SECTION

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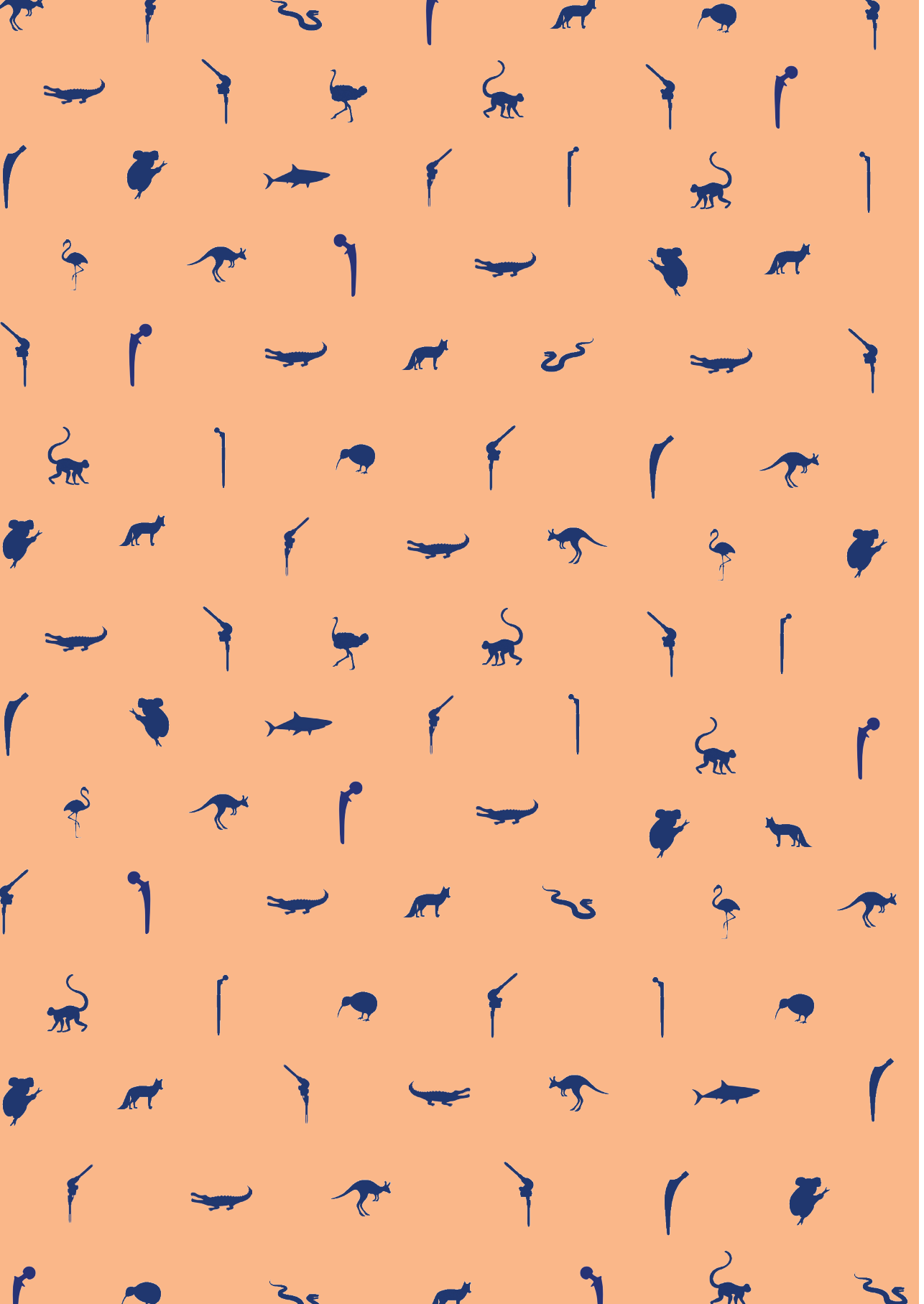

CHAPTER

6

Similar rate of infection eradication for functional articulating, prefabricated and custom–made spacers in two-stage revision of the infected total hip

A literature review

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ABSTRACT

Background Nowadays, two-stage revision with the use of an antibiotic-loaded interval spacer is therapy of choice in late periprosthetic joint infection for most surgeons. For the spacer, either a prefabricated, functional articulating or custom made spacer can be used. Little is known about which type of spacer provides optimal outcome after two-stage revision. The aim of this study was to determine which type of spacer provides the best results, when used in two-stage revision of an infected THA.

Methods We performed a systematic review of the literature to analyse which type of interval spacer provides highest infection eradication rate and best functional outcome after a minimum two year follow-up. Exclusion criteria were follow-up of less than 2 years, single-stage revision, or two-stage revision without use of a spacer.

Results Twenty-five studies were included. Infection eradication rate was similar with rates of 96%, 93% and 95% for the prefabricated-, functional articulating- and custom made spacers respectively. Functional outcome was scarcely described. Postoperative HHS was 81, 90 and 83 respectively.

Interpretation Functional articulating spacers achieve a comparable rate of infection eradication in the treatment of periprosthetic hip joint infections as compared to preformed or custom-made antibiotic-loaded spacers. There is insufficient evidence concerning rehabilitation and functional outcome after two-stage revision hip arthroplasty to advocate or discourage the use of either kind of interval spacer.

Keywords: antibiotic-loaded spacer, functional articulating spacer, periprosthetic joint infection, total hip arthroplasty, two-stage revision.

INTRODUCTION

Periprosthetic joint infection (PJI) is a devastating complication after primary and revision arthroplasty. The number of total knee and hip arthroplasties performed yearly is expected to increase drastically in the coming decades.[1] Even if the percentage of PJI can be decreased, this will cause an increase in the absolute number of PJI requiring treatment. This development asks for standardized evidence based protocols describing the best type of treatment for PJI. Debridement, antibiotics and implant retention are treatment of first choice in case of early infection after total hip arthroplasty (THA).[2, 3] In case of late or persisting infection, one- or two-stage revision needs to be performed according to global consensus.[3, 4] The use of different kinds of spacers in two-stage revision surgery has been widely debated in the past years.[5, 6] Various preformed spacers are available, as well as functional articulating spacers and spacers custom made by individual surgeons following a local protocol.

The aim of this study was to determine which type of spacer should be used during the interval of two-stage revision of an infected THA. First, we hypothesize that functional articulated spacers achieve infection eradication results comparable to other types of spacers. Second, we hypothesize that the rehabilitation period is shorter and patients' functional outcome is improved after two-stage revision with the use of a functional articulated spacer. In addition, we compared the incidence of spacer-related complications between the groups.

