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Outcome of short versus long interval in two-stage exchange for periprosthetic joint infection: a prospective cohort study

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Abstract

Introduction A two-stage exchange is the standard treatment approach for chronic periprosthetic joint infection (PJI). While a 6–8 week interval is commonly used before reimplantation, the optimal length of the prosthesis-free interval has not yet been determined. We evaluated the influence of a short (< 4 weeks) and long (≥ 4 weeks) interval on reinfection rate and functional outcome of hip and knee PJI.

Methods In this prospective cohort, patients undergoing two-stage revision for PJI were assigned to prosthesis reimplantation after a short (< 4 weeks) or long (≥ 4 weeks) interval. All patients received standardized antimicrobial therapy, which consisted of antibiogram-adapted, non-biofilm-active antibiotics during the interval and an antimicrobial combination therapy with biofilm-active antibiotics after reimplantation. Follow-up was performed for infection, joint function, pain, need for care and quality of life.

Results Thirty-eight patients undergoing two-stage revision for PJI (18 hips and 20 knees) were included. Short interval was used in 19 patients having a mean interval of 17.9 days (range 7–27 days), long interval in 19 patients having a mean interval of 63.0 days (range 28–204 days). At a mean follow-up of 39.5 months (range 32–48 months), 37 of 38 patients (97.4%) were infection-free. One failure occurred among patients with long interval and none among patients with short interval. Functional results (ROM, HHS, KSS, VAS) and quality of life (SF-36) were similar in both groups. Patients treated with long interval required cumulatively additional 204 inpatient days for nursing care compared to patients with short interval.

Conclusions This study suggests that two-stage exchange with short interval has a similar outcome than with long interval, when highly active antibiotic therapy is used. Patient inconvenience and care costs due to immobilization were lower when strategies with a short interval were used.

Keywords Periprosthetic joint infection · Two-stage revision · Interval length · Hip arthroplasty · Knee arthroplasty · Infection management

Introduction

With an increasingly aged population, the number of arthroplasties is expected to further rise in industrialized nations, accompanied by a growing number of periprosthetic joint infections (PJI) [6, 22]. Improved diagnostic methods and standardized definition criteria cause further increase in the infection rates [27, 30]. Two-stage prosthesis exchange is currently the most commonly used surgical procedure for PJI. The reimplantation of the prosthesis is typically performed after an interval of 6–8 weeks [5, 11, 23]. However, the optimal length of the prosthesis-free interval remains unknown and has not been systematically compared. We hypothesized that the prosthesis-free interval may be

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shortened with a bactericidal and biofilm-active antibiotic treatment, resulting in faster mobilization and potentially better outcome.

In a prospective study, we compared the treatment outcome using a short (< 4 weeks) versus long (≥ 4 weeks) prosthesis-free interval in patients with PJI, in whom a two-stage prosthesis exchange was performed. The short and long strategy was applied in two consecutive periods, during which the antimicrobial treatment was standardized and followed a predetermined PJI management algorithm [32]. Beside the infection outcome (cure rate), also the functional results and nursing care burden were evaluated.

Patients and methods

Study population and design

We prospectively included consecutive patients with PJI undergoing two-stage prosthesis exchange from January through December 2013 at our institution. The study was conducted in a large tertiary healthcare center, providing advanced specialty care to a population of about four million inhabitants. The institutional ethics committee reviewed and approved the study protocol (EA1/028). Informed consent was obtained from all individual participants included in the study. All procedures during the study were in accordance with the ethical standards and with the Helsinki Declaration of 1975, revised in 2000.

Study design

Patients were not randomized but consecutively included in two periods with different treatment strategies. In the first period, the prosthesis was reimplanted after a long interval of ≥ 4 weeks, whereas in the second period, the prosthesis was reimplanted after a short interval of < 4 weeks. Patients with acute PJI (i.e. early postoperative infection occurring < 1 month after implantation or haematogenous infections with < 3 weeks of symptom duration) were excluded, as they would have been treated with debridement, exchange of mobile parts and retention of the prosthesis. Patients with critical soft tissue conditions or isolation of difficult-to-treat microorganisms [2] were also excluded.

