stage exchange arthroplasty?

Consensus
A well performing articulating spacer provides better function for the patient in between the stages of total hip arthroplasty (THA). These are especially preferred for patients who are likely to have a spacer in place for longer than 3 months.

Delegate Vote
Agree: 89%, Disagree: 7%, Abstain: 4% (Strong Consensus)

Justification

There are 26 original articles (excluding case reports, review articles, and technical reports) analyzing the functional outcomes of patients who have undergone two-stage exchange for PJI of the hip. Most of the available studies report functional outcome according to the Harris Hip Score (HHS). We found 1 level 1 study, 2 level 2 studies, 2 level 3 studies, and 21 level 4 studies.

A few studies that evaluated patient function between stages for resection arthroplasty and reimplantation detected a superior outcome for patients receiving articulating spacers compared to those with non-articulating spacers.[42,47–71]

Question 4: Is there a functional difference in the use of non-articulating or articulating spacers for the treatment of PJI in the hip, at a minimum of 2 years after reimplantation?

Consensus

There is a non-significant trend in functional improvement with articulating compared to non-articulating spacers, but the panel believes that this is still of value to the patient.

Delegate Vote

Agree: 81%, Disagree: 12%, Abstain: 7% (Strong Consensus)

Justification

There are 26 original articles (excluding case reports, review articles, and technical reports) analyzing the functional outcomes of patients who have undergone two-stage exchange for PJI of the hip. Most of the available studies report functional outcome according to the HHS. We found one level 1 study, 2 level 2 studies, 2 level 3 studies, and 21 level 4 studies. The majority of the reports comparing the mid-term outcome of surgical treatment for PJI revealed a better functional outcome (as measured by the HHS) for patients who received articulating spacers compared to non-articulating spacers. The average reported HHS for all patients receiving articulating spacers (898 cases) after an average follow-up of 50 months was 83 (range 68–98 points; SD = 8.2), compared to the HHS of 81 points (range, 78–83 points; SD = 2.3) for those receiving non-articulating spacers (63 patients) after an average follow up of 61 months.[42,47–71]

Question 5: Is there a difference in reimplantation (surgical ease) with the use of non-articulating or articulating spacers for the treatment of PJI in the knee and hip?

Consensus

Yes. Reimplantation surgery is easier overall in patients receiving articulating spacers compared to non-articulating spacers.

Delegate Vote

Agree: 81%, Disagree: 8%, Abstain: 11% (Strong Consensus)

Justification

As far as we could find there were no studies that directly compared the ease of reimplantation of spacers between patients receiving non-articulating or articulating spacers. However, based on anecdotal reports it appears that the use of articulating spacers facilitates reimplantation surgery. Better soft tissue tension, improved ability of the patient to move the joint in the interim between resection and reimplantation, and better restoration of anatomy may all be reasons for this difference.

Question 6: Is there a difference with regards to control of infection with the use of articulating or non-articulating spacers in the knee?

Consensus

No. The type of spacer does not influence the rate of infection eradication in two-stage exchange arthroplasty of the knee.

Delegate Vote

Agree: 89%, Disagree: 6%, Abstain: 5% (Strong Consensus)

Justification

Evaluation of the peer-reviewed literature revealed 59 original articles (excluding case reports, review articles, and technical reports) related to this subject. There were no level 1 studies that examined the success of surgical treatment with regard to infection control. There were 5 level 2 studies, 11 level 3 studies, and 43 level 4 studies.[1–59]

Eleven studies compared the eradication of infection rates through the use of articulating or non-articulating spacers. We analyzed all available literature, including 1,557 cases treated with articulating spacers and 601 cases treated with non-articulating spacers. The eradication rate of 91.5% (132 cases of reinfection) was higher with the use of an articulating spacer at latest mean follow-up of 42 months. The eradication rate was 87.0% (78 cases of reinfection) using a non-articulating spacer at 56 months follow-up. It is possible that the longer follow-up for the non-articulating spacer cohort may explain the slight difference in infection control between the non-articulating and articulating spacer cohort. A further limiting factor for comparison of both groups might relate to the differences in organism profile (low vs high virulence), patient age, and comorbidities. None of the studies performed a multivariate analysis to isolate the use of spacer as an independent factor influencing the outcome of surgical treatment with regard to infection control.[1–6,8–27,29–46,72–85]

Question 7: Is there a difference with regards to control of infection with the use of articulating or non-articulating spacers in the hip?