METHODS

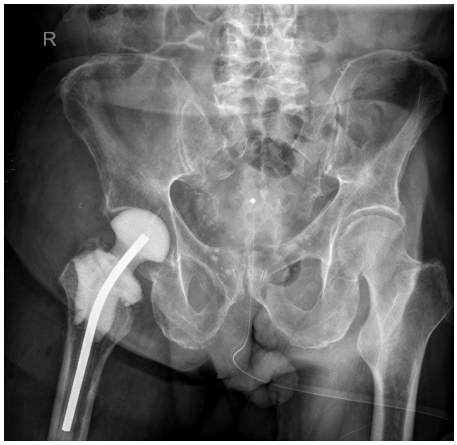
A review protocol was constructed and registered at PROSPERO international prospective register of systematic reviews (http://www.crd.york.ac.uk/PROSPERO/) with reference number CRD42014014324.

The search term can be found in appendix 1. The search was limited to adult humans and the databases (Pubmed/Medline, Embase, and Cochrane Library) were searched from 1978 to April 1st 2015. The lists of references of retrieved publications were manually checked for additional studies potentially meeting the inclusion criteria and not found by the electronic search. One-stage revision, two-stage revision without use of a spacer, in vitro studies and studies with a follow-up of less than two years were exclusion criteria. Studies on objective or functional outcome were selected and more closely reviewed by one of the authors (EV) and verified by a second author (DJM).

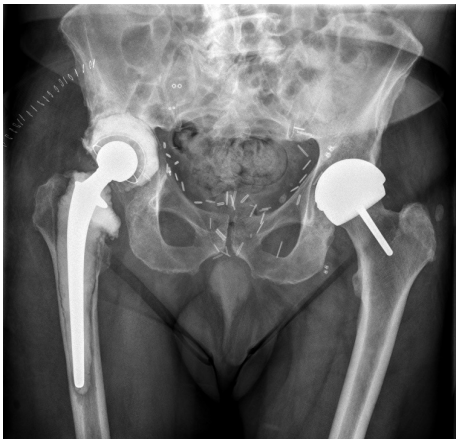
We extracted all information regarding the level of evidence, mean years of follow-up, number of patients initially included in the study and the number of patients available for follow-up, baseline patient characteristics and baseline clinical and laboratory findings. Data regarding type of spacer and antibiotics used, timing of second stage surgery, tissue culture results, postoperative regimen, functional outcome and patient satisfaction were extracted. The type of spacer was identified and studies were divided into three groups. Group I comprised studies using a preformed spacer (such as the Spacer-G) (figure 1A), group II comprised studies using a functional articulating spacer (Figure 1B) and group III comprised studies using a custom made spacer either from a prefabricated template or manufactured by the individual surgeons following a local protocol.

Figure 1

A. postoperative radiograph of a patient with a prefabricated antibiotic-loaded hip spacer of the right hip.



B. postoperative radiograph of a patient with an antibiotic-loaded functional articulated spacer of the right hip.



A spacer is considered a functional articulating spacer when patients are encouraged to bear partial to full weight and rehabilitation is stimulated. Functional articulating spacers consist of (parts of) regularly used prosthetic hip devices combined with antibiotic cement. An example is the PROSTALAC spacer. A spacer is considered a custom made spacer when a mold (either prefabricated or constructed by the authors of the original article) is used intraoperatively to construct a cement spacer, with or without the addition of any kind of internal stabilization.

The data included in the articles were extracted by one author (EV) and verified by a second (DJM). Primary outcome was success rate of infection eradication, defined as retention of the revision prosthesis at final follow-up without signs of recurrent infection. Secondary outcomes were the number of adverse events or complications and patient satisfaction and functional recovery as measured by patient reported outcome measures (PROMs).

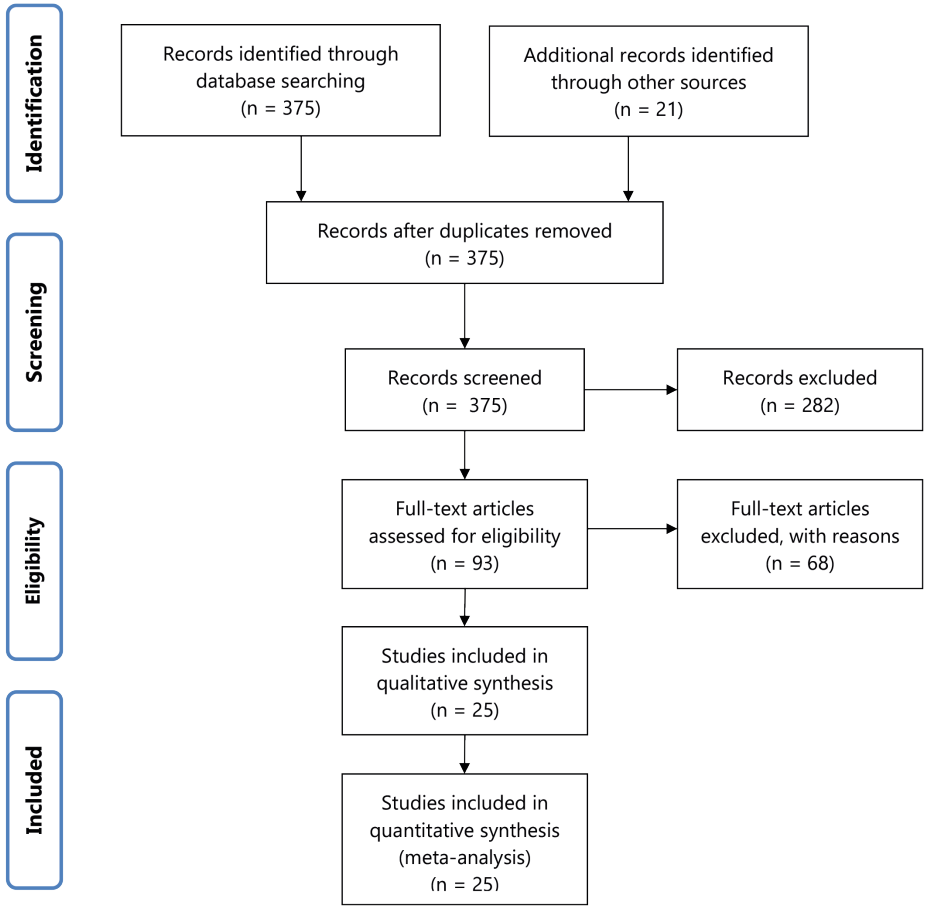
Studies were graded according the scoring system of the Grading of Recommendations Assessment, Development and Evaluation (GRADE) working group (http://www.gradeworkinggroup.org/index.htm). In short, for studies on therapy or prognosis, Level I is attributed to well designed and performed randomized controlled trials, Level II are cohort studies, Level III are case–control studies, Level IV are case series and Level V are expert opinion articles.

