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Use of Hinged Implants for Multistage Revision Knee Arthroplasty for Severe Periprosthetic Joint Infection: Remission Rate and Outcomes After a Minimum Follow-Up of 5 Years

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A B S T R A C T

Background: In severe periprosthetic joint infection after total knee arthroplasty (TKA), multistage procedures are indicated for ongoing signs of infection after implant removal during the spacer interval of an intended 2-stage exchange. In these cases, several additional debridement and spacer exchange surgeries may be necessary. Herein, we analyzed the complications, remission rates, and functional outcomes after multistage revision arthroplasty using hinged TKAs.

Methods: Patients (n = 79) treated with multistage revision arthroplasty after chronic periprosthetic joint infection of the knee were included (2010 to 2018). During the prosthesis-free interval, a static spacer containing antibiotic-loaded bone cement was implanted. The mean number of surgeries, including implant removal and revision arthroplasty, was 3.8 (range, 3 to 8). The mean duration from implant removal to revision arthroplasty was 83 days (range, 49 to 318). Complications, remission, and mortality were analyzed after a minimum follow-up of 5 years. Outcomes were assessed based on the Knee Society Score (KSS) and the Western Ontario McMasters University Osteoarthritis Index.

Results: During follow-up, 24 (30.4%) patients underwent revision surgery, with a mean time to surgical revision of 99 weeks (range, 1 to 261). After follow-up, the infection-free remission rate and overall mortality were 87.3 and 11.4%, respectively. The mean KSS was 74.3 (range, 24 to 99), the KSS Function Score was 60.8 (range, 5 to 100), and the Western Ontario McMasters University Osteoarthritis Index 30.2 (range, 5 to 83).

Conclusions: In difficult-to-treat cases, multistage revision arthroplasty showed high remission rates and low mortality after a follow-up of 5 years. The overall revision rate was comparably high, accounting for early and late reinfections most of the time. In cases of implant survival, functional outcomes comparable to those of revision hinge TKA reported in the literature can be achieved. Therefore, multistage procedures with additional debridement steps should be performed in cases of ongoing infections in intended 2-stage procedures.

Periprosthetic joint infection (PJI) is a devastating complication after total knee arthroplasty (TKA), and its growing incidence is being increasingly recognized as a medical challenge and economic burden [1]. An estimated $1.1 billion will be spent on the treatment of PJI of the knee in the United States alone by 2030 [2]. While acute PJI of the knee can be successfully treated with the Debridement, Antibiotics, and Implant Retention procedure or single-stage exchange arthroplasty [3,4], management of chronic and late-onset PJI is more complex. Surgical management depends on patient-derived factors, pathogens, and the status of soft and bony tissue [5,6]. While there is yet no gold standard for the treatment of PJI with TKA [6], 2-stage exchange remains the current procedure of choice, with remission rates more than 85% [7]. However, reported

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Informed consent was obtained from each patient.

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outcomes vary depending on the inclusion criteria and treatment strategies, as success rates depend on host grade [8].

When an intended 2-stage revision arthroplasty fails because of signs of ongoing infection after prosthesis removal, additional surgeries become necessary [9]. For PJI of total hip arthroplasty, multistage and 2-stage exchange showed comparable outcomes [10]. However, data on outcomes are lacking after multistage exchange TKA for PJI.

In the case of multistage revision after PJI of TKA, every debridement and spacer exchange step hampers the remaining bone stock and soft-tissue quality. Owing to bone loss and soft-tissue damage, there is a regular need for implants with a high constraint, such as rotating-hinge TKA (RH-TKA), to avoid arthrodesis or amputation. In recent years, outcomes after RH-TKA have been reported to continuously improve given the new implant designs [11]. However, implant survival rates of RH-TKA after septic revision are often lower than those of aseptic RH-TKA [12–14].

The aim of this study was to analyze infection remission, implant survival, and functional outcome after multistage revision arthroplasty using an RH-TKA in chronic and late-onset PJI of the knee. Patients were included after a minimum follow-up of 5 years. Owing to the often-underlying multiple comorbidities in patients, complex microbiological findings, and aggravating complications with each revision in chronic and late-onset PJI after TKA requiring multistage revision, we hypothesized lower remission and implant survival rates after a 5-year follow-up than in 2-stage revisions.

Materials and Methods

Patient Characteristics

Between January 1, 2010 and December 31, 2018, 79 patients from a specialized PJI referral center were retrospectively included when chronic PJI of the knee was treated using a multistage revision with RH-TKA (Table 1). All patients were treated using a multistage revision protocol with a mean of 3.80 surgeries (range, 3 to 8; Appendix Figure 1) per patient, including implant removal and revision arthroplasty. The mean duration from implant removal to revision arthroplasty was 83.4 days (range, 49 to 318). Baseline patient and treatment characteristics are listed in Table 1. The mean follow-up time was 8.1 years (range, 5 to 14), with a minimum follow-up of 5 years. Included patients were initially expected to undergo a 2-stage exchange, but the treatment failed because of signs of ongoing infection in the prosthesis-free interval, making another surgical revision necessary. Patients who had a previous history of PJI or implant revisions for PJI were excluded. The study was approved by the Institutional Review Board, and informed consent was obtained from all patients.