Definitions

For definition of PJI, the proposesd European Bone and Joint Infection Society (EBJIS) as working definition criteria were used [32]. According to these criteria, PJI was diagnosed when at least one of the following criteria was present: (i) macroscopic purulence around the prosthesis, (ii) presence of sinus tract, (iii) increased synovial fluid leukocyte count (> 2000 leukocytes/µl or > 70% granulocytes), (iv) significant microbial growth in synovial fluid, periprosthetic tissue or sonication culture, (v) positive histopathology, corresponding to type 2 or type 3 periprosthetic membrane [15]. Periprosthetic tissue culture was considered positive if (i) ≥ 1 specimen was positive in highly virulent organisms (such as *S. aureus*, Enterobacteriaceae, streptococci, *Candida* spp.) or (ii) ≥ 2 specimen showed microbial growth of a low-virulent pathogen (coagulase-negative staphylococci, *Cutibacterium* (formerly *Propionibacterium*) spp. and other bacteria of the normal skin microbioma). Sonication was considered positive if > 50 colony-forming units (CFU)/ml sonication fluid grew [25].

Difficult-to-treat microorganisms are organisms, for which no biofilm-active antibiotics exist, including rifampin-resistant staphylococci, quinolone-resistant gram-negative rods, enterococci and fungi [31].

Surgical and antimicrobial therapy

All patients underwent complete removal of the prosthesis and debridement by three orthopaedic surgeons experienced in septic surgery, followed by antimicrobial therapy for a minimum of 12 weeks. Antibiotic therapy was not discontinued before prosthesis reimplantation and no diagnostic joint aspiration was performed. Patients treated with a short interval remained inpatients until reimplantation, whereas patients treated with long interval were transferred home or in rehabilitation or geriatric unit for the 4–6 weeks. The reimplantation was not performed, if the postoperative wound was continuously draining or the C-reactive protein values were not continuously decreasing. In this case, an additional revision was performed.

Explantation technique: explantations were performed following a standardized procedure for each patient. In THA patients either a transgluteal or posterior approach was used depending on previously used approaches or the on the use of a transfemoral approach. In TKA patients the medial parapatellar approach was used. After removal of a cemented implant, special care was taken to remove residual bone cement from the interface. If this could not be achieved endomedullary, cement residuals were removed either via a bony window or a transfemoral approach in THA patients. Cementless implants were either removed endomedullary or using a transfemoral approach in THA patients with long porous coated stems. Osteotomies were closed with cerclages. After removal of implants/cement, a thorough debridement was performed including endomedullary curettage with the removal of all infected membranes and sequestra followed by a complete synovectomy of the joint. If cartilage residues were present at the patella in knee patients, these were removed. In all patients, irrigation was performed with saline using pulse lavage.

In THA patients the situs was closed with adaptation of the muscles, the iliotibial tract, subcutis and cutis, leaving a resection arthroplasty. In TKA patients all patients received a static spacer as described in the next paragraph followed by suturing capsule, subcutis and cutis. Drains were used in all patients.

Antimicrobial therapy All patients received antibiotics only after the microbiological specimens had been harvested during explantation. All patients initially received broad spectrum antimicrobial treatment for the first 7–10 days, the standard regimen being vancomycin or daptomycin combined with ampicillin/sulbactam. In cases where an organism had been identified previously, which would not have been covered by this regimen, the antibiotics were adapted. After 7–10 days, the antibiotics regimen was narrowed according to the microbiological findings up to that time if possible. Patients received intravenous antibiotics during 2 weeks after explantation and for 1–2 weeks after reimplantation. After discharge, oral antibiotics were given. Rifampin and ciprofloxacin were never given during the interval, but were only started when the wound was dry after reimplantation. SI patients received a 12-week course of antibiotics after explantation. LI patients received antibiotics from explantation until a minimum of 6 weeks after reimplantation, for in total, a minimum of 12 weeks. The patient with the long interval of 204 days was discontinued of antibiotics 10 weeks after reimplantation and received the standard 6 weeks therapy after reimplantation.

Joint status during interval

Either resection arthroplasty (for THA) or implantation of a static spacer (for TKA) was performed. Static spacers consisted of bone cement containing 0.5 g gentamicin/ 40 g PMMA (Palacos R + G, Heraeus Medical, Wehrheim, Germany) to which 2 g vancomycin/ 40 g PMMA were added. Bone cement was centrally augmented with intramedullary steel pins or rods.

All perioperative complications and detected microorganisms were recorded. Patients were followed for reinfection, need for care during the interval and functional outcome. In both, THA and TKA patients, mobilization after implant removal was performed with partial weight bearing as soon as the patient was physically able to walk (with aids). Upon reimplantation, patients were mobilised with a full weight bearing.

Statistical analysis

Statistical analysis was performed using IBM SPSS Statistics 25 (IBM Corp., Armonk, USA). The descriptive statistics is noted in numbers (percentage) or mean (range) as appropriate. The Mann–Whitney-*U* test was used where the data was non-parametric and the *t* test for parametric data. Statistical significance was assumed for all p values < 0.05.

