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Original article

The benefits of systematic intraoperative sampling during lower limb arthroplasties due to sequelae from prior osteoarticular infections: A retrospective study of 92 cases

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ABSTRACT

Introduction: Osteoarticular infections (OAIs) of native joints lead to cartilage damage which may require subsequent arthroplasty. There is no consensus on systematic intraoperative microbiological sampling when performing an arthroplasty on a native joint with a history of OAI. We carried out a retrospective study to: (1) identify the frequency of the persistence of the microorganism(s) involved during the initial, presumed cured OAI, when performing an arthroplasty for sequelae of osteoarthritis, (2) to find an association between the length of time between the OAI and arthroplasty, and the recurrence of bacterial infection, (3) to assess the influence of the presence of hardware on the risk of infectious recurrence.
Hypothesis: Systematic sampling is justified during a subsequent arthroplasty after an OAI, even after a prolonged period.
Material and method: This single-center, retrospective descriptive study included all patients whose indication for arthroplasty resulted from osteoarthritis, osteitis or bacterial osteomyelitis of a native joint, or in the aftermath of an infection post osteosynthesis. All patients were considered to have recovered from the initial infection at the time of the arthroplasty. Between 2008 and 2019, 92 patients were included in the study, with an average age of 56.5 years (range: 21–97 years). OAI occurred at a mean age of 35 years (range: 1–84 years). The average time from OAI to implantation was 15 years (range: 1–65 years). The bacteria most frequently found in the initial OAI was *Staphylococcus aureus*, involved in 35.8% of cases ($n = 33/92$).
Results: The intraoperative samples came back positive in 17% of cases ($n = 16/92$), including 9 positive for the same bacteria as the OAI (56%, $n = 9/16$). For these 16 cases, the time between the OAI and the arthroplasty was 1 year for 5 patients, between 1 and 15 years for 5 patients and greater than 15 years for 6 patients. For 3 positive patients, the information on the initial microorganism was not known and 4 patients were positive for a bacterium different from the initial one. The time from the initial OAI to the arthroplasty was not associated with positive results ($p = 0.38$). There was no significant difference between a positive culture at the time of arthroplasty and the initial type of OAI [native joint versus presence of hardware and/or open fracture ($p = 0.41$)].
Conclusion: The results of this work suggest there is value in microbiological sampling when performing an arthroplasty on a previously infected joint, regardless of the duration of the infection.
Level of evidence: IV; retrospective study.

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1. Introduction

Osteoarticular infections (OAIs), including septic arthritis and osteomyelitis/osteitis, are an important cause of morbidity in orthopedics [1]. The incidence of septic arthritis, of native joints or after surgery, is estimated at 4–10 per 100,000 inhabitants in developed countries [1]. Osteomyelitis, occurring mainly in children, has an estimated incidence of 10 per 100,000 population [2–5]. The management of an OAI is a medico-surgical emergency that can involve a life-threatening prognosis at an early stage and can also endanger the functional prognosis at a later stage, with a possible transition to chronicity. Unless treated promptly and adequately, OAIs in children and adults can lead to a wide spectrum of residual deformities requiring surgical treatment in adulthood. In the hip and knee, the sequelae can be joint deformity, ankyloses and early osteoarthritis leading to disabling pain and major functional limitation [6–9]. In this context, total hip arthroplasty (THA) or total knee arthroplasty (TKA) offer therapeutic solutions to restore joint function and relieve pain. One of the major concerns is the recurrence of the initial OAI following arthroplasty, which can lead to complex prosthetic revision surgeries, major morbidity for patients, and significant additional economic costs [10,11].

An analysis of the recurrence of infection in these indications identified varying results and recommendations in the literature [11–14]. To date, there is no consistent approach to systematic intraoperative microbiological sampling, when performing an arthroplasty after OAI sequelae [12–14]. Since samples are not taken systematically, there is little data in the literature on the long-term persistence of a quiescent microorganism in situ, and on the benefit of sampling, at a later stage, from the initial infection. A delay of more than 10 years is generally recommended to limit the risk of recurrent infection [12–14].

Faced with this lack of consensus, systematic microbiological sampling occurs in our center for these indications and often leads to antibiotic therapy. Therapy remains until final microbiological results are obtained, and may be extended for 3 months if the cultures are positive and adapted to the antibiograms. We carried out a retrospective study in order to:

- study the frequency of the persistence of the microorganism(s) involved during the initial, presumed cured OAI, when performing an arthroplasty for sequelae of osteoarthritis;
- to find an association between the length of time between the OAI and arthroplasty and the recurrence of bacterial infection;
- to assess the influence of the presence of a hardware on the risk of reinfection.