Consensus

No. The type of spacer does not influence the rate of infection eradication in two-stage exchange arthroplasty of the hip.

Delegate Vote

Agree: 95%, Disagree: 3%, Abstain: 2% (Strong Consensus)

Justification

An evaluation of the peer-reviewed literature revealed 65 original articles (excluding case reports, review articles, and technical reports) related to this matter. Most[55] of the available studies are level 4 studies, followed by 5 level 3 studies and 4 level 2 studies. Only 1 level 1 study was available.[9,42,47–72,74,78,86–120]

Based on the available literature, we found 2,063 infected THA cases treated with articulating and 354 infected THA cases treated with non-articulating spacers. The eradication rate was slightly higher with the use of an articulating spacer with 92.5% (154 cases of reinfection) at latest follow-up of 43.4 months. The eradication rate was 90.7% (33 cases of reinfection) at latest follow-up of 49.6 months using a non-articulating spacer. Again, the confounding variables here may be the differences in follow-up, organism profile, patient age, patient comorbidities, and numerous other factors that influence the outcome of surgical intervention for PJI. None of the studies performed a multivariate analysis to isolate the type of spacer as an independent factor influencing control of infection.

Question 8: Is there a difference with regards to control of infection between different types of articulating spacers used in the knee?

Consensus

Control of the infection is no different between different types of articulating spacers in the treatment of infected TKA.

Delegate Vote

Agree: 90%, Disagree: 5%, Abstain: 5% (Strong Consensus)

Justification

Evaluation of the available peer-reviewed literature revealed 45 original articles (excluding case reports, review articles, and technical reports). There were no level 1 studies. There were 5 level 2 studies, 11 level 3 studies, and 29 level 4 studies.[1,3–6,8–10,12–14,16–18,21–25,27,29,30,32,33,35–38,40–45,51,72,73,77,79–82,85]

We evaluated the outcome of combined cohorts, which included 1,492 infected TKA cases treated with different articulating spacers (PROSTALAC, Depuy, Warsaw, IN, $n = 314$ cases; Hoffmann technique, $n = 410$; cemented molds, $n = 716$; and Spacer K, $n = 52$ cases). The eradication rate was higher with the use of a Spacer K with 94.2% (three cases of reinfection) followed by the Hoffmann technique with 93.7% (26 cases of reinfection), and cemented molds with 91.6% (60 cases of reinfection) in the treatment of infected TKA. The eradication rate with the use of the PROSTALAC spacer was 91.1% (28 cases of reinfection).

Question 9: Are there contraindications for the use of non-articulating and/or articulating spacers?

Consensus

There are no clear contraindications for the use of non-articulating or articulating spacers, other than the technical feasibility of the procedure. In patients with massive bone loss and/or lack of integrity of soft tissues or ligamentous restraint, strong consideration should be given to the use of non-articulating spacers.

Delegate Vote

Agree: 92%, Disagree: 3%, Abstain: 5% (Strong Consensus)

Justification

Based on available evidence, it is difficult to determine if there are any contraindications for the use of either spacers in the knee or the hip. However, expert surgeons who treat patients with PJI of the hip and knee on a frequent basis feel that the use of articulating spacers in patients with massive bone loss or lack of soft tissue or ligamentous integrity may lead to dislocation of the spacer. In addition, some surgeons prefer to use non-articulating spacers in patients with compromised soft tissue around the joint in order to prevent motion and allow better soft tissue healing. However, this practice has not been evaluated scientifically. We also analyzed the spacer complication rate using articulating and non-articulating hip spacers. The overall complication rate was 11.6% using articulating spacers and 6.9% using non-articulating spacers.[9,47–72,74,78,86–120] The higher complication rate for articulating spacers should be noted.

Question 10: Are there any differences in functional outcome between manufactured spacers versus surgeon-made dynamic spacers used in the knee?

Consensus

There is no difference in functional outcome between manufactured spacers versus surgeon-made articulating spacers used in the knee. However, issues of cost, ease of use, and antibiotic delivery should be considered.