Results

Demographic data

Thirty-eight patients undergoing two-stage revision for PJI (18 hips and 20 knees) were included. Patient demographics are summarized in Table 1. Patients were equally distributed concerning age, American Society of Anesthesiologists Physical Status Classification System (ASA), and microbial spectrum. The latter reflected the common distribution of bacteria among PJI patients [20]. Patients treated with long interval had a higher number of previous revisions, but an identical number of revisions due to PJI, and had a lower preoperative Harris Hip Score ($p = 0.008$) in patients with hip PJI.

Perioperative and follow-up evaluation (Table 2)

The mean interval between implant removal and reimplantation was 63 days (range 28–204 days) in patients with long interval and 17.9 days (range 7–27 days) in patients with short interval. One patient in the LI group had an interval of 204 days, because he delayed the reimplantation due to personal reasons until that time. Excluding this patient, the range of the interval in the LI was 28–89. All patients in the LI group were dependent on additional care during the prosthesis-free interval. Among patients who were discharged home to family members or acquaintances, a nursing institution was involved in 2 cases. Eight patients were transferred to a geriatric ward, where they spent a total of 204 inpatient days.

Infection treatment failure

One patient in the long-interval group suffered from a persistent infection and underwent a second two-stage exchange, whereas in the short-interval group no treatment failure had occurred until the last follow-up evaluation. The duration of hospital stay was identical in the short- and long-interval groups. This was because the same antibiotic regimen was applied in both groups, which consisted of an initial intravenous therapy after ex- and reimplantation. Patients of the long-interval group were switched to oral therapy after discharge until reimplantation. All patients were treated orally from 1 week after reimplantation.

Table 1 Patient characteristics

	Short-interval group (SI)	Long-interval group (LI)
Age (years)	66.8 (37–76)	69.9 (40–88)
ASA[a]	2.3 (2–3)	2.5 (1–3)
BMI[b] (kg/m²)	31.5 (23.5–45.4)	29.9 (19.8–50.6)
Sex		
Male	9	5
Female	10	14
Joint (Hips/Knees)	10/9	10/9
Patient history		
Previous exchange surgeries (Hips/Knees)	7/4	10/6
Previous septic exchanges (Hips/Knees)	1/4	1/4
Diabetes mellitus (total)	4	6
Immunsuppression	0	0
Malignancies in patient history	2	1
Rheumatoid Arthritis	1	2
Time implantation to explantation (years)	4.2 (0.4–14.4)	5.7 (0.5–18.4)
Microbial spectrum		
Coagulase-negative staphylococci	17	16
Staphylococcus aureus	2	3
Propionibacterium acnes	2	2
E. coli	0	1
Streptococci	0	2
Others	1	5
Culture-negative	5	1

Values given as mean and range

[a]American Society of Anesthesiologists physical status classification system

[b]Body mass index given as kg per m^2 body surface

Table 2 Perioperative and follow-up parameters

	Short-interval group (SI)	Long-interval group (LI)
Inpatient parameters[a]		
Interval explantation to implantation (days)	17.9 (7–27)	63.0 (28–204)
Hospital stay (days)	28.0 (21–45)	26.0 (20–57)
Intensive care unit stay (days) (explantation)	0.5 (0–1)	0.5 (0–2)
Follow-up at > 32 months		
Decayed	1	1
Stay in geriatric ward (days)	0	204
Relapse of PJI	0	1
Revision due to infection	1	3
Revision due to aseptic cause	1	2

[a]Values given as mean and range

Functional outcome and quality of life

Analysis of the patients' joint function and pain scores at the time of discharge and during long-term follow-up revealed no statistically significant differences between the short- and long-interval groups. All groups showed an improvement in range of motion, Knee Society or Harris Hip Score (Fig. 1) and VAS pain (Fig. 2) after two-stage exchange. Noticeable was the high standard deviation, which reflects the typical broad functional spectrum of PJI patients despite successful therapy of infection. This could also be observed looking at quality of life with the SF-36 questionnaire as depicted in Fig. 3. All patients showed a good improvement of both, the mental and physical health components of the SF-36. Long and short interval did not differ after short- and long-term follow-up.