RESULTS

The search resulted in a total of 375 related studies, of which 93 studies were selected for additional review of the full text. A total of twenty-five studies met our inclusion criteria and were included for data analysis (Figure 2).[4, 7-30] The studies were published from 1997 to 2014. General characteristics of the included studies can be found in table 1. All reported averages in Table 3 are sample size weighted. Pooling of the overall results was not possible due to the clinical heterogeneity of the data. As a consequence no statistical analysis could be performed. Outcome after treatment will also depend on extent of infection, delay in treatment, virulence and susceptibility of infecting agents, quality of surgical debridement, type and extent of antibacterial treatment, compliance with treatment and so on. These potential confounders were in general poorly reported and when described heterogeneity of these factors was too large to analyze the effect on outcome.

Seven studies described preformed spacers, eight studies described functional articulating spacers and ten studies described custom made spacers. The only functional outcome measure used both pre- and postoperatively in at least one study per group was the Harris Hip Score (HHS)[31], outcome measures used only pre- or postoperatively were not further analyzed.

Figure 2: PRISMA flow diagram



Group I; prefabricated spacers

A total of 389 patients in seven studies were treated with two-stage revision of an infected hip arthroplasty with the use of a prefabricated antibiotic-loaded spacer.[9, 17, 19, 21-23, 30] In all studies the Spacer-G/Interspace was used. Characteristics of the patients, type of spacer, causative micro-organisms and complications can be found in tables 1, 2 and 3. Re-infection occurred in 4% of patients, resulting in a treatment success rate of 96% (range 80-98%). Mean interval between the first and second stage procedure was thirteen weeks. The second stage procedure was performed in 97% of originally included patients. Mean preoperative HHS was 28, which improved to 84 postoperatively after the second stage.[22, 23]

Group II; functional spacers

A total of 527 patients in eight studies were treated with two-stage revision of an infected hip arthroplasty with the use of a functional articulating antibiotic-loaded spacer.[7, 11, 12, 16, 18, 25, 26, 29] Characteristics of the patients, type of spacer, causative micro-organisms and complications can be found in tables 1, 2 and 3. Re-infection occurred in 7% of patients, resulting in a treatment success rate of 93% (range 76-100%). Mean interval between the first and second stage procedure was sixteen weeks. The second stage procedure was performed in 89% of originally included patients. Patients retaining the functional spacer were not accounted for when calculating time between first and second stage. Mean preoperative HHS was 53, which improved to 90 postoperatively after the second stage.[32]

Group III; custom made spacers

A total of 534 patients in ten studies underwent two-stage revision with the use of a custom made spacer.[4, 8, 10, 13-15, 20, 24, 27, 28] The study by Hsieh et al describes two groups of patients, which were both included in this study and were analysed separately.[14] In six studies prefabricated molds were used, in the other five studies spacers were intra-operatively molded by hand. Spacers were enforced by K-wires in four studies, by a Küntscher nail in 2 studies, by a rush pin in two studies and by a modular head and stem in one study. In two studies no reinforcement was used. Characteristics of the patients, type of spacer, causative micro-organisms and complications can be found in tables 1, 2 and 3. Re-infection occurred in 5% of patients, resulting in a treatment success rate of 95% (range 86-100%). Mean interval between the first and second stage procedure was eleven weeks. The second stage procedure was performed in 97% of originally included patients. Mean preoperative HHS was 39, which improved to 81 postoperatively after the second stage.[4, 13, 20]

Table 1; General characteristics

Author	Year	Level of evidence	N of hips stage 1	Age	M	F	Type of spacer	N of hips stage 2	Failure	Success (%)	Patients available for follow-up (n)	FU (months)
Group 1; Prefabricated spacers												
Cherubino	2013	3	30	71	17	13	Spacer-G/InterSpace	29	1	97	30	72
Magnan	2001	4	10	72	7	3	Spacer-G/InterSpace	8	2	80	10	35
Neumann	2012	4	44	x	25	19	Spacer-G/InterSpace	42	1	98	44	67
Pattyn	2010	3	61	65	30	31	Spacer-G/InterSpace	61	2	96	61	36
Pignatti	2010	4	41	59	16	25	Spacer-G/InterSpace	40	1	98	41	64
Romano	2011	3	20	56	9	11	Spacer-G/InterSpace	20	1	95	20	57
Romano	2012	4	183	60	61	122	Spacer-G/InterSpace	183	10	94	162	60
Group 2; Functional spacers												
Biring G	2010	3	99	72	52	47	Prostalac	48	4	89	48	144
Fink	2009	4	44	69	20	16	Functional spacer	39	0	100	39	35
Hofmann	2005	4	42	64	15	12	Functional spacer	35	1	96	27	76
Leung	2011	4	50	64	20	18	Prostalac	38	9	76	38	58
Masri	2007	4	31	65	21	10	Prostalac	29	3	90	29	47
Tsung	2014	4	76	72	37	38	Functional spacer	42	12	84	76	80
Wentworth	2002	3	135	66	66	69	Functional spacer	118	24	83	135	x
Younger	1997	4	50	67	22	28	Functional spacer	48	3	94	50	43

Table 1; General characteristics (continued)

Author	Year	Level of evidence	N of hips stage 1	Age	M	F	Type of spacer	N of hips stage 2	Failure	Success (%)	Patients available for follow-up (n)	FU (months)
Group 3; Custom made spacers												
Cabrita	2007	1	38	54	x	x	Custom spacer	33	4	89	38	48
Durbhakula	2004	3	20	70	12	8	Custom spacer	18	2	90	20	38
Hsieh	2004	3	42	61	32	10	Custom spacer	40	3	93	42	55
Hsieh Group 1	2009	4	51	59	27	19	Custom spacer	49	4	91	49	50
Hsieh Group 2			56	62	33	20	Custom spacer	53	4	89	53	37
Ibrahim	2014	3	125	68	x	x	Custom spacer	125	5	96	125	103
Klouche	2012	3	46	67	26	20	Custom spacer	46	4	91	46	35
Oussedik	2010	4	39	x	x	x	Custom spacer	39	2	96	39	60
Schwartzkopf	2014	4	56	62	27	29	Custom spacer	48	8	86	56	32
Whittaker	2009	4	44	69	21	22	Custom spacer	44	5	93	44	49
Yamamoto	2003	4	17	62	6	11	Custom spacer	17	0	100	17	38

n = number; M = male; F = female; X = not reported

Table 2: bacteria isolated at first stage procedure.