Table 1
Baseline Patient Characteristics and Implants Used.

N (sex [women/men]) (%)	79 (39 [49.4]/40 [50.6])
Mean age (years)	67 (38 to 87)
Body mass index (BMI)	29.4 (21.2 to 44.3)
Charlson Comorbidity Index	1.0 (0 to 8)
Charlson Comorbidity Index, age adapted	3.3 (0 to 12)
Comorbidities (%)	
Smoking	11 (13.9)
Diabetes mellitus	9 (11.4)
Hypertension	50 (63.3)
Infected TKA (%)	
Bicompartmental knee arthroplasty	77 (97.5)
Unicompartmental knee arthroplasty	2 (2.5)
Rotating-hinge implants (%)	
BPKS	43 (54.4)
RHK Revision	33 (41.8)
Mutars GenuX MK	3 (3.8)

TKA, total knee arthroplasty; BPKS (Peter Brehm, Weisendorf, Germany); RHK Revision (Zimmer, Warsaw, Indiana, United States); Mutars GenuX MK (Implantcast, Buxtehude, Germany).

Diagnostic Criteria

Knee PJI was defined according to the guidelines of the Musculoskeletal Infection Society and retrospectively confirmed using the 2018 International Consensus Meeting criteria [15]. A chronic or late-onset infection was defined according to the guidelines of the Infectious Diseases Society of America (IDSA) [16,17].

To facilitate antimicrobial therapy, a preoperative diagnostic arthrocentesis was performed to analyze the cell count, differential leukocyte count, and microorganisms of the synovial fluid, whenever possible. Preoperative diagnostic arthrocentesis was performed in 69 (87.3%) patients. Antimicrobial therapy was withheld for at least 2 weeks prior to the collection of the synovial fluid and the first surgical intervention. During each surgical intervention, 3 to 5 periprosthetic tissue samples were obtained for microbiological and histopathological testing [18]. The incubation time for microbiological samples was 14 days. Furthermore, the white blood cell count and C-reactive protein level were routinely checked, per the IDSA guidelines [16]. In cases of fever, aerobic and anaerobic blood cultures were tested, and blood procalcitonin levels were assessed and monitored.

Surgical Procedure

All patients were intended to be treated with a 2-stage exchange protocol, per the IDSA treatment guidelines [17]. During the first surgery, the TKA, including bone cement, was removed, and bone and soft tissues were debrided. A total of 3 to 5 tissue samples for microbiological and histopathological analyses were obtained. After the removal of all components, a static polymethylmethacrylate (PMMA) spacer was used. Hoffmann II External Fixation System rods (Stryker, Kalamazoo, Michigan, USA) were each inserted in the femoral and tibial intramedullary canals, coupled with rod couplings, and encapsulated using PMMA cement. Antibiotic-loaded PMMA was used, containing gentamicin. In cases with known microbiological specimens and an antibiogram owing to preoperative arthrocentesis or previous surgery, bone cement was loaded with antibiogram-specific antibiotics whenever possible. In these cases, local antibiotics used in PMMA were gentamicin and vancomycin, gentamicin and clindamycin, or gentamicin and meropenem (individually mixed during surgery). Local antibiotics were not used with other delivery systems than the PMMA spacer. A calculated systemic antimicrobial therapy was initiated using amoxicillin and clavulanic acid, and adapted to antibiograms when available. A total of 6 weeks of antibiotic therapy were administered: 2 weeks intravenously and 4 weeks with highly bioavailable oral treatment.

All included patients underwent at least one additional surgical revision and, therefore, a multistage treatment protocol (Figure 1). The decision for revision surgery in the prosthesis-free interval was made based on clinical signs of infection (wound drainage, redness, overheating, and signs of sepsis) and increasing white blood cell count or C-reactive protein blood levels after the exclusion of other possible causes [19]. None of the patients included in the study were revised for other reasons than ongoing signs of infection. Failure of the static spacer did not occur in any of the patients. In these cases, the spacer was removed, bone and soft tissue were debrided, 3 to 5 tissue samples were collected, and patients were fitted with a new static PMMA spacer. The antibiotic regimen was restarted, and patients were treated with

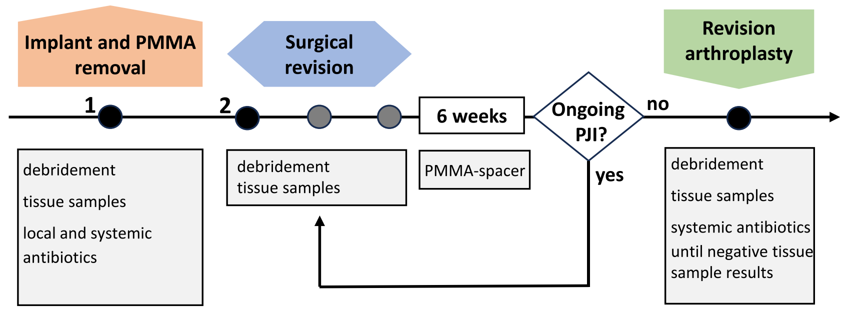

Fig. 1. Therapy algorithm of multistage revision arthroplasty for periprosthetic joint infection of the knee. After implant removal and implantation of a static spacer (surgery 1), surgical revisions including exchange of spacer were performed when signs of ongoing infection are present. At least one surgical revision was performed, making the therapy a multistage revision. After 6 weeks of antibacterial therapy, patients were re-evaluated for signs of ongoing infection and subsequently underwent rotating-hinge arthroplasty in the event of infection-free re-evaluation.