Delegate Vote

Agree: 89%, Disagree: 5%, Abstain: 6% (Strong Consensus)

Justification
Evaluation of the available peer-reviewed literature revealed 50 original articles (excluding case reports, review articles, and technical reports). None of the studies were level 1. There were 6 level 2 studies, 11 level 3 studies, and 33 level 4 studies.[1–50]

We analyzed 1,525 infected TKA cases treated with either a handmade spacer ($n = 1074$) or manufactured spacers ($n = 451$). The mean flexion at latest follow-up was tendentially higher with a mean of 101.9° (range 77–115°; SD = 8.3) using a handmade spacer compared to a mean of 90.2° (range 63–106°; SD = 12.3) with a manufactured spacer.[1,3–10,12–14,16–19,22–25,27–29,31–45,72,73,75,77,79–82,84,85,108]

Question 11: Are there any differences in the rate of infection control between manufactured spacers versus surgeon-made articulating spacers used in the knee?

Consensus
There are no differences in the rate of infection control between manufactured spacers and surgeon-made articulating spacers used in the knee. However, issues of cost, ease of use, and antibiotic delivery should be considered.

Delegate Vote
Agree: 93%, Disagree: 2%, Abstain: 5% (Strong Consensus)

Justification
Evaluation of the available peer-reviewed literature revealed 50 original articles (excluding case reports, review articles, and technical reports). None of the studies were level 1. There were 6 level 2 studies, 11 level 3 studies, and 33 level 4 studies.[1–50]

We analyzed 1,525 infected TKA cases treated with either a handmade spacer ($n = 1,074$) or manufactured spacers ($n = 451$). The eradication rate was comparable with the use of a handmade spacer with 92.2% (84 reinfections) compared to the use of an industry-made spacer with 90.5% (43 reinfections).[1,3–10,12–14,16–19,22–25,27–29,31–45,72,73,75,77,79–82,84,85,108]

Question 12: Are there any differences in functional outcome between manufactured spacers versus surgeon-made dynamic spacers used in the hip?

Consensus
There is no difference in functional outcome between manufactured spacers versus surgeon-made articulating spacers used in the hip. However, issues of cost, ease of use, and antibiotic delivery should be considered.

Delegate Vote
Agree: 89%, Disagree: 7%, Abstain: 4% (Strong Consensus)

Justification
Evaluation of the available peer-reviewed literature revealed 55 original articles (excluding case reports, review articles, and technical reports). There were one level 1 study, 4 level 2 studies, 4 level 3 studies, and 46 level 4 studies.[9,47–54,56–59,61–67,70,71,72,74,78,86–88,90–98,100–108,110–113,115,117,119,120,123]

We analyzed 1,925 infected THA cases treated with either a handmade spacer ($n = 1,011$) or manufactured spacer ($n = 914$). The mean HHS at latest follow-up was also comparable using a handmade spacer (mean 84.9; range 68–97.8; SD = 8.7) or manufactured spacer (mean HHS = 82.3; range 70–93 points; SD = 8.0).

Question 13: Are there any differences in the rate of infection control between manufactured spacers versus surgeon-made dynamic spacers used in the hip?

Consensus
There is no difference in the rate of infection control between manufactured spacers versus surgeon-made articulating spacers used in the hip. However, issues of cost, ease of use, and antibiotic delivery should be considered.

Delegate Vote
Agree: 94%, Disagree: 3%, Abstain: 3% (Strong Consensus)

Justification
Evaluation of the available peer-reviewed literature revealed 55 original articles (excluding case reports, review articles, and technical reports). There were one level 1 study, 4 level 2 studies, 4 level 3 studies, and 46 level 4 studies.[9,47–54,56–59,61–67,70,71,72,74,78,86–88,90–98,100–108,110–113,115,117,119,120,123]

We analyzed 1,925 infected THA cases treated with either a handmade spacer ($n = 1,011$) or manufactured spacer ($n = 914$). The infection control rate with the use of a handmade spacer was 94.0% (61 reinfections) which was similar to the use of a manufactured spacer with 93.5% (59 reinfections).

Question 14: Which antibiotic should be used and how much of it should be added to cement spacers?