Author	S. epidermidis	S. aureus	MRSA/ MRSE	E. faecalis	Multiple Gram+	Strep species	Gram– (undefined)	E. coli	P. aeruginosa	negative cultures	Other
Group I											
Cherubino	5	8			5	2		2		8	
Magnan	1	1				1	1	1	1	4	
Neumann	6	10	5			7	2	2	2		7
Pattyn	13	14	8	1	4	6				11	4
Pignatti	8	7	9	2	10	1				4	
Romano	3	7	4	1					1	4	
Romano	36	38	38	5			13	5	14	68	13
Total	**51**	**85**	**64**	**9**	**19**	**17**	**16**	**10**	**18**	**99**	**24**
Group II											
Biring	26	22	10		20	12	10	3		5	1
Fink	25	4	3	7		1	4				3
Hofmann	1	6	3	2		1	2	1	2	5	
Leung F			38								
Masri	10	11	1	1	3	1	2				
Tsung	30	16	3	2	1	8	3	4	2	7	1
Wentworth	38	28				4	2	2			21
Younger	24	7			2	9	3	1	1		1
Total	**86**	**94**	**58**	**12**	**26**	**36**	**26**	**11**	**5**	**17**	**27**

Table 2: bacteria isolated at first stage procedure. (continued)

Author	S. epidermidis	S. aureus	MRSA/ MRSE	E. faecalis	Multiple Gram+	Strep species	Gram– (undefined)	E. coli	P. aeruginosa	negative cultures	Other
Group III											
Cabrita	10	23		10		6	23	4	1		3
Durbhakula	4	6	2	2		4		1			1
Hsieh	9	14		2	3		4	3	6		1
Hsieh Gr1	11	4	12	1	1	3	3	2	5	4	
Hsieh Gr2	10	5	15	1	2	2	2	5	8	3	
Ibrahim	35	29	14		16	11	19			13	7
Klouche	12	5	12	1	4	5					7
Oussedik	19	3	6		6		2	3	3		
Schwartzkopf	2	13	1		2	6	2		1	16	22
Whittaker	27	3	2	7		5					
Yamamoto	8		3					1	1	4	
Total	**48**	**105**	**67**	**24**	**34**	**42**	**55**	**19**	**25**	**40**	**41**

Table 3: Complications.

Complication	Group 1	Group2	Group 3
After 1st stage			
Spacer dislocation	13%	4%	3%
Spacer fracture	0%	0%	2%
Femur fracture	4%	4%	1%
Re-infection during spacer	5%	6%	14%
Repeat 1st stage procedure	5%	3%	6%
After 2nd stage			
Re-infection after 2nd stage	4%	7%	5%
Recurrent dislocation	2%	3%	2%
Revision for infection	2%	4%	2%

All shown numbers are percentage per group.

DISCUSSION

The aim of this study was to perform a systematic review of the literature to investigate which type of antibiotic-loaded spacer provides the best outcome in patients treated with two-stage revision for an infected arthroplasty of the hip. Our first hypothesis was that functional spacers would provide a comparable rate of infection control as compared to custom made or preformed antibiotic-loaded spacers. Our results show comparable good results for the three types of spacers when considering infection control, with control rates ranging between 93% and 96%. Patients receiving antibiotic suppression therapy after two-stage revision were considered failure of treatment.

Our second hypothesis was that patients treated with a functional spacer would experience a shorter rehabilitation time and better functional results as compared to patients treated with custom made or preformed antibiotic-loaded spacers. While functional and patient reported outcome after primary total hip arthroplasty has extensively been described in literature, functional outcome after revision total hip arthroplasty for PJI has scarcely been reported. Of all included studies only one study[17] describes postoperative range of motion, no studies report patient satisfaction. The only frequently used outcome measure was the HHS, which showed comparable postoperative scores in all groups. Other outcome measures were used less than twice per group and gave insufficient data to compare between groups of spacers. The original studies did not report on rehabilitation protocols. We had insufficient data to prove or disprove our second hypothesis.

Most complications are evenly distributed among the three groups, except for dislocation. The incidence of spacer dislocation is high in the prefabricated spacer group as compared to both other groups (13% versus 4% and 3% respectively). Although this appears to be a large difference, significance levels could not be calculated, due to heterogeneity of the original data. The difference can be explained by the possibility for the orthopaedic surgeon to adjust functional spacers and custom made spacers to the situation in an individual patient, considering for instance femoral shaft size, neck length, offset deficiency, acetabular size or bone loss. The prefabricated spacers are only available in a limited number of sizes resulting in overstuffing or instability in some patients, which might lead to spacer dislocation.

Remarkably, in 11% of patients in group 2 no second stage procedure was performed. This high incidence was caused by patients refusing second stage surgery because they were satisfied with the functional result after first stage placement of the functional articulating spacer. Outcome measures and functional results such as walking distance and range of motion were not specifically reported for the group of patients refusing second stage surgery.

There are differences in bacteriology between the three groups. Group 1 contains a high number of culture negative cases, especially in the study by Romano et al.[30] These patients might have a positive influence on the outcome, as infection has not been objectified during primary surgery and bacteria might have been absent in the patients.

A weak point of this study is the lack of quality of evidence. There is an absence of level 1 evidence comparing different kinds of spacers in the two-staged treatment of PJI of the hip. Functional outcome and patient satisfaction after one- or two-stage revision of the infected total hip arthroplasty have only scarcely been described and therefore could not be presented in the results. Also, due to the lack of information in and heterogeneity of the original data concerning extent of infection, delay in treatment, virulence and susceptibility of infecting agents, quality of surgical debridement, type and extent of antibacterial treatment, compliance with treatment, type of antibiotic in the spacer cement and timing of second stage procedure the effect of these factors on outcome could not be analyzed. We acknowledge these could be confounding factors.