at least 6 weeks of antibiotic therapy. After at least 6 weeks of antibiotic treatment and a 2-week observation period after antibiotic cessation and with no ongoing signs of infection, revision arthroplasty using RH-TKA was performed (Figure 2). Indications for RH-TKA were loss of bone stock or damage to the collateral ligaments.

The implants used in this study are RHK Revision (Zimmer, Warsaw, Indiana, USA), BPKS (Peter Brehm, Weisendorf, Germany), and Mutars GenuX MK (Implantcast, Buxtehude, Germany). Implants were cemented using gentamicin-loaded PMMA or gentamicin-vancomycin—loaded PMMA in cases with known pathogens susceptible to vancomycin. During revision arthroplasty, another 3 to 5 tissue samples were obtained. Patients received at least 2 weeks of antibiotic treatment. After negative tissue cultures, the antibiotic treatment was discontinued after 2 weeks. In the case of positive microbiological cultures during revision arthroplasty, the duration of antibiotic treatment was reset to 6 weeks, including biofilm-active antibiotics. Furthermore, in cases of positive microbiological cultures during revision arthroplasty or signs of acute PJI, the Debridement, Antibiotics, and Implant Retention procedure was carried out as previously described [19].

Outcome Assessments

The primary end point was remission of infection and implant survival after a minimum follow-up of 5 years. Remission of PJI was defined as the absence of clinical, radiological, and biological signs of infection at follow-up according to the Delphi consensus criteria [20]. Complications as well as mortality were analyzed using patients' medical data, additional telephone interviews, and national databases on mortality when necessary.

The secondary end points were clinical and functional outcomes. The functional outcome was evaluated using the Knee Society Score (KSS) and the Western Ontario McMasters University Osteoarthritis Index (WOMAC). Quality of life (QoL) was assessed using the Short-Form Health Survey 12 (SF-12). The scores were confirmed after a minimum follow-up of 5 years. Due to the retrospective design of the study, preoperative scores were not available. However, we compared the results of the functional outcome to the literature in the discussion section. Functional outcome was assessed for 52 (65.8%) patients who had complete datasets for the KSS, WOMAC, and SF-12 scores.

The microbiological specimens of the included patients were analyzed throughout the surgical revisions. Furthermore, possible influencing variables such as age, comorbidities, body mass index, and Charlson Comorbidity Index were also collected and included in the analysis.

Data Analyses

Data were collected and analyzed using IBM SPSS (Statistical Package for Social Sciences) (Statistics, version 29 (IBM, Armonk, New York, USA). Continuous variables were presented as means (range), ordinal variables as medians (interquartile range), and nominal variables as numbers (%). Data normality was verified using a graphical method and Shapiro-Wilk tests. Group comparisons were made using Student's *t*-tests for continuous normally distributed variables, Mann-Whitney U tests for continuous or ordinal non-normally distributed variables, and *Chi*-square tests for categorical variables. Kaplan-Meier survival curves were used to analyze implant survival and mortality, with *post hoc* log-rank tests used to report differences between groups. Multivariable logistic regression models were used to stratify variables associated with remission of infection and mortality. The statistical significance of the model was reported with *Chi*-squares and *P* values, and variances were explained using Nagelkerke's R2. $P < 0.05$ was considered to indicate statistically significant differences.

Results

Microbiological Testing

At least one bacterium was isolated in 37 (46.8%) patients, of whom 19 had coagulase-negative *Staphylococci*. When bacteria were not present (false negative results), other parameters according to the International Consensus Meeting criteria [15] confirmed PJI. During implant removal, 48 (60.8%) patients had positive intraoperative tissue samples. The results of intraoperative tissue samples for 2 patients could not be retrieved because of external implant removal. In 4 (5.1%) patients, no bacteria were detected throughout the multistage revision process. A total of 12 (15.2%) patients had positive microbiological tissue samples during revision arthroplasty. Of these, 5 were positive for the same bacteria as in the revision process, 4 patients had different bacteria, and 3 had no positive test result before. In 28 (35.4%) patients, polymicrobial specimens (more than one bacterium per sample) were detected (Table 2).