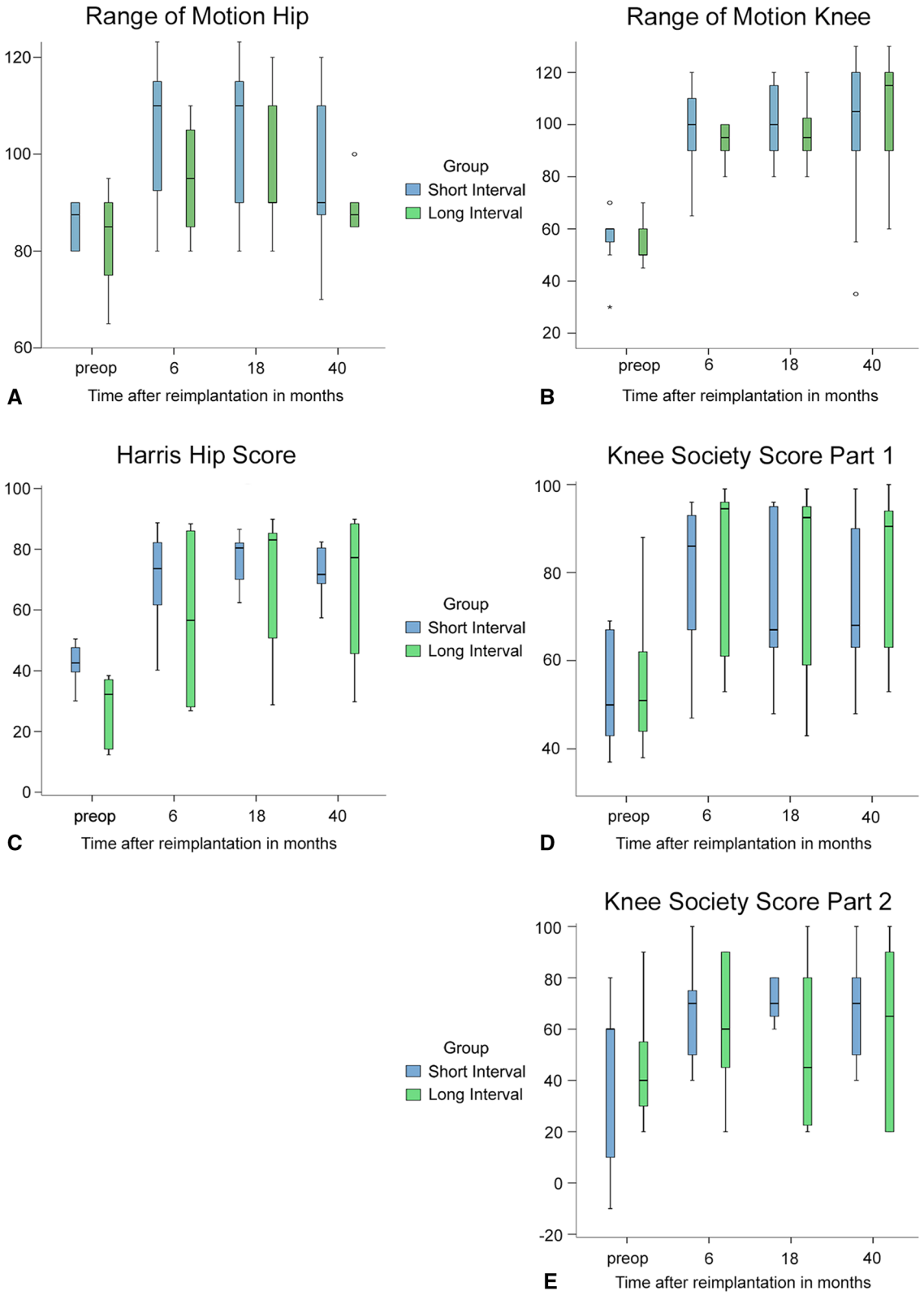

Fig. 1 No difference in function after long- and short-interval two-stage exchange. Improvement of Harris Hip Score (HHS) in hip patients (**a**) and Knee Society Score (KSS) part 1 (**b**) and part 2 (**c**) in knee patients