This study creates a comprehensive overview of the available literature on the use of antibiotic-loaded spacers in two-stage revision arthroplasty of the infected prosthetic hip joint. With the challenge of an increasing number of infected total hip revisions

ahead, there is a need for an evidence based approach to the treatment of PJI after total hip arthroplasty. Literature comparing functional outcome between various spacers in two-stage revision of the hip is absent. Various studies have investigated the outcome of one-stage versus two-stage revision arthroplasty[6] or difference in outcome of two-stage revision with the use of different types of spacers including cement beads and Girdlestone procedures.[5, 15, 33-36] None of these studies have described functional outcome after revision arthroplasty of infected total hip arthroplasty.

Functional spacers may improve the congruence of the joint compared to preformed spacers, but up to date there have been no reports investigating whether clinical performance during and after two-stage revision is better with a functional spacer.

The international consensus meeting[3] concerning periprosthetic joint infections organized in 2013 resulted in the following statements: (1) the type of spacer does not influence the rate of infection eradication in two-stage exchange arthroplasty of the hip, (2) a period of antibiotic therapy of 2 to 6 weeks after removal of the infected implant is recommended, (3) there is no definitive evidence in the literature as to the optimal time interval between the two stages, reports vary from 2 weeks to several months. As could be expected after reading the recommendations from the international consensus meeting, we have found a large variety in treatment protocols described in literature.

Research should focus on finding the preferred type of treatment and type of spacer to combine a high success rate of infection treatment with a good functional and patient reported outcome. There is a need for a large, prospective study evaluating patient satisfaction and functional outcome after two-stage revision hip arthroplasty comparing various kinds of antibiotic-loaded spacers. Secondly, research should focus on the optimal timing of the second stage procedure.[37]

Functional articulating spacers achieve a comparable rate of infection eradication in the treatment of periprosthetic hip joint infections as compared to preformed or custom-made antibiotic-loaded spacers. There is insufficient evidence concerning rehabilitation and functional outcome after two-stage revision hip arthroplasty to advocate or discourage the use of either kind of interval spacer.

CONTRIBUTION OF AUTHORS

All authors have made substantial contributions to study design, data collection, manuscript draft and/or manuscript revision.

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CONFLICT OF INTEREST AND FUNDING

No funding was received for this study. We have no conflict of interest to mention.

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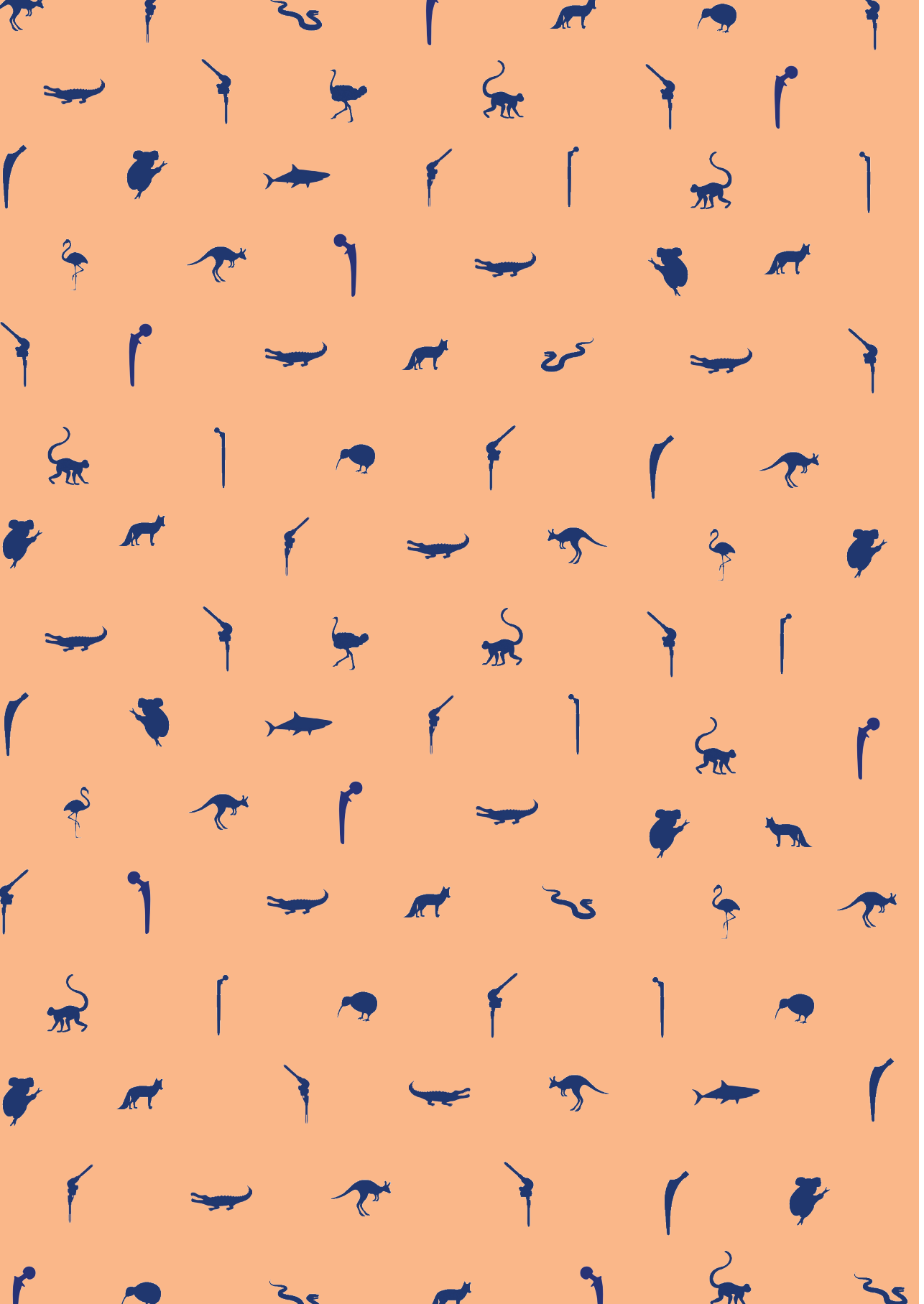
APPENDIX 1:

A search term with Boolean operators was constructed: ((spacer[all fields] OR two-stage[all fields]) AND (((“hip”[MeSH Terms] OR “hip”[All Fields]) AND (“arthroplasty”[MeSH Terms] OR “arthroplasty”[All Fields])) OR (“arthroplasty, replacement, hip”[MeSH Terms] OR (“arthroplasty”[All Fields] AND “replacement”[All Fields] AND “hip”[All Fields]) OR “hip replacement arthroplasty”[All Fields] OR (“total”[All Fields] AND “hip”[All Fields] AND “replacement”[All Fields]) OR “total hip replacement”[All Fields]))) AND ((“infection”[MeSH Terms] OR “infection”[tiab] OR “infections”[tiab]) OR (revision[All Fields] AND (“hip”[MeSH Terms] OR “hip”[All Fields]))).