Complications, Remissions, and Mortalities

Surgical revision within 30 days after completing multistage revision arthroplasty was necessary in 4 (5.1%) patients. Of these, 3 were successfully treated for postoperative infection and prolonged wound secretion with no implant removal. A patient was treated for a traumatic patellar tendon rupture. A total of 24 (30.4%) patients underwent surgical revision during follow-up, with a

Fig. 2. Case report of a patient who had late onset periprosthetic joint infection of a bicondylar total knee arthroplasty. (A) Before admission to our center, implant retention using resorbable calcium-based local antibiotics was tried without success. (B) The patient was referred to our unit, and the implant was removed and replaced by a gentamicin-loaded polymethylmethacrylate spacer using 2 fixator rods and a fixator coupling (Stryker, Kalamazoo, Michigan, United States). (C) Due to ongoing clinical signs of infection with *S. epidermidis* found in tissue samples, surgical revision with an exchange of spacer using vancomycin-loaded and gentamicin-loaded PMMA was performed. (D) After 6 weeks of systemic antibacterial treatment, the patient received revision arthroplasty using a BPKS (Peter Brehm, Weisendorf, Germany) rotating-hinge prosthesis.

mean time to surgical revision of 98.7 weeks (range, 1.1 to 260.7). The reasons for revision after multistage revision arthroplasty using a hinged implant are listed in Table 3.

After a minimum follow-up of 5 years, 13 (16.5%) implants were removed (implant survival rate: 83.5%). For treatment after implant removal see Table 3. The indication for implant removal was recurrent PJI in 10 of 13 patients. Therefore, the PJI remission rate was 87.3% after a minimum follow-up of 5 years. In a multivariable logistic regression model for reinfection, positive microbiological findings during reimplantation were significantly associated with reinfection during follow-up (Appendix Table 1). After maximum follow-up, the implant survival rate was 77.2% and the remission rate was 81.0% (Figure 3). All 4 patients who had recurrent PJI after $>$ 5 years of follow-up had a prior infection due to unrelated reasons. Mortality after the minimum follow-up of 5 years was 11.4% (Table 4). No patient died due to sepsis or immediate postoperative complications. Risk factors were assessed in a multivariable logistic regression model for mortality during follow-up. Age and Charlson Comorbidity Index were significantly associated with an increased risk of mortality (Appendix Table 2).

Functional Outcomes

The mean KSS was 74.3 (range, 24 to 99), KSS Function Score was 60.8 (range, 5 to 100), and WOMAC score was 30.2 (range, 5 to 83). Of the 52 patients, 23 (44.2%) reported a KSS of $\geq$ 80, and 33 (63.5%) reported a KSS of $\geq$ 70 (Figure 4). QoL was assessed using the SF-12, with a mean score of 37.5 (range, 15 to 56) on the physical scale and

Table 2
Bacterial Load per Patient and Bacteria Detected During Implant Removal, Revision Surgery, and Revision Arthroplasty (Multiple Detections Included).

Bacterial Detection	Implant Removal	Surgical Revision(s)	Revision Arthroplasty
Number of bacteria per patient, n (%)			
No bacteria detected	31 (39.2)	49 (62.0)	67 (84.8)
One bacterium	25 (31.6)	22 (27.8)	11 (13.9)
Two bacteria	17 (21.5)	8 (10.1)	2 (2.5)
Three bacteria	3 (3.8)	0	0
Four bacteria	1 (1.3)	0	0
Bacterial spectrum, n			
Staphylococcus epidermidis	14	12	7
Staphylococcus aureus	15	3	1
Enterococcus faecalis	7	1	
Methicillin-resistant *Staphylococcus epidermidis*	6	3	4
Escherichia coli	5		
Methicillin-resistant *Staphylococcus aureus*	3	4	
Streptococcus dysgalactiae	4	1	
Staphylococcus capitis	2	2	
Cutibacterium acnes	2	4	
Bacillus subtilis	1	2	
Klebsiella pneumoniae	1	1	
Staphylococcus warneri	1	1	
Proteus mirabilis	1	1	
Staphylococcus haemolyticus	1		
Enterobacter cloacae	1		
Enterococcus faecium	1		
Staphylococcus lugdunensis	1		
Streptococcus oralis	1		
Staphylococcus xylosus	1		
Bacillus cereus	1		
Streptococcus mitis	1		
Finegoldia magna	1		
Streptococcus gordonii	1		
Proteus vulgaris		1	
Streptococcus salivarius		1	
Micrococcus luteus		1	
Bacteroides fragilis			1

In 2 cases, microbiological specimens of implant removal were unknown because of external implant surgery.

Table 3
Reasons for Revision Surgery Within the Minimum Follow-Up Duration of 5 Years and Maximum Follow-Up.

Complications	Number of Patients, n (%)	Treatment, n (%)
Early complications (0-30 days)		
Postoperative prolonged wound secretion	2 (2.5)	DAIR procedure, 2 (2.5)
Postoperative hematoma	1 (1.3)	DAIR procedure, 1 (1.3)
Patellar tendon tear	1 (1.3)	Reconstruction, 1 (1.3)
Minimum follow-up (30 days to 5 years)		
Periprosthetic joint infection	10 (12.6)	Multistage revision, 5 (6.3) Arthrodesis, 3 (3.8) Above knee amputation, 2 (2.5)
Aseptic loosening	1 (1.3)	Two-stage revision, 1 (1.3)
Arthrofibrosis	3 (3.8)	Arthrolysis, 3 (3.8)
Periprosthetic femoral fracture	3 (3.8)	Plate osteosynthesis, 3 (3.8)
Extensor mechanism damage (femoral nerve damage)	1 (1.3)	Arthrodesis, 1 (1.3)
Stem fracture	1 (1.3)	Two-stage revision, 1 (1.3)
Retropatellar arthrosis	1 (1.3)	Patella resurfacing, 1 (1.3)
Maximum follow-up (> 5 years)		
PJI after urosepsis	2 (2.5)	Arthrodesis, 1 (1.3) Permanent fistula, 1 (1.3)
PJI after empyema of the foot	1 (1.3)	Arthrodesis, 1 (1.3)
Aseptic loosening	1 (1.3)	Two-stage revision, 1 (1.3)
PJI after femoral fracture surgery	1 (1.3)	Multistage revision, 1 (1.3)
PJI after spine surgery	1 (1.3)	Arthrodesis, 1 (1.3)