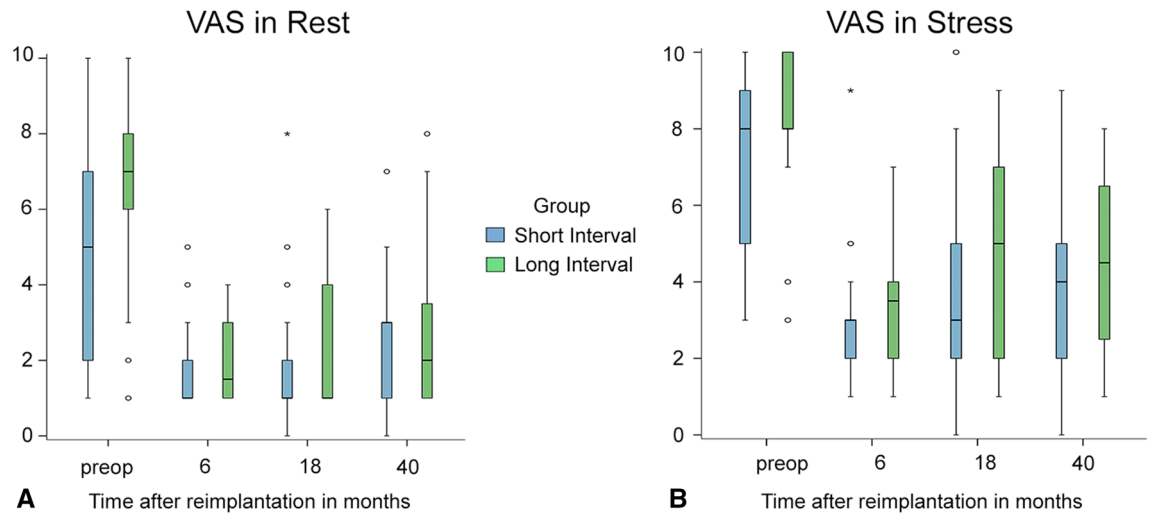

Fig. 2 No difference in pain after two-stage reimplantation between long- and short-interval groups. **a** Pain in physical rest and **b** pain in physical stress. Visual analogue scale: 0 = no pain, 10 = worst pain imaginable

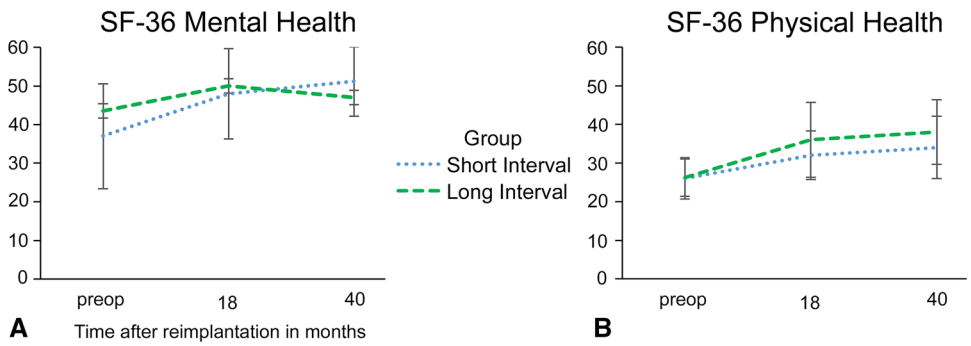

Fig. 3 No difference in quality of life after two-stage reimplantation between long- and short-interval groups. SF-36 Mental Component Summary (**a**) and Physical Component Summary (**b**)

Complications

Long-interval group An 86-year-old female, who underwent a two-stage TKA exchange with an interval of 41 days, died 3 months after reimplantation at home. An autopsy was not performed as the family declined. A 75-year-old female, who underwent THA reimplantation after 63 days, experienced a stroke during her hospital stay. At the time of last contact, she had fully recovered from her stroke. The prosthesis showed no signs or symptoms of infection. A 72 year-old female suffered from a reinfection of her streptococcal PJI of the knee at 5 months after reimplantation. This patient had been revised due to persistent secretion with debridement, irrigation and change of mobile parts 10 days after reimplantation. The patient underwent a second 2-stage prosthesis exchange and was without reinfection at the latest follow-up. Three patients of the LI group (16%) were revised for aseptic causes: TKA dislocation due to a rupture of the medial capsule and a symptomatic haematoma in the same patient, a quadriceps tendon rupture and an incomplete removal of a drainage tube. One TKA patient from the same group received an exchange of the spacer and a second debridement due to suspicion of a persistent infection (although the microbiological results were negative).

Short-interval group a 67-year-old male patient receiving a high dose of anticoagulation due to a coronary stent developed a subcutaneous haematoma, which had to be revised by local evacuation. This patient died due to an intracerebral bleeding 9 months after reimplantation. A 75-year-old female patient with a Steinmann-pin augmented static spacer of the knee suffered from an anterior femoral outbreak of the pin after mobilization, which was addressed at the time of reimplantation without previous revision. One 66-year-old patient suffered a knee PJI 8 months after reimplantation. In this patient, initially a low-virulent organism (Staphylococcus epidermidis) was isolated, whereas later, a highly virulent Staphylococcus aureus grew. Therefore, this PJI is categorized as a new haematogeneous infection rather than persistent or relapsing infection. In addition, the patient underwent dental treatment 4 weeks before PJI symptoms manifested. Debridement, irrigation and PE liner-exchange

was performed and the patient remained infection-free during a consecutive follow-up time of 36 months.