Consensus
The type of antibiotic and the dose needs to be individualized for each patient based on the organism profile and antibiogram (if available) as well as the patient's renal function and allergy profile. However, most infections can be treated with a spacer with Vancomycin (1–4 g per 40 g package of cement) and gentamicin or tobramycin (2.4–4.8 g per 40 g package of cement). We provide a list of all available antibiotics and the range of doses to be used against common infecting organisms.

Delegate Vote
Agree: 89%, Disagree: 7%, Abstain: 4% (Strong Consensus)

Justification
Some antibiotics become deactivated during the exothermic setting of polymethylmethacrylate (PMMA) cement and hence cannot be used in spacers. A list of all available antibiotics and the organisms against which they are active is provided (Table 1).

Although there are some studies claiming that the addition of high doses of antibiotic to PMMA cement is possible and does not carry the risk of systemic toxicity, the majority of surgeons have had experience with patients who developed renal toxicity following the use of an antibiotic-impregnated cement spacer. There are three main factors that influence the elution of antibiotic from PMMA spacers and the potential for renal toxicity. This includes the type of PMMA cement used (with high-viscosity cements containing MA-MMA copolymers having better antibiotic elution profiles than other acrylic bone cement formulations), renal function of the patient, and the manner in which the spacer is made and positioned in the infected joint. The larger the surface area of the spacer, the higher the antibiotic elution will be from the given spacer. Some surgeons place a ball of cement spacer in the joint, whereas others may place numerous PMMA beads in the soft tissue or the intramedullary canal. The treating surgeon needs to consider both of these options when operating on a patient with an infected joint.

We did not find any evidence in favor of or against any of the commercially available PMMA cements that may be used in fashioning a spacer. Two of the most commonly used PMMA cements, namely Palacos and Simplex cement, were compared. We analyzed the available data with regard to infection control rates between these two cement types. Overall, 1,160 infected TKA cases were included. In 811 out of 1,160

Table 1. Available Antibiotics and Anti-Fungals Which Can Be Used in Spacers

Antibiotic group	Type of antibiotic	Activity against	Dose per 40 g cement (g)
Aminoglycoside	Tobramycin	Gram-negative bacteria such as *Pseudomonas*	1–4.8
Aminoglycoside	Gentamicin	Gram-negative bacteria-*Escherichia coli*, *Klebsiella* and particularly *Pseudomonas aeroginosa*. Also aerobic bacteria (not obligate/facultative anaerobes)	0.25–4.8
Cephalosporin, 1st gen	Cefazolin	Gram-positive infections, limited Gram negative coverage	1–2
Cephalosporin, 2nd gen	Cefuroxime	Reduced Gram-positive coverage, improved Gram-negative coverage	1.5–2
Cephalosporin, 3rd gen	Ceftazidime	Gram-negative bacteria, particularly *Pseudomonas*	2
Cephalosporin, 4th gen	Cefotaxime	Gram-negative bacteria, no activity against *Pseudomonas*	2
Cephalosporin, 5th gen	Ceftaroilne	Gram-negative bacteria, no activity against *Pseudomonas*	2–4
Fluoroquinolone	Ciprofloxacin	Gram-negative organisms including activity against *Enterobacteriaciae*	0.2–3
Glycopeptide	Vancomycin	Gram-positive bacteria, including methicillin-resistant organisms	0.5–4
Lincosamide	Clindamycin	Gram-positive cocci, anaerobes	1–2
Macrolide	Erythromycin	Aerobic gram-positive cocci and bacilli	0.5–1
Polymyxin	Colistin	Gram-negative	0.24
β-Lactam	Piperacillin not available Piptzobactam	Gram-negative bacteria (particularly *Pseudomonas*), Enterobacteria and anaerobes	4–8
β-Lactam	Aztreonam	Only Gram-negative bacteria	4
β-Lactamase inhibitor	Tazobactam	Gram-negative bacteria (particularly *Pseudomonas*), Enterobacteria, and anaerobes in combination with Piperacillin	0.5
Oxazolidinones	Linezolid	Multidrug-resistant Gram-positive cocci such as MRSA	1.2
Carbapenem	Meropenem	Gram-positive and Gram-negative bacteria, anaerobes, *Pseudomonas*	0.5–4
Lipopeptide	Daptomycin	Only gram-positive organisms	2
Antifungals	Amphotericin	Most fungi	200
Antifungal	Voricanazole	Most fungi	300–600 mg