Only final treatment is listed. There is 1 patient who was listed twice due to early postoperative wound infection with successful surgical revision including the Debridement, Antibiotics, and Implant Retention procedure and re-infection 7 years later after surgery of a femoral fracture with multistage revision arthroplasty.
PJI, periprosthetic joint infection; DAIR, Debridement, Antibiotics, and Implant Retention procedure.

55.0 (range, 24 to 68) on the mental scale. There were no differences in scores between different implant systems (GenuX MK was excluded for group comparisons because of the low case number).

Discussion

In chronic and difficult-to-treat PJI of TKA, 2-stage revision arthroplasty remains the standard procedure [7]. In difficult-to-treat PJI, ongoing signs of infection after implant removal may be present. In these cases, additional surgical debridement and spacer exchange steps are necessary, resulting in a multistage approach.

To date, the outcomes in these cases remain unclear. Higher mortality and lower success rates in accordance with restrictive functional outcomes are expected. To our knowledge, this is one of the largest studies evaluating complications, infection remission, and functional outcome with a minimum follow-up of 5 years after multistage revision arthroplasty using RH-TKA for PJI. We identified an infection remission rate of 87.3% and an overall mortality rate of 11.4% after 5 years. After maximum follow-up, the infection remission rate was 81%.

The 2 most common microorganisms isolated in this study were *S. epidermidis* (37.4%; including methicillin-resistant *Staphylococcus epidermidis*) and *S. aureus* (15.4%), which are consistent with previous reports of bacterial spectra for 2-stage revisions [21,22]. In a recent study, microorganisms in the first-stage and second-stage procedures of the 2-stage procedure were compared, showing an increase in *S. epidermidis* and *Cutibacterium acnes* in the second-stage procedure with decreasing numbers of *S. aureus* and *Streptococci* [21], a trend that was also noted in our study. Coagulase-negative *Staphylococci* were recently shown to be associated with low treatment success in PJI [23], which explains the presence of ongoing signs of infection after implant removal in our study. Moreover, in 28 (35.4%) patients, polymicrobial infection was present, and 4 (5.1%) patients were culture-negative, which was shown to be a negative predictor for the outcome after the first step of a 2-stage procedure [24,25]. Hence, patients in our study presented with a complex microbiological spectrum, which likely played a role in ongoing infection after implant removal, making 2-stage revision impossible. In accordance with a meta-analysis that identified a positive culture during reimplantation as a risk factor for reinfection [26], 8 of 12 patients who had positive cultures had their implant removed because of PJI recurrence during follow-up.

Multistage revision arthroplasty was performed in patients after an intended 2-stage revision with ongoing signs of infection after implant removal. Several studies have reported the outcome of 2-stage revision arthroplasties for knee PJI [27–29]. A recently published multicenter study with long-term results after 2-stage revision by Kildow et al. [27] showed an infection remission rate of 85.4% in 178 patients (n = 13, 7.3% underwent multistage revision) after a mean of 6.6 years. The comparison of these studies with ours is hampered by the low patient numbers treated with multistage revision. However, another study on 2-stage septic