CHAPTER

7

Improved Patient Reported Outcome and Infection Eradication Rate with Functional Articulating Spacers in Two-Stage Revision of the Infected Hip

(submitted)

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ABSTRACT

Introduction Two-stage revision arthroplasty with an antibiotic-loaded spacer is treatment of choice in chronically infected total hip arthroplasties. Interval spacers can be functional articulating or prefabricated. Functional results of these spacers have scarcely been reported. We retrospectively compared patient reported outcome and infection eradication rate after two-stage revision arthroplasty for periprosthetic joint infection of the hip with the use of a functional articulating or prefabricated spacer.

Materials and Methods All patients with two-stage revision of a hip prosthesis between 2003 and 2016 were retrospectively included. Patients were divided into two groups; patients treated with a functional articulating spacer or with a prefabricated spacer. Patients completed the Hip Osteoarthritis Outcome Score and the EQ-5D and EQ-VAS scores. Primary outcomes were patient reported outcome and infection eradication after two-stage revision. The results of both groups were compared to the patient acceptable symptom state (PASS).

Results We consecutively treated fifty-five patients with a prefabricated spacer and fifteen patients with a functional articulating spacer of the hip. Infection eradication rate for functional articulating and prefabricated spacers were 93% and 78% respectively. More patients in the functional articulating spacer group reached the PASS for the HOOS pain, HOOS QoL and EQ-VAS.

Conclusions Functional articulating spacers seem to lead to improved patient reported functional outcome, better infection eradication rate and less perioperative complications after two-stage revision arthroplasty of an infected total hip prosthesis, compared to prefabricated antibiotic-loaded spacers.

Failure of two-stage revision and subsequent explantation of the prosthesis leads to very poor quality of life.

Keywords: Periprosthetic joint infection; total hip arthroplasty; functional articulating spacer; hip revision.

INTRODUCTION

When a periprosthetic joint infection (PJI) persists after a debridement, antibiotics and implant retention procedure of an infected prosthesis, or when onset of infection is delayed or late, the PJI is considered chronic.[1, 2] Two-stage revision arthroplasty is the standard treatment for chronic PJI of the hip.[3] Antibiotic-loaded interval spacers have proven to be effective in eradicating the infection.[3-5] In contrast to a Girdlestone situation the antibiotic-loaded hip spacer keeps the soft tissues at length during the interval period.[6] Antibiotic-loaded interval spacers can be either functional articulating, prefabricated or custom-made peroperatively with or without the use of a prefabricated mold.[4] The infection eradication rates for these types of spacers are comparable, while the complication rates of prefabricated spacers are reported to be higher.[4, 7, 8] Dislocation of prefabricated hip spacers is the most common complication occurring during the spacer interval, which is probably caused by the limited number of options available to adjust the prefabricated spacer to the patients' anatomy.[4]

Repetitive surgery on a joint causes soft tissue trauma, which can lead to periarticular fibrosis and impaired range of motion.[6, 9] Therefore, orthopaedic surgeons have been trying to find a type of antibiotic-loaded spacer with the same efficacy in infection eradication, but also facilitating range of motion exercises and ambulation during the spacer period.[7, 10, 11] Since the functional articulating spacers allow the patient normal activity during the interval period, they may be a good solution for these functional problems and thereby also decrease morbidity and impairments of the patients to a certain extent. Patient related functional assessment of hip function after two-stage revision of the infected total hip arthroplasty (THA) with the use of a functional articulating has only scarcely been reported, and these studies did not compare the outcome of the different types of spacers.[10, 11]

We retrospectively reviewed all patients treated with two-stage revision of an infected hip arthroplasty with the use of either a prefabricated or a functional articulating spacer between 2003 and 2016. We hypothesized functional articulating spacers lead to improved patient reported outcome, fewer complications and shorter in-hospital stay, while maintaining a comparable infection eradication rate as compared to prefabricated antibiotic-loaded hip spacers.

METHODS

The STROBE statement was adhered to while constructing the study and writing the manuscript.

Patients

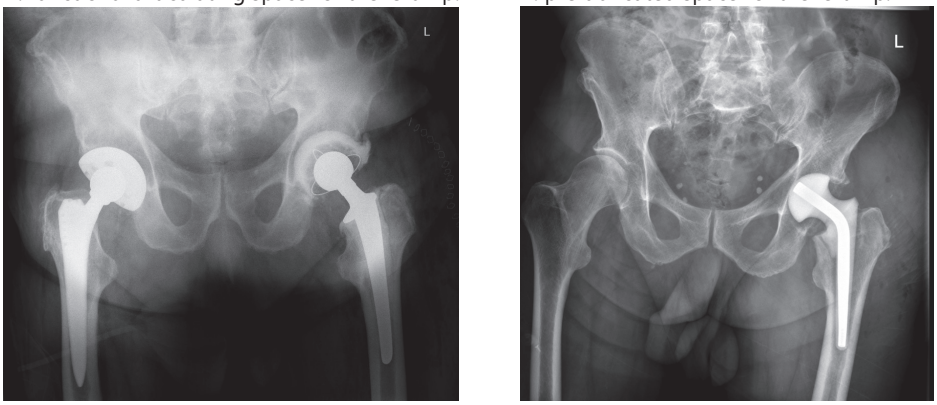
After approval by the local medical ethics committee, the records of all patients whom had two-stage revision arthroplasty of the hip between 2003 and 2016 were retrospectively reviewed. All patients with chronic periprosthetic joint infection of the hip that were treated with two-stage revision arthroplasty with the use of an interval spacer and with follow-up of at least twelve months were included in the study. Exclusion criteria were two-stage revision without the use of a spacer, patients treated with one-stage revision and follow-up of less than twelve months. Extent of bone loss was not an exclusion criterion for either kind of spacer.