The hypothesis is that it is justified, even at a later stage from the OAI, to take systematic samples during the subsequent performance of an arthroplasty.

2. Patients and methods

2.1. Patients

We carried out a single-center, retrospective descriptive study, based on primary hip and knee arthroplasties performed across the orthopedics and septic traumatology department of the Lille University Hospital since 2008. This date corresponds to the digitalization of medical data and the creation of CRIOAC-G4 Lille Tourcoing, with the systematization of Multidisciplinary Concertation Meetings (MCM).

We included all patients whose indication for arthroplasty was a sequel of osteoarthritis, osteitis or bacterial osteomyelitis, of a native joint or following osteosynthesis. The osteosynthesis hardware must have been removed before the arthroplasty procedure was performed. All the patients were considered cured of the initial infection when performing the arthroplasty, with a minimum follow-up of one year from the OAI, and not presenting with any clinical or biological inflammatory syndromes when undergoing the arthroplasty.

The exclusion criteria were active OAIs during surgical management and patients with osteochondral sequelae of non-bacterial origin. We chose not to exclude patients for whom bacteriological documentation from the initial OAI was not available. Those considered to have a history of infection at the operated site were derived from clinical data or analysis of their medical file (operative report, history of fistula, consultation letters indicating an infection without specifying the germs found or the antibiogram).

Two hundred and eighty-four primary arthroplasties (185 THA and 99 TKA) were implanted in the orthopedics/septic traumatology unit between 2008 and 2019, 92 of which corresponded to primary prostheses meeting the criteria for inclusion and exclusion (Fig. 1). Among them, there were 50 hip arthroplasties and 42 knee arthroplasties. The excluded patients corresponded to coding errors ($n = 58$), to arthroplasty less than one year after the OAI ($n = 82$), or arthroplasty after removal of a prosthesis ($n = 52$) (Fig. 1). These were 44 women and 48 men, with an average age of 56.5 ± 19 years (range: 21–97 years). The bone and joint infection responsible for the destruction of the joint occurred at a mean age of 35 ± 23 years (range: 1–84 years). The arthroplasty was performed at a mean age of 50 ± 19 years (range: 15–85 years), with a mean time of 15 ± 16.9 years (range: 1–65 years) between OAI and arthroplasty (Table 1). The bacteria most frequently identified in the initial OAI was *Staphylococcus aureus* (33/92; 35.8%). Nine cases corresponded to osteoarticular tuberculosis. For 31 patients, or 33.7% ($n = 31/92$), we could not find the agent responsible for the initial infection (Table 2). Among these patients, 18 presented with an OAI of a native joint and 13 with osteosynthesis hardware or an open fracture. Twenty-seven preoperative joint aspirations were performed at the discretion of the surgeon.

3. Methods

In our practice, intraoperative sampling is systematic when performing arthroplasties on sequelae of OAI, regardless of the duration between the OAI and the arthroplasty, or the microorganism identified during the initial infection. Therefore, all patients benefited from multiple samples according to the protocol of the Reference Center for Osteoarticular Infections (CRIOAC), Lille-Tourcoing, as well as antibiotic therapy lasting until the final results were obtained, 15 days after the operation. The surgical method, however, was the same whether there was a history of infection or not. In the event of positive samples, the patient was treated with targeted antibiotic therapy for a specified duration.

3.1. Assessment method

The main characteristics of the initial infection and of the arthroplasty, the time between the two events, and the microbiological results of the samples taken during the two events, were collected, as well as the performance of a preoperative joint aspiration, if it had been carried out. We compared the results of the microorganisms identified during the initial OAI, and during the intervention, as well as a possible joint aspiration preceding the arthroplasty ($n = 27$). The microbiological diagnosis was established at the time of the arthroplasty according to the MSIS 2018 and ICM 2013 recommendations [15–17], and after presentation and discussion of the file in a CRIOAC multidisciplinary consultation meeting [18]. In addition, we investigated whether a new episode of OAI had