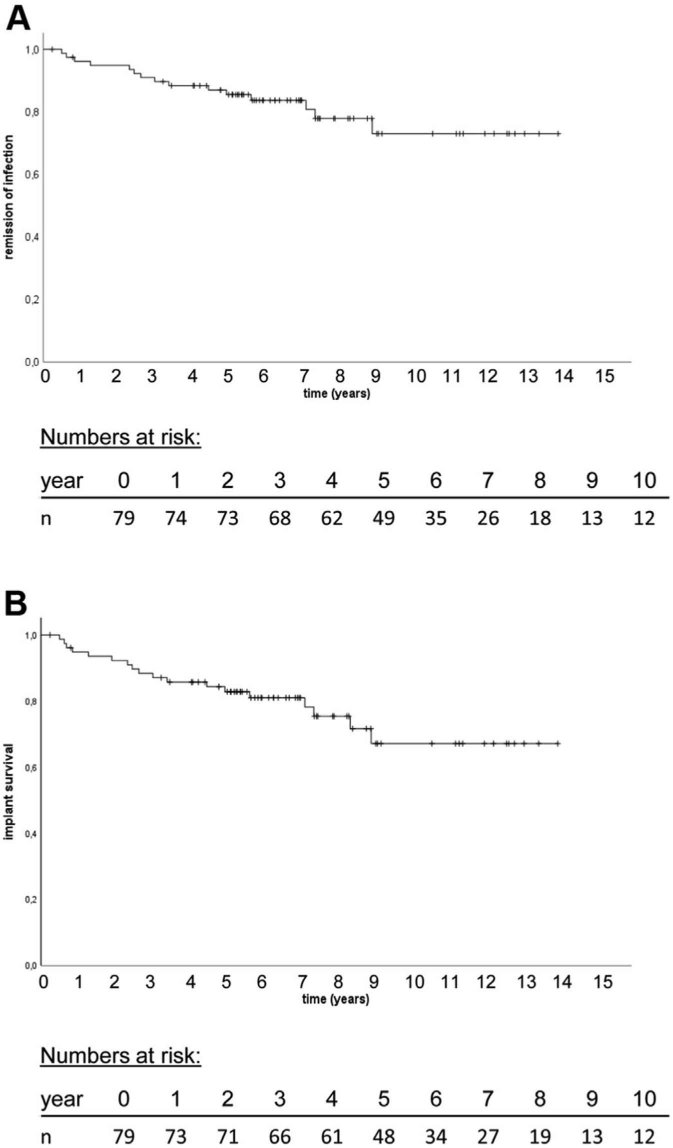

Fig. 3. Kaplan-Meier survival curves for (A) infection-free remission and (B) implant survival for any reason.

revision of infected TKA showed that additional surgical revisions prior to revision arthroplasty in 46 of 245 patients (19%) were not a risk factor for reinfection [28]. In contrast, a study by Tan et al. [30] demonstrated poor outcomes in 90 of 533 patients who underwent a 2-stage exchange with at least one additional spacer exchange for PJI compared to patients who did not require a spacer exchange. Notably, the bacterial spectrum differed with a higher prevalence of *S. aureus*, and their patients had more comorbidities and a higher body mass index than patients in our study. Complication rates for all causes are reportedly higher after RH-TKA than bicondylar TKA because of many factors such as implant size, time of surgery, and mechanical failures, especially in the context of septic revisions. In a recent meta-analysis by Yoon et al., there is no significant difference in implant survival rates using constrained condylar knee implants compared to RH-TKA, but aseptic revisions are included in the meta-analysis, and septic revisions are described as a risk factor for revision independent of the implant design [31]. A study including only RH-TKA for septic revision in 46 patients, of whom 5 underwent multistage revision, reported a higher surgical revision rate of 55.9% than the 36.7% in our study at the final follow-up [29]. The difference in revision rates is mainly a result of fewer septic revisions in our study, which might be attributed to better infection control following multistage revisions. The implant survival rate owing to septic revision after a 5-year follow-up of 2-stage revision arthroplasty using RH-TKA for knee PJI is reportedly 67.1% to 93% [12,27,28,32,33]. Thus, a PJI remission rate of 87.3% in this study can be considered adequate.

Table 4
Mortality After 3 Months, 5 Years, and Maximum Follow-Up Including Reasons for Mortality When Available.

Reasons for Mortality	Number of Patients, n (%)
Early mortality (0-3 months)	1 (1.3)
Sepsis	0
Postoperative complication (eg, thromboembolic)	0
Age, death at home, no further information	1 (1.3)
Unknown	0
Minimum follow-up (3 months to 5 years)	8 (10.1)
Sepsis	0
Heart failure	1 (1.3)
Cancer	1 (1.3)
Age, death at home, no further information	6 (7.6)
Unknown	1 (1.3)
Maximum follow-up (> 5 years)	11 (13.9)
Sepsis	0
Age, death at home, no further information	8 (10.1)
Unknown	3 (3.8)

No patient died due to sepsis or postoperative complications. For most patients, the reason for mortality was natural causes due to age (without further post-mortem examination).

In our study, all patients who had recurrent PJI of RH-TKA after 5 years had an unrelated infection prior to the PJI. Diagnostic and treatment procedures unrelated to the arthroplasty have long been discussed in the literature as risk factors for hematogenous PJI, with recently increasing interest [34,35]. Patients who underwent septic revision, especially with RH-TKA, are at higher risk of reinfection [36], and therefore, prevention of reinfection, particularly in the presence of other infections, is crucial even many years after revision arthroplasty. Preventing a reinfection of the RH-TKA is of particular importance because treatment options offer only modest implant survival rates with poor functional outcomes [37], and salvage procedures are often necessary [38].

Mortality after 2-stage revision arthroplasty for PJI of the knee is reported to be 11 to 16% after 2 years [12,28] and up to 33.1% after 5 years [27,39]. Mortality rates after 2-stage revision arthroplasty in chronic PJI have recently been compared to rates of cancer, with high mortality being attributed to not only the comorbidities and complications but also the risks of the 2 major surgeries [27]. Hence, patient survival likely faces a higher risk in multistage compared to 2-stage approaches for chronic PJI. Nevertheless, mortality was only 11.4% after 5 years, and no patient died due to sepsis or postoperative complications. Implant removal was not associated with mortality, but patient age, and comorbidities were factors causing high mortality rates. Given the mortality rates, the use of articulating spacers during spacer exchange should be considered as an option for definitive treatment [40]. Moreover, the high mortality rates may cause a bias and underestimate the reinfection rates.