Intervention

During first-stage surgery the infected prosthesis including bone cement, if present, was removed using a posterolateral approach. After meticulous debridement a functional articulating - or a prefabricated antibiotic-loaded interval spacer was inserted (Figure 1A and 1B, respectively). The functional articulating spacers are made of commonly used femoral and acetabular cemented components. During insertion the antibiotic-loaded cement is not pressurized and care is taken to have no cement distal to the tip of the stem. The type of antibiotics used in the cement can be adjusted to the causative pathogen found in the preoperative cultures. The surgeon has several options to optimize offset and neck length of the femoral component, and offset, version and inclination of the acetabular component. The spacer enables patients to practice full range of motion and patients are allowed to walk bearing 50% to full body weight, irrespective of the extent of bone loss. Prefabricated antibiotic-loaded hip spacers are commercially available with different stem lengths and head sizes. During the spacer interval the prefabricated spacer allows patients to practice range of motion of the hip. Weight-bearing during the spacer interval is usually limited to less than 25% of body weight. The two groups of patients were treated consecutively, there were no differences in selection criteria for either type of treatment. Initially the prefabricated spacers were used, later the functional articulating spacers. The concentration of antibiotics in the cement were the same in both groups.

All included patients were treated with antibiotics according to the recommendations postulated by Zimmerli and colleagues in 2004.[2] The type of antibiotic treatment was decided in close consultation with a microbiologist and an infection specialist. Two weeks before the second stage procedure antibiotics were discontinued to achieve a two-week antibiotic free interval. During the study period there were no other changes to the treatment practice, except for the implementation of the functional articulating spacers in 2014.

Figure 1
A. functional articulating spacer of the left hip. B. prefabricated spacer of the left hip.



Data and Patient Reported Outcome Measures

General patient characteristics, complications during treatment and infection status were retrieved from patients' records. At follow-up patient reported outcome was measured using the Hip Osteoarthritis Outcome Score (HOOS), EQ-5D-3L (EQ5D) and the EQ-5D quality of life thermometer (EQ-VAS) were used to assess patient reported outcome.[12, 13] The HOOS is a validated score for patients with osteoarthritis of the hip and consists of five domains: symptoms (5 questions), pain (10 questions), activities (17 questions), sports (4 questions) and quality of life (4 questions). Using all answers a score can be calculated with range of scores between 0-100, with 100 as the optimal score. The EQ-5D is a questionnaire that is developed to describe and value health across a wide range of disease areas. The EQ-5D comprises of 5 dimensions: mobility, self-care, usual activities, pain/discomfort and anxiety/depression. The patient indicates his health state on one of three levels: no problems, some problems or extreme problems, labelled 1-3. The scores can be converted into a value -0.500 to 1.00, with 1.00 as the optimal score. The EQ-5D also contains a visual analogue scale for quality of life (EQ-VAS), where patients can indicate their perceived quality of life on a range of scores 0-100, with 100 as the optimal score.

Primary outcomes were patient related outcome measure scores (PROMs) and infection eradication after second-stage procedure. Secondary outcomes were complications reported during the spacer period and at final follow-up.

Data analysis

The results of the subscores of the HOOS and the result of the EQ-5D were compared to the patient acceptable symptom state (PASS) as described for patients following

primary total hip arthroplasty by Paulsen and colleagues.[14] The PASS for the HOOS, EQ-5D and EQ-VAS are 91 (HOOS Pain), 88 (HOOS-PS), 83 (HOOS QoL), 0.92 (EQ-5D Index), and 85 (EQ-VAS), respectively.[14]

Patients were analyzed for the type of spacer they were treated with. To be able to compare patient reported outcome after successful treatment and to determine patient reported outcome after failed two-stage revision and subsequent treatment, the PROMs of successfully and unsuccessfully treated patients were analyzed separately.

Failure of treatment was defined as persisting infection at final follow-up, removal of the hip prosthesis or use of suppressive antibiotics at follow-up.[15] Descriptive statistics, mean and range are used to represent the demographics of the patients. For numerical variables we used students' t-tests were used to assess the level of significance for differences between the groups, with 95% confidence intervals, for binary outcome we used Fisher's exact test. Calculations and statistical analyses were performed using Excel and SPSS software.

RESULTS

Patient characteristics and general outcome

Between 2003 and 2016 we consecutively treated fifty-five patients with a prefabricated spacer and fifteen patients with a functional articulating spacer. General patient characteristics and infection characteristics are listed in Table 1 and 2. All live patients completed the PROMs. The results of HOOS and EQ-5D scores are displayed in Figure 2.

Table 1: General patient characteristics

	Functional articulating spacer group	Prefabricated spacer group	p
Number of patients	15	55	
Age (range)	66 (58-76)	68 (33-88)	N.S.
Gender female	8	25	N.S.
BMI (range)	27 (20-35)	27 (19-41)	N.S.
BMI > 30	3	13	N.S.
Diabetes	4	8	N.S.
ASA 1/2/3	1 / 11 / 3	3 / 30 / 22	N.S.
Post-traumatic (fracture)	6	9	< 0.05
Months follow-up (range)	24 (16-85)	51 (13-129)	< 0.005

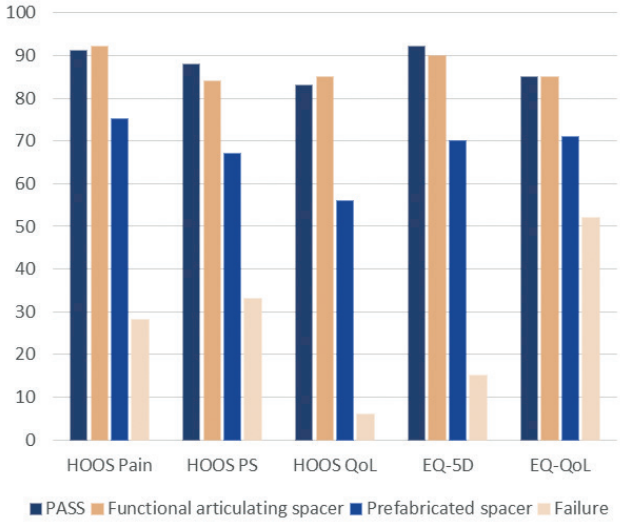
N.S. = Not significant. BMI = Body mass index. ASA = American Society of Anesthesiologists score.

Table 2: Infection characteristics, causative pathogens

	Functional articulating spacer group	Prefabricated spacer group
CoNS	10	18
S. aureus	0	9
S. epidermidis	0	1
Propioni Acnes	0	5
E. faecalis	2	2
E. coli	0	1
P. aeruginosa	0	1
H. parainfluenzae	0	1
Corynebacterium	0	2
Aerococcus christensenii	0	1
Group B Streptococcus	1	0
Candida albicans	0	2
Culture negative	0	4
Polymicrobial	2	8

CoNS = *Coagulase Negative Staphylococcus.*

Figure 2: patient reported outcome measure results at follow-up



The results of the EQ5D score are multiplied by 100 for reasons of readability.
HOOS = Hip Osteoarthritis Outcome Score
PASS = Patient Accepted Symptom Scale as described by Paulsen [14].
QoL = Quality of life.