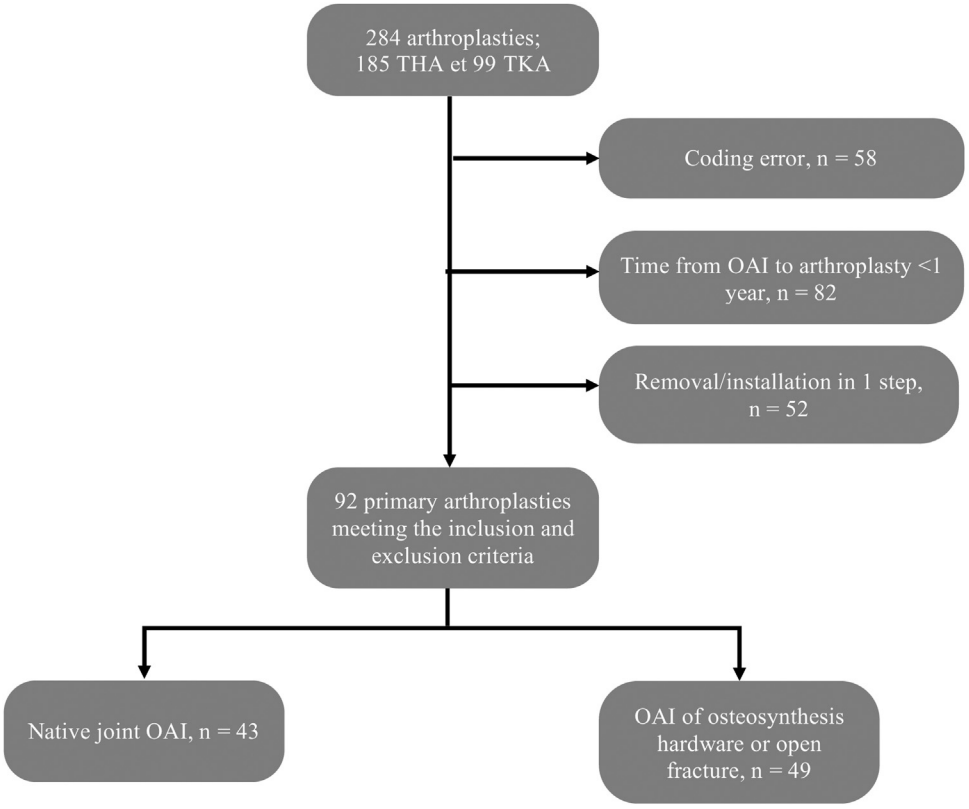

Fig. 1. Patient selection flowchart.

Table 1
Main characteristics according to the initial type of OAI.

	Total population *n* = 92	Native joint group *n* = 43	Osteosynthesis hardware and/or open fracture group *n* = 49
Average age (range)	56.5 (21–97)	56.1 (21–97)	57.02 (28–92)
Average age of arthroplasty (range)	50 (15–85)	49.9 (15–85)	51 (17–84)
Average age of OAI (range)	35 (1–84)	31.7 (1–84)	38 (1–78)
Average time from OAI to arthroplasty (range)	15 (1–65)	18.9 (1–65)	12.9 (1–61)
Number of positive samples	16	6	10

OAI: osteoarticular infection.

Table 2
Bacteria found during the initial OAI.

Bacteria found during the initial OAI	Number (total = 92)	Percentage
Gram + cocci	48	52.2
Staphylococcus aureus	33	35.8
Streptococcus dysgalactiae	4	4.3
Methicillin-resistant *Staphylococcus aureus*	2	2.1
Enterococcus faecalis	2	2.1
Staphylococcus epidermidis	2	2.1
Streptococcus haemolyticus	1	1.1
Streptococcus oralis	1	1.1
Streptococcus agalactiae	1	1.1
Streptococcus corynossus	1	1.1
Staphylococcus warneri	1	1.1
Escherichia coli	2	2.1
Mycobacterium tuberculosis	9	9.7
Pseudomonas aeruginosa	2	2.1
Kingella kingae	1	1.1
Unidentified bacteria or result not available	31	33.6

OAI: osteoarticular infection.

Table 3
Information about positive patients.