In each group, positive microbiology results (all coagulase-negative staphylococci) were obtained in 1 TKA and 3 THA patients (21% of each group) at the time of reimplantation. This was the original bacterium in seven of these patients one patient was initially diagnosed with a *Staphylococcus aureus* PJI.

Discussion

This study suggests that using highly active biofilm-active antibiotic treatment is associated with similar treatment outcome using a short interval in two-stage septic revision surgery. Furthermore, these findings demonstrate that the inconvenience and care costs associated with immobilization can be reduced by the implementation of a SI approach.

The levels of infection control reported here were equal to or superior to those available in the literature [4, 9, 16, 17, 24]. Antibiotics with activity against biofilms are able to target bacteria within non-sterile settings, such as encountered during one-stage revision procedures. Early reimplantation (e.g. 2–3 weeks after implant removal) provides several advantages in the treatment of PJI, including faster mobilization, treatment of patients within a single hospital stay and better soft tissue conditions in terms of contraction and surgical dissection. In addition, the few reported cure rates from single institutions seem to be equal compared with the traditional concept [7, 10].

Hsieh et al. retrospectively compared patients treated with short and long antibiotic regimens after THA removal. Both patient groups were implanted with a spacer and reimplanted after an interval of 3 months [13]. In our study, all patients received a minimum of 12 weeks of antimicrobial treatment. As we did not use biofilm-active antibiotics (e.g. rifampin or ciprofloxacin) during the interval (to prevent the development of resistance against these critical substances), patients in the SI group received these antibiotics for a longer time than LI patients, representing a possible bias in our study. However, this can also be interpreted as a further advantage of the SI approach.

With SI, an antibiotic-free period and joint aspiration before reimplantation are not possible. However, we did discontinue antibiotics in none of our patients, including LI patients, as there is no evidence supporting this practice [11, 14, 26, 28].

Moreover, it is possible that a reimplantation after 6 weeks, with 2 weeks of antibiotic treatment plus a 4-week holiday period, would concur with a time of bacterial growth in cases of bacterial persistence, such as was detected in 21% of our patients (both in the SI and LI groups). The detection of bacteria also after the long interval challenges the concept behind the use of the LI approach (i.e. to cure the infection before reimplantation) and favours the application of the SI approach, in which a positive microbiology at the time of reimplantation is accepted [1].

Difficult soft tissue conditions due to scarring and contraction are frequently encountered in patients with hip resection arthroplasties or static knee spacers after a long interval, which can result in the necessity of extensive soft tissue release to enable joint exposition and implantation of the new components. This is typically not the case in SI patients, in which scarring and contraction still remain at low levels.

The primary treatment aim in septic revision arthroplasty is to achieve good joint function with a low level of pain and a good quality of life. In our cohort, these criteria were met in most patients, with a decrease of VAS pain over time in both hip and knee patients, as well as improvements in HHS and KSS up to the latest follow-up. SF-36 scores also displayed an increase 18 months after surgery, but stayed at these levels between short and long-term follow-up. High standard deviations in all functional parameters reflected the typical pattern of patients treated with two-stage revisions for PJI. Despite a successful eradication of the infection and an improvement of joint function, pain and quality of life, the patient cohort remains inhomogeneous and many of these patients lack a good functional outcome. Our data indicate a larger variation of functional outcomes after long interval revision compared to the SI group despite similar preoperative values. Nevertheless, this analysis has to be confirmed in larger cohorts.

The problems of a long prosthesis-free interval are evident and are mainly caused by the impaired mobilization of the patients. Disadvantages of the LI approach include a high demand for additional care without full weight bearing ability and impairment of daily activities (e.g. stair climbing and entering a car). In our cohort, all patients were dependent on additional help in the prosthesis-free interval. In the LI group, this help was often provided by friends and family members after discharge, although a nursing service was used in 2/19 cases and 8/19 patients needed to be transferred to a geriatric ward for the period of the interval, resulting in an additional 204 inpatient days compared to the SI group.

Full mobility is the state of lowest morbidity for patients and, therefore, should be the aim of all orthopaedic procedures. High mortality rates have been reported in patients undergoing two-stage exchange with long intervals. Berend et al. reported a 4% mortality between stages and a 7% mortality within 90 days of reimplantation [3]. Toulson et al. reported a mortality rate of 25.7% within 2 years in their patients undergoing two-stage THA exchange [29]. Here, we report the death of 1 LI group patient 3 months and of 1 SI group patient 9 months after reimplantation. Although our data is not sufficient to suggest reduced mortality with

a shortening of the interval during two-stage exchange, we propose that a reduction in the period of limited mobility is highly likely to reduce the rate of classical complications associated with immobility, such as pneumonia, decubitus and deep venous thrombosis related events. Such complications are often observed in patients undergoing long interval procedures. Although we mostly avoided such complication within our patients, one patient did suffer from cerebral infarction during the LI period.