Chen et al. [32] reported the functional outcomes of 31 patients after 2-stage septic revision arthroplasty using RH-TKA with a mean KSS of 70.7 and a KSS function of 56.5 points, which are comparable to our study. According to a recent study validating the KSS for TKA, these results can be considered *fair*; however, primary cruciate-retaining TKA was investigated to set the categories [41].

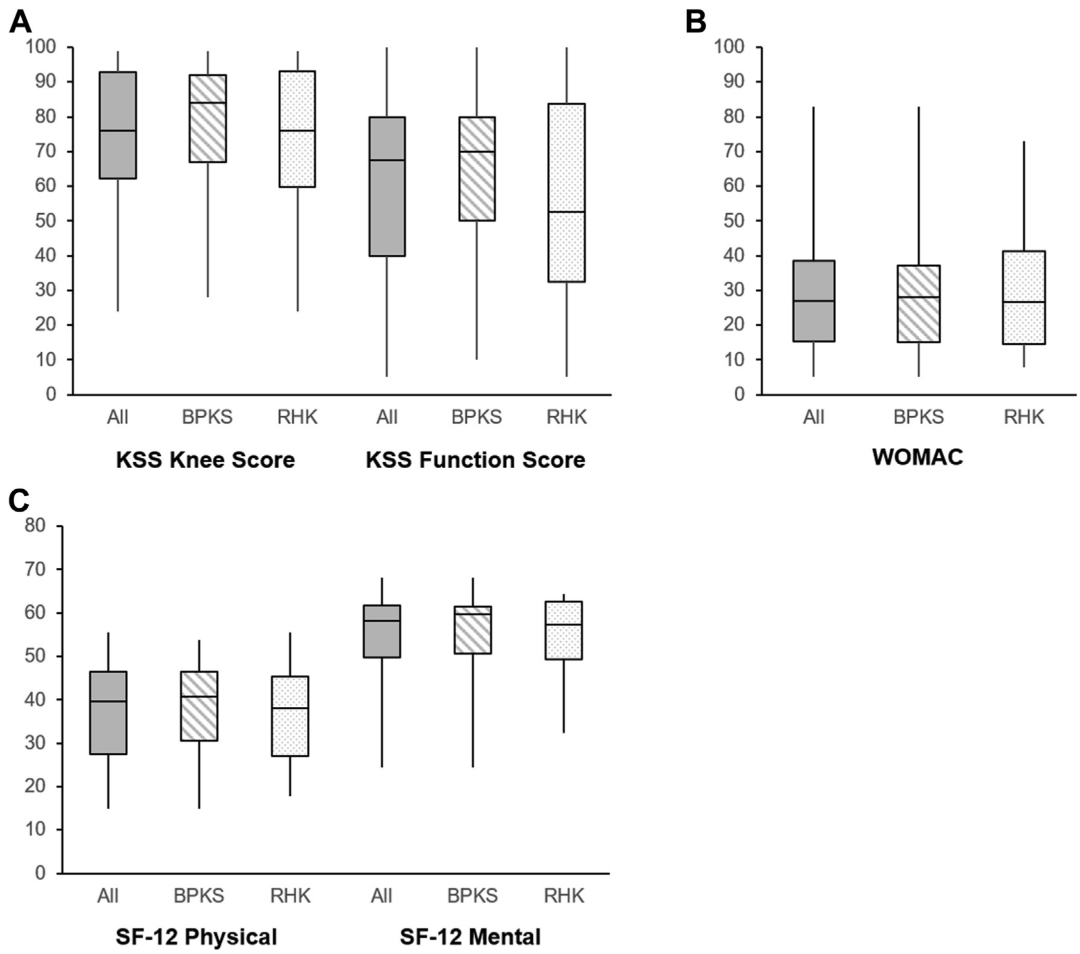

Fig. 4. Functional outcome of 52 patients assessed using (A) Knee Society Score (KSS), (B) Western Ontario McMasters Universities Osteoarthritis Index (WOMAC), and (C) Short-Form Health Survey 12 (SF-12). There were no significant differences between patients who received the BPKS or RHK (revision) implant for KSS knee ($P = .583$), KSS function ($P = 0.257$), WOMAC ($P = .804$), SF-12 physical ($P = 0.224$), and SF-12 mental ($P = 0.957$) scores. GenuX MK was excluded for functional follow-up because of the low case number; BPKS (Peter Brehm, Weisendorf, Germany); RHK Revision (Zimmer, Warsaw, Indiana, USA).

Only a few studies report functional outcomes after RH-TKA using WOMAC scores. Recently, a mean postoperative WOMAC score of 19.3 points has been reported for mainly aseptic RH-TKA [42], making comparison among studies difficult. In a recent meta-analysis and systematic review, septic revision TKA showed significantly lower KSS scores compared to aseptic revision TKA among different implant types [42,43]. In comparison to constrained condylar knee implants, rotating-hinge revision TKA was found to have significantly lower functional outcome scores [31]. However, mainly aseptic revision TKA was included. Shen et al. found RH-TKA to have superior function outcomes in septic revisions with bone defects, while unlinked constrained prostheses offer superior outcomes in aseptic revisions with bone defects of similar grade [44]. QoL was assessed using the SF-12 score, with a mean score of 37.5 on the physical scale and 55.0 on the mental scale. Mental scores are falling in accordance with a reference population, but physical scores are lower [45]. This observation is confirmed by a recently published review on patient-reported outcome measures of patients who had a PJI, showing comparable mental and physical scores for the SF-12 [46]. However, matched studies did not show significant differences in QoL among patients who had a septic revision and primary or aseptic revision arthroplasty [46].