	Initial bacteria	Bacteria found	Results if aspiration performed	Time between OAI and arthroplasty	Type of location	Initial OAI Type
Patient 1	NA	*Cutibacterium acnes*	Negative	17 years	THA	NJ
Patient 2	*Staphylococcus aureus*	*Staphyloccocus capitis*	–	1 year	THA	OHOF
Patient 3	*Staphylococcus aureus*	*Staphylococcus aureus*	–	1 year	THA	OHOF
Patient 4	*Staphylococcus aureus*	*Staphylococcus aureus*	–	18 years	THA	NJ
Patient 5	*Mycobacterium tuberculosis*	*Mycobacterium tuberculosis*	Negative	3 years	THA	NJ
Patient 6	*Mycobacterium tuberculosis*	*Cutibacterium acnes*	–	1 year	THA	NJ
Patient 7	*Staphylococcus aureus*	*Staphylococcus aureus*	–	37 years	THA	OHOF
Patient 8	*Staphylococcus aureus*	*Staphylocoque capitis*	Negative	28 years	THA	OHOF
Patient 9	*Streptococcus dysgalactiae*	*Streptococcus dysgalactiae*	–	2 years	THA	OHOF
Patient 10	NA	*Staphylococcus hominis*	–	34 years	THA	NJ
Patient 11	NA	*Staphylococcus epidermidis*	Negative	33 years	TKA	OHOF
Patient 12	*Staphylococcus epidermidis*	*Staphylococcus epidermidis*	–	8 years	TKA	OHOF
Patient 13	*S. aureus* résistant à la méticilline	*S. aureus* résistant à la méticilline	–	4 years	TKA	OHOF
Patient 14	*Staphylococcus capitis*	*Staphylococcus capitis*	Positive	1 year	TKA	NJ
Patient 15	*Staphylococcus aureus*	*Cutibacterium acnes*	Negative	13 years	TKA	OHOF
Patient 16	*Pseudomonas aeruginosa*	*Pseudomonas aeruginosa*	Negative	1 year	TKA	OHOF

OAI: osteoarticular infection; THA: total hip arthroplasty; TKA: total knee arthroplasty; NJ: native joint group; OHOF: osteosynthesis hardware and/or open fracture group; NA: data not available.

Table 4
Patients with OIA following arthroplasty.

	Bacterium: initial OAI	Specimens: 1st intention arthroplasty	Bacterium: 1st intention arthroplasty	Bacteria: washing out of arthroplasty	Time between arthroplasty and the new OAI episode	Type of location	Initial AIO type
Patient A	*Streptococcus dysgalactiae*	Negative	–	*Streptococcus gallolyticus*	4 years	THA	OHOF
Patient B	NA	Negative	–	*Staphylococcus epidermidis*, *Staphylococcus ominis*	2 months	TKA	OHOF
Patient 4 from Table 2	*Staphylococcus aureus*	Positive	*Staphylococcus aureus*	*Staphylococcus aureus*, *Streptococcus agalactiae*	7 months	THA	NJ
Patient D	*Staphylococcus aureus*	Negative	–	*Staphylococcus aureus*	2.5 years	TKA	OHOF

OAI: osteoarticular infection; NA: data not available; NJ: native joint group; OHOF: osteosynthesis hardware and/or open fracture group.

occurred after the time of arthroplasty, at the last available follow-up, regardless of the result of the intraoperative samples.

3.2. Statistical analyzes

The normality of the numerical parameters was verified graphically and by the Shapiro–Wilk test.

The comparison of the sample results, according to the hardware, was carried out by the Chi^2 test, and according to the time between the OAI and the arthroplasty by the Mann–Whitney test. All data including missing data, were analyzed with the assumption of maximum bias. The significance threshold used was set at 5%. The statistical analysis was performed using SAS software, version 9.4 (SAS Institute, Cary, NC, USA) by the Biostatistics Unit of the Lille University Hospital.

4. Results

4.1. Persistence of the initial microorganism

The operative samples taken during the arthroplasty came back positive in 17% of cases ($n = 16/93$). Among the positives, 9 corresponded to the same bacteria as that of the initial OAI, i.e. 56% ($n = 9/16$) of the patients, for 3 patients we had no information on the microorganism of the initial infection and in 4 cases, the microorganisms were different (Table 3). For the 92 patients, the mean follow-up time from the initial arthroplasty was 4.35 years (1 to 16 years), and among these, 4 had had an infection of the arthroplasty at the mean follow-up of 21.7 months (range: 2 months–48 months), of which only 1 had been positive during the intraoperative sampling and two patients were positive for the same microorganisms as that of the initial OAI (Table 4).