This study has several limitations. First, the patient groups were small with 19 SI and 19 LI patients. However, to our knowledge this is the largest cohort to date analysed for the outcome of a short interval in two-stage revision and the only study, where both approaches have been compared. Second, randomisation was not performed, which could bias our results. We tried to reduce this bias by including the patients in two consecutive blocks. Nevertheless, our results should be confirmed in a randomized study, which analyses the use of a short and a long interval in septic revision arthroplasty in a larger number of patients.

Third, three different surgeons did the exchange procedures, thereby introducing interindividual differences in surgical handling as a possible bias. However, at our institution, we adhere to standardized regimens also for surgical treatment of PJI. The respective protocols, according to which patients were surgically treated have been described in the methods section.

Fourth, the use of spacers in the THA patients could have ameliorated mobilization, however, due to problems that have been reported with spacer implantation, such as the risk of periimplant fracture, dislocation, acetabular erosion, bacterial colonization of the spacer, and the risk of emergence of resistance, we decided against spacer use in our patient collective [8, 12, 18].

Currently, one of the major obstacles of short interval exchange surgery in Germany is the fact that if a patient receives ex- and reimplantation within one hospital stay or even if readmission for reimplantation takes place within 30 days of discharge after the first stay, this is reimbursed as one case, creating a significant deficit. This pushes surgeons in to the usage of long intervals because these can be coordinated in a way that two cases can be reimbursed. With the growing knowledge and more successful treatment of PJI with modern approaches, it can be expected that these irregularities will be corrected in the near future [19, 21].

In conclusion, our study indicates that an SI could be as effective in controlling infection as the LI approach during two-stage exchange for PJI. A shortening of the prosthesis-free time reduces immobility and allows swifter remobilization with a functional joint.

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Compliance with ethical standards

Conflict of interest All authors declare that they have no conflict of interests.

References

1. Akgun D, Muller M, Perka C, Winkler T (2017) A positive bacterial culture during re-implantation is associated with a poor outcome in two-stage exchange arthroplasty for deep infection. Bone Jt J 99-B(11):1490–1495
2. Akgun D, Perka C, Trampuz A, Renz N (2018) Outcome of hip and knee periprosthetic joint infections caused by pathogens resistant to biofilm-active antibiotics: results from a prospective cohort study. Arch Orthop Trauma Surg 138: 635–642
3. Berend KR, Lombardi AV Jr, Morris MJ, Bergeson AG, Adams JB, Sneller MA (2013) Two-stage treatment of hip periprosthetic joint infection is associated with a high rate of infection control but high mortality. Clin Orthop Relat Res 471(2):510–518
4. Born P, Ilchmann T, Zimmerli W et al (2016) Eradication of infection, survival, and radiological results of uncemented revision stems in infected total hip arthroplasties. Acta orthopaedica 87(6):637–643
5. Burnett RS, Kelly MA, Hanssen AD, Barrack RL (2007) Technique and timing of two-stage exchange for infection in TKA. Clin Orthop Relat Res 464:164–178
6. Hall MJ, DeFrances CJ, Williams SN, Golosinskiy A, Schwartzman A (2010) Centers for Disease Control and Prevention/ National Center for Health Statistics National hospital discharge survey: Summary 2007. National Health Statistic Reports 26 Oct 2010, no 29, pp 1–21
7. De Man FH, Sendi P, Zimmerli W, Maurer TB, Ochsner PE, Ilchmann T (2011) Infectiological, functional, and radiographic outcome after revision for prosthetic hip infection according to a strict algorithm. Acta Orthop 82(1):27–34
8. Duncan CP, Masri BA (1995) The role of antibiotic-loaded cement in the treatment of an infection after a hip replacement. Instr Course Lect 44:305–313
9. Engesaeter LB, Dale H, Schrama JC, Hallan G, Lie SA (2011) Surgical procedures in the treatment of 784 infected THAs reported to the Norwegian Arthroplasty Register. Acta Orthop 82(5):530–537
10. Erhart J, Jaklitsch K, Schurz M, Vecsei V, Ehall R (2010) Cementless two-staged total hip arthroplasty with a short term interval period for chronic deep periprosthetic infection. Technique and long-term results. Wien Klin Wochenschr 122(9–10):303–310
11. Hoell S, Moeller A, Gosheger G, Hardes J, Dieckmann R, Schulz D (2016) Two-stage revision arthroplasty for periprosthetic joint infections: What is the value of cultures and white cell count in synovial fluid and CRP in serum before second stage reimplantation? Arch Orthop Trauma Surg 136(4):447–452
12. Hope PG, Kristinsson KG, Norman P, Elson RA (1989) Deep infection of cemented total hip arthroplasties caused by coagulase-negative staphylococci. J Bone Jt Surg Br Vol 71(5):851–855
13. Hsieh PH, Huang KC, Lee PC, Lee MS (2009) Two-stage revision of infected hip arthroplasty using an antibiotic-loaded spacer: retrospective comparison between short-term and prolonged antibiotic therapy. J Antimicrob Chemother 64(2):392–397