This study has some potential limitations. Although data on mortality are available for all patients, reasons for mortality are not available for all patients, and some patients might have reduced life expectancy as an indirect consequence of PJI (e.g., impaired mobility). However, no patient died due to the immediate consequences of PJI (e.g., postoperative sepsis). There were 2 patients who underwent external implant removal, which might suggest potential variations in medical management, but the patients were transferred to our center within the first few days, and the external treatment was identical to our treatment as described above. Furthermore, we acknowledge that signs of ongoing infection, especially clinical signs, rely on individual decision-making without objective criteria. Moreover, there is a selection bias due to the specialization in septic revisions toward more severe cases at our center. Despite these limitations, this study adds significant information to the literature regarding complications, remission of infection, and mortality after multistage septic RH-TKA. Our data may be used to improve treatment for chronic PJI of the knee, and surgeons should be aware of the outcome presented when deciding on optimal therapeutic strategies.

In conclusion, this study highlights the challenges in managing chronic PJI of the knee with a multistage procedure: difficult-to-treat microbiological specimens, high surgical revision and mortality rates, and a reinfection rate of 12.7% after 5 years of follow-up, increasing to 19.0% after maximum follow-up. This reiterates the ongoing risk of reinfection for unrelated causes and calls for patient education and prevention strategies. In the case of sufficient multistage revision arthroplasty using RH-TKA, patients can expect a fair functional outcome that falls in accordance with reported outcomes for revision arthroplasty using RH-TKA for other indications in the literature.

CRediT authorship contribution statement

Matthias Schnetz: Writing – review & editing, Writing – original draft, Visualization, Validation, Supervision, Methodology, Investigation, Formal analysis. **Larissa Ewald:** Writing – original draft, Visualization, Investigation, Formal analysis. **Tim Jakobi:** Writing – review & editing, Visualization, Investigation, Formal analysis. **Alexander Klug:** Writing – review & editing, Visualization, Validation, Supervision, Methodology, Formal analysis. **Reinhard Hoffmann:** Writing – review & editing, Supervision, Resources, Project administration, Conceptualization. **Yves Gramlich:** Writing – review & editing, Visualization, Validation, Supervision, Resources, Project administration, Methodology, Formal analysis, Conceptualization.

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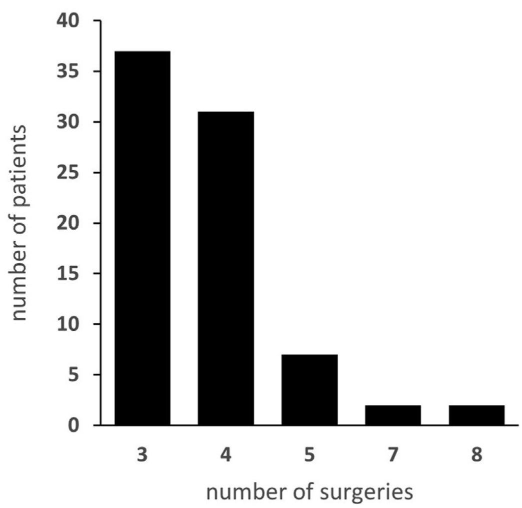
Appendix



Appendix Figure 1. Distribution of the number of surgeries for the patients included in the study. The mean number of surgeries was 3.8 (standard deviation: 1.1). The first surgery was implant removal and the implantation of a static spacer in every patient. At least one revision with spacer exchange was performed before revision arthroplasty using a rotating-hinge implant, making the treatment a multistage effort. Number of surgeries, including the removal of the initial implant and reimplantation.

Appendix Table 1
Variables Included in the Multivariable Logistic Regression Model for Risk for Remission of Infection ($\chi^2 = 14.160$; $P = 0.003$; $R^2 = 0.264$).

Variable	*P* Value
Positive microbiological tissue samples from revision arthroplasty	**<0.001**
Number of surgeries until revision arthroplasty	0.130
Coagulase-negative *Staphylococci* during any surgery	0.532

$P < 0.05$ was considered to indicate statistically significant differences (bold).

Appendix Table 2
Variables Included in the Multivariable Logistic Regression Model for Risk of Mortality ($\chi^2 = 15.587$; $P = 0.016$; $R^2 = 0.329$).

Variable	*P* Value
Charlson Comorbidity Index	**0.011**
Age at time of surgery	**0.044**
Implant removal during follow-up	0.206
Surgical revision during follow-up	0.894
Body mass index	0.774
Number of surgeries until revision arthroplasty	0.755

$P < 0.05$ was considered to indicate statistically significant differences (bold).