4.2. Association between positive samples and time between OAI and arthroplasty

The time between the OAI and arthroplasty was 1 year for 5 patients, between 1 and 15 years for 5 patients and greater than 15 years for 6 patients. The time between the initial infection and arthroplasty was not statistically associated with the positivity of intraoperative samples during arthroplasty ($p = 0.38$) (Table 5). Among the 9 patients positive for bacteria identical to that of the initial OAI, the mean interval between OAI and arthroplasty was 12 years (range: 1–37 years).

4.3. Association between positive samples and OAI of a native joint or hardware

Among these 92 patients, 43 had had an OAI of a native joint, i.e. 46.7% ($n = 43/92$) while 49 patients presented with an OAI of osteosynthesis hardware or of an open fracture, i.e. 53.3% ($n = 49/92$). There was no significant difference between a positive culture during arthroplasty and the type of initial OAI [native joint versus presence of hardware and/or open fracture, (X^2 [1,

Table 5
Association between positive samples and time between OAI and arthroplasty.

	Time between OAI and arthroplasty				
	1 year	> 1 to 15 years	> 15 years	Total	
Results of intraoperative samples					
+	5 (21%)	5 (18%)	6 (15%)	16 (17%)	
–	19 (79%)	23 (82%)	34 (85%)	76 (83%)	
Total	24	28	40	92	$p = 0.38$

OAI: osteoarticular infection.

Table 6
Association between positive samples and OAI of a native joint or on material.

	OAI of a native joint	OAI on osteosynthesis hardware and/or open fracture	Total	
Sampling results peroperative				
+	6 (14%)	10 (20%)	16 (17%)	
–	37 (86%)	39 (80%)	76 (83%)	
Total	43	49	92	$p = 0.41$

OAI: osteoarticular infection.

$n = 92$] = 0.66 $p = 0.41$) (Table 6)]. Only one of the 27 joint aspirations performed before arthroplasty was positive (*Staphylococcus capitis* corresponding to the microorganism found during the arthroplasty).

5. Discussion

In our series, the bacteriological samples were positive in 17.4% ($n = 16/92$) of the cases at the time of the arthroplasty performed following osteoarthritis or osteomyelitis. Nine (9.8%) of the patients in the study had the same bacteria as the OAI on the samples taken during the arthroplasty, which was performed, on average, 12 years after the initial OAI. There was no significant difference between the frequency of positive intraoperative samples and the time between OAI and arthroplasty. Finally, there was no difference in the positivity of the samples between patients with OAI of the native joint and OAI of the osteosynthesis hardware or open fracture.

In a 1991 study, analyzing 44 patients who underwent hip arthroplasty after bacterial OAI in childhood, Kim et al. [12] observed no recurrence of infection in patients with an interval between OAI and arthroplasty ranging from 11 to 40 years with a mean of 19.9 years. This study was only interested in OAIs of native hip joints, occurring in childhood, and with an interval of at least 10 years between the two events. In our study, the minimum time between the OAI and the arthroplasty, for the patient to be considered cured, was 1 year. This period is significantly less than those found in the literature which recommend much longer time before implantation. Other studies showed a zero rate of reinfection in patients who had a hip OAI in childhood, such as Luo et al. [19], who did not identify any recurrence of infection in 101 patients who had undergone hip arthroplasty after OAI of a native joint with a mean interval of 24 years (range: 11–43 years) and a mean follow-up of 6.1 years after surgery. The same results were found by Kim et al. [14], in a study of 170 hip arthroplasties secondary to OAI in childhood, with only one recurrence of infection reported in a patient with a 7-year interval between the OAI and arthroplasty. A systematic review of the literature published in 2020 [20] concerning 12 publications about arthroplasties on sequelae of OAI of native hip joints, concluded that an average rate of reinfection was low at 0.9% (range: 0–2.6) after an average follow-up period of 8.2 years, but slightly longer than that reported in the context of conventional primary arthroplasty [21]. However, Bauer et al. [22] observed 7/23 (30.4%) positive intraoperative samples during hip or knee arthroplasty on presumed cured OAIs, after an average of 5 years. These results included arthroplasties after OAI knee sequelae, for which the literature found higher reinfection rates [9,23,24]. Thus, Seo et al. [9] identified a positive sample rate of 9.7% for TKA with a history of infection, demonstrating a result closer to our study.