14. Janz V, Bartek B, Wassilew GI, Stuhlert M, Perka CF, Winkler T (2015) Validation of synovial aspiration in girdlestone hips for detection of infection persistence in patients undergoing 2-stage revision total hip arthroplasty. J Arthroplast 31: 684–687
15. Krenn V, Morawietz L, Perino G et al (2014) Revised histopathological consensus classification of joint implant related pathology. Pathol Res Pract 210(12):779–786
16. Kunutsor SK, Whitehouse MR, Blom AW, Beswick AD, Team I (2015) Re-infection outcomes following one- and two-stage surgical revision of infected hip prosthesis: a systematic review and meta-analysis. PloS ONE 10(9):e0139166
17. Kunutsor SK, Whitehouse MR, Lenguerrand E, Blom AW, Beswick AD, Team I (2016) Re-infection outcomes following one- and two-stage surgical revision of infected knee prosthesis: a systematic review and meta-analysis. PloS One 11(3):e0151537
18. Lautenschlager EP, Jacobs JJ, Marshall GW, Meyer PR Jr (1976) Mechanical properties of bone cements containing large doses of antibiotic powders. J Biomed Mater Res 10(6):929–938
19. Lieb E, Hanstein T, Schuerings M, Trampuz A, Perka C (2015) Reduction of treatment duration in periprosthetic infection with a fast-track concept is economically not feasible. Z Orthop Unfall 153(6):618–623
20. Lutro O, Langvatn H, Dale H et al (2014) Increasing resistance of coagulase-negative staphylococci in total hip arthroplasty infections: 278 THA-revisions due to infection reported to the Norwegian arthroplasty register from 1993 to 2007. Adv Orthop 2014:580359
21. Muller M, Trampuz A, Winkler T, Perka C (2018) The economic challenge of centralised treatment of patients with periprosthetic infections. Z Orthop Unfall 156:407–413
22. OECD (2012) Health at a Glance. OECD iLibrary
23. Parvizi J, Gehrke T, Chen AF (2013) Proceedings of the international consensus on periprosthetic joint infection. Bone Jt J 95-B(11):1450–1452
24. Pivec R, Naziri Q, Issa K, Banerjee S, Mont MA (2014) Systematic review comparing static and articulating spacers used for revision of infected total knee arthroplasty. J Arthroplast 29(3):553–557 **(e551)**
25. Portillo ME, Salvado M, Trampuz A et al (2013) Sonication versus vortexing of implants for diagnosis of prosthetic joint infection. J Clin Microbiol 51(2):591–594
26. Preininger B, Janz V, von Roth P, Trampuz A, Perka CF, Pfitzner T (2017) Inadequacy of joint aspiration for detection of persistent periprosthetic infection during two-stage septic revision knee surgery. Orthopedics 40(4):231–234
27. Rak M, KavcIc M, Trebse R, Co RA (2016) Detection of bacteria with molecular methods in prosthetic joint infection: sonication fluid better than periprosthetic tissue. Acta Orthop 87(4):339–345
28. Restrepo C, Schmitt S, Backstein D et al (2014) Antibiotic treatment and timing of reimplantation. J Orthop Res 32(Suppl 1):S136–S140
29. Toulson C, Walcott-Sapp S, Hur J et al (2009) Treatment of infected total hip arthroplasty with a 2-stage reimplantation protocol: update on "our institution's" experience from 1989 to 2003. J Arthroplast 24(7):1051–1060
30. Trampuz A, Piper KE, Jacobson MJ et al (2007) Sonication of removed hip and knee prostheses for diagnosis of infection. N Engl J Med 357(7):654–663
31. Trampuz A, Zimmerli W (2008) Diagnosis and treatment of implant-associated septic arthritis and osteomyelitis. Curr Infect Dis Rep 10(5):394–403
32. Zimmerli W, Trampuz A, Ochsner PE (2004) Prosthetic-joint infections. N Engl J Med 351(16):1645–1654