The dose ranges reveal only the reported doses in the analyzed studies and are not recommendations.[1–134] Again, the type of antibiotic and the dose needs to be individualized for each patient based on the organism profile and antibiogram (if available) as well as the patient's renal function and allergy profile.

cases Palacos cement (69.9%) was used and in the remaining 349 cases Simplex cement was used (30.1%). The eradication rate was similar with a 91.6% rate of eradication (68 cases of reinfection) using Palacos cement compared to Simplex cement with an eradication rate of 89.4% (37 cases of reinfection).[1–4,7–10,12–14,17,18,28–30,32,33,36,38,40,41,43,72,73,76–78,80–84,108]

We also analyzed the available data for infected THA cases. We included 1,454 cases (Palacos, $n = 1{,}201$; and Simplex, $n = 253$). The infection control rate was similar in both groups with a rate of 93.7% (16 cases of reinfection) for Simplex and 93.8% (74 cases of reinfection) for Palacos cement.[3,9,47,48,50–54,56,60–66,70,72,73,78,87,90–92,94,95,98,100,102,104,105,108,110,113,115,117,119,123]

Question 15: What is the optimal technique for preparing a high-dose antibiotic cement spacer (mixing, when and how to add antibiotics, and porosity)?

Consensus

There is no consensus on the best method of preparation of high-dose antibiotic cement spacers.

Delegate Vote

Agree: 93%, Disagree: 3%, Abstain: 4% (Strong Consensus)

Justification

The pharmacokinetics of antibiotic release from the matrix is influenced by numerous factors, including the porosity of the cement (high viscosity cement containing MA-MMA copolymers have been shown to have better antibiotic elution profiles than other acrylic bone cement formulations) dose and type of antibiotics added to PMMA, and the shape and surface area of the spacer.

One of the basic principles of spacer preparation is recognition that local antibiotic concentration must be clearly above the minimal inhibitory concentration and have minimal bactericidal concentrations of the infecting organism.[124] In general, the spacers should generate high local concentrations of antibiotic without associated systemic toxicity. Elution of antibiotics from the cement has been shown to be highest in the first 24–72 h after surgery.[125] It seems that the initial high elution from the cement is a result of mechanical erosion of the spacer surface. The prolonged release over weeks relates to the antibiotic-loaded bone cement itself.[126]

Another factor influencing the efficacy of antibiotic release from spacers includes the combination of antibiotics used, fatigue life of PMMA, and mixing technique. Antibiotic combinations can alter the elution characteristic of each agent; therefore, as one antibiotic dissolves, porosity increases and changes the surface, which allows for increased elution of other antibiotics. For instance, it has been shown that there was a statistically significant increase in the elution of vancomycin when the dose of tobramycin was increased from 2.4 g to at least 3.6 g in the mixture.[108]

General principles of mixing antibiotics to cement

Antibiotic needs to be bactericidal, in powder form to allow better integration with cement,[127] sterile, heat/thermo stable, and soluble in water.

The technical aspects of preparing a spacer include

For preparation of antibiotic-loaded cement for the spacer, some technical aspects apply. As the dosage of antibiotics increases, the difficulty of incorporating the antibiotics into the cement during the mixing process increases. In these situations, mixing the cement powder and monomer for 30 s,[134] followed by the addition of the antibiotic powder in multiple small doses, will facilitate incorporation. It is also advisable to crush clumps of antibiotic, although some irregularity in the antibiotics is acceptable, and may be preferable for early elution of active antibiotics. Hand mixing in a bowl without vacuum is recommended as bubbles facilitate elution of the antibtioics.[130] Addition of fillers such as Xyletol or Ancef may improve the elution of active antibiotics.[122,131–133] The addition of a high amount of antibiotic to cement will decrease the fatigue strength and increase the fracture risk. The addition of more than 4.5 g of powder substantially weakens the cement. For most antibiotic spacers, elution of antibiotics is a primary concern over the mechanical property, but the surgeon must keep this in mind for structural spacers.

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