Functional articulating spacer group

Fifteen patients were treated with a functional articulating spacer of the hip. At a mean follow-up of 24 months (range 15-85 months) one patient had died due to reasons unrelated to treatment.

The mean operating time of the first-stage surgery was 160 minutes (range 116-290 minutes). Patients were admitted to the orthopaedic ward for median thirteen days (range 5-34 days) after the first stage procedure. Spacer dislocation occurred in two patients. Both patients experienced one dislocation each, which was treated with a closed reduction in both patients. The mean duration of the spacer interval was eight weeks (range 5-12 weeks).

The mean operating time of the second stage surgery was 139 minutes (range 88-188 minutes). After the second stage procedure patients were admitted for a median six days (range 3-12 days) postoperatively. Results of the PROMs are listed in Table 3 and Figure 2, PASS was reached for the mean score of the HOOS pain, HOOS QoL and EQ-VAS.

We consider one patient as failure of treatment. Infection persisted after two-stage revision, therefore a Girdlestone situation was created.

Table 3: Patient reported outcome measure results and comparison of the groups.

	Functional articulating spacer group	Prefabricated spacer group	p
Number of patients	15	55	
HOOS total (SD)	88 (6)	67 (14)	<0.01
HOOS pain (SD), % PASS	92 (6), 54%	75 (14), 8%	<0.01
HOOS PS (SD), % PASS	85 (6), 15%	67 (14), 3%	<0.01
HOOS QoL (SD), % PASS	85 (12), 46%	56 (21), 5%	<0.01
EQ-5D (SD), % PASS	0.90 (0.17), 46%	0.69 (0.30), 5%	<0.01
EQ-VAS (range), % PASS	85 (65-100), 46%	71 (45-85), 3%	<0.05

HOOS = hip osteoarthritis outcome score. PASS = patient acceptable symptom state. QoL = quality of life. VAS = visual analogue scale.

Prefabricated spacer group

Fifty-five patients were treated with a prefabricated spacer of the hip. At a mean follow-up of 51 months (range 13-129 months) ten patients had died, five of these patients had died due to reasons unrelated to treatment.

The mean operating time of the first-stage surgery was 186 minutes (range 70-360 minutes). Patients were admitted to the orthopaedic ward for median thirty-one days (range 5-114 days) after the first stage procedure. Ten patients experienced dislocation of the spacer. In these ten patients a total of twenty-five dislocations occurred. Revision of the spacer because of multiple dislocations was performed in seven patients. The mean duration of the spacer interval was eight weeks (range 2-28 weeks).

The mean operating time of the second stage surgery was 165 minutes (range 75-326 minutes). After the second stage procedure patients were admitted for a median twenty-two days (range 3-63 days) postoperatively. After the second-stage procedure dislocation of the hip prosthesis occurred in two patients, both of these patients were treated with a closed reduction. Results of the PROMs are listed in Table 3 and Figure 2, none of the mean outcomes reached the PASS.

We considered twelve patients as failure of treatment. Persistent infection occurred in eight patients, re-infection with a different bacteria was present in four patients. Two patients were treated with lifelong suppressive antibiotics. Two patients underwent subsequent two-stage revision which was successful in both. Eventually a Girdlestone situation was created in eight patients. Five of the failure patients had died at time of final follow-up.

Comparison of the groups

With respect to the functional outcome, the HOOS and its subscores (all $p<0.01$), the EQ-5D ($p<0.01$) and the EQ-VAS scores ($p<0.05$) were all significantly better for patients successfully treated with a functional articulating spacer compared to patients successfully treated with a prefabricated spacer. The infection eradication rates were 93% and 78% ($p>0.05$) for patients treated with a functional articulating spacer and for patients treated with a prefabricated spacer respectively.

The mean duration of the first-stage procedure was not statistically different ($p=0.14$), and neither was the second-stage procedure ($p=0.13$), for the functional articulating and prefabricated groups respectively. The duration of time patients were admitted to the hospital was significantly shorter for the patients with a functional articulating spacer, both after first-stage surgery ($p<0.01$), as well as after the second-stage procedure ($p<0.01$).

The number of patients with a spacer dislocation was not significantly different for the functional articulating or prefabricated spacer group ($p>0.05$). However, the number of dislocations per patient experiencing a dislocation was significantly higher for patients with a prefabricated spacer ($p<0.01$). Revision of the spacer due to recurrent dislocations was performed more often in the prefabricated spacer group, without reaching significance ($p=0.15$).

Failure patients

We considered thirteen patients as failure of treatment after two-stage revision of the hip. Mean age of these patients was sixty-seven years (range 50-88 years) at first-stage surgery. There were ten females and three males. Mean Body Mass Index (BMI) was 32 (range 24-37). Seven patients were American Society of Anesthesiologists score (ASA) 3, the other six were ASA 2. Five patients had died at final follow-up, all of these patients had ASA 3. The eight patients who were alive at follow-up completed the HOOS, EQ-5D and EQ-VAS questionnaires and scored mean 20 (range 5-39), 0.1486 (range -0.128-0.693) and 52 (range 30-80) respectively. None of the patients reached PASS for any of these outcomes. Two of these seven patients received lifelong suppressive antibiotic therapy, the others had a Girdlestone situation.

DISCUSSION

This study compared patient reported outcome, infection eradication rate and complications for functional articulating spacers and prefabricated spacers used in two-staged revision arthroplasty for PJI of the hip. Infection eradication rate seemed higher for patients treated with a functional articulating spacer than for patients treated with a prefabricated spacer (93% versus 78% respectively). Both these infection eradication rates are in concordance with the literature.[10, 11]

The patients treated with a functional articulating spacer achieved patient reported outcome scores above or close to the PASS, reflecting an acceptable state of functioning from a patient's perspective as described by Paulsen, whereas the patients treated with a prefabricated spacer achieve much lower scores.[14] The results of the HOOS, EQ-5D and EQ-QoL show patients treated with a functional articulating spacer achieved significantly higher scores compared to the patients treated with a prefabricated spacer. The difference may be partially explained by heterogeneity of the two patient groups, however correcting for age and comorbidity made no difference. We think these higher scores adequately reflect the better functional recovery of patients with a functional spacer, which has large implications for long-term quality of life.