The study by Sultan et al. [24], of 62 patients who required hip or knee arthroplasty with a history of a native joint OAI, and a follow-up of 4.4 years, showed an increased risk of having a periprosthetic infection, at 8% ($n = 5/62$). They therefore concluded that patients with a history of native joint infection were at greater risk of periprosthetic infections, particularly smokers, and should benefit from special monitoring. The results provided by our study are consistent with the idea that patients with a history of OAI are more at risk of bacterial reinfection than patients having had a conventional primary arthroplasty, with a positive rate of our samples much higher than that of the literature.

In our study, more than half of the patients had a history of OAI of osteosynthesis hardware. These patients were not considered in the studies available in the literature, but many of them benefited from several surgeries that posed an infection risk, especially if trauma with an open fracture was involved, for example. This may explain the higher proportion of positive samples, although no significant relationship was found between the rate of positive patients according to the type of prior infection. In addition, amongst the patients in this study, samples were taken systematically during the operation. It is possible that the use of standardized criteria available in the literature [15,16] defining the positive cases, overestimates the positivity rate of samples compared to studies which define positive cases based on the clinical and paraclinical expression of the infection, from patient follow-up. The number of positive samples from a microorganism different to the initial one was low ($n = 4$) and could be explained by an unknown initial infectious agent, or by contamination during implantation. We use the MSIS criteria, so at least 2 positive samples are needed, which reduces contamination, but due to low numbers, do not allow reliable conclusions to be made.

One of the strengths of this study is the systematic nature of bacteriological sampling for this indication, regardless of the time interval between OAI and arthroplasty. In fact, all patients with a history of OAI who underwent arthroplasty in our unit, benefited from intraoperative bacteriological sampling. In addition, no other study in the literature considers all patients who had an OAI cured before an arthroplasty. In our study, we considered both the history of hip and knee native joint OAI but also OAI of osteosynthesis hardware and osteomyelitis which may explain the important

difference between our results and those of literature. The data in the literature does not establish a time, between the initial OAI and the arthroplasty, beyond which the resurgence of an infection can be excluded. The negativity of the preoperative joint aspiration does not present sufficient sensitivity in this study to exclude this hypothesis. We therefore propose that sampling should remain systematic in this context, applying the guidelines for septic arthroplasty revisions, particularly for postoperative antibiotic therapy while awaiting results and as per the sensitivity profile of the microorganisms of the initial infection, when these data are available [18].

This study has several limitations:

- the large number of patients whose initial bacteria were not found ($n = 31/92$) which may have led us to keep patients who potentially had non-bacterial arthritis. In these cases, the diagnosis was based on a set of precise clinical arguments reported by the patient, or the practitioner who provided the initial care, and after a detailed analysis of their medical file (operating report, history of fistula, consultation letters indicating an infection without specifying the germs found or the antibiogram);
- the heterogeneity of our patients within an average sample size that could lead to confusion or comparison bias. Indeed, the inclusion of all patients, regardless of OAI results, confers a heterogeneous population despite only 92 patients. However, the two groups were well balanced since there were 43 native joint OAIs versus 49 OAIs of osteosynthesis hardware or open fracture. In addition, uniform management reduced the risk of measurement bias;
- statistical analyzes carried out could not find significant results due to a lack of power from the low number of positive results ($n = 16/92$), particularly for the analysis between the time between the OAI and arthroplasty, and the positivity of the samples;
- finally our results do not allow our conclusions to be generalized to subgroups such as arthroplasties for sequelae of simple hip or knee OAIs occurring in childhood because our numbers are not large enough.

6. Conclusion

The results of this work suggest that primary arthroplasties performed at a formerly infected site should be performed routinely as septic revisions, regardless of the length of time between the arthroplasty and the initial infection.

Disclosure of interest

Henri Migaud is editor-in-chief *Orthopedics & Traumatology: Surgery & Research* related to this study, and outside of this work declares to be an educational consultant for Zimmer-Biomet, Corin-Tornier, SERF and MSD. Sophie Putman declares that, outside of this work, she is an educational and research consultant for Tornier-Corin. Eric Senneville does not declare any conflicts in relation to this work but outside this work, he is a consultant for MSA ZImmer-Biomet and Diaxonhit. The other authors declare that they have no competing interest.

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Authors' contribution

Nicolas Mainard: conception, writing, editing.

Eric Senneville: conception, writing, editing, responsible for CRIOAC G4.

Marie Titecat and Caroline Loiez: microbiological data management, editing.

Sophie Putman, Pierre Martinot, Julien Dartus: surgery, editing.

Hervé Dezeque: editing.

Marc Saab: writing, editing.

Henri Migaud: surgery, design, writing, editing.

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