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Satisfactory and Similar Outcomes After Knee Arthroplasty Revisions in One or Two Stages for Infection, Following a Surgical Strategy Based on Robust Guidelines

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A B S T R A C T

Background: This study aimed to assess the outcomes of a one-stage or two-stage strategy after revision total knee arthroplasty for periprosthetic joint infection.
Methods: This single-center retrospective study included all TKA revisions for chronic infection operated on between 2010 and 2021, with at least two years of follow-up. The surgical strategy was based on the recommendations from the Philadelphia Consensus 2018. Patients were classified into five overlapping groups: mechanical failure, septic failure, controlled infection, cure of infection, and complete healing. Revision was defined as the need for further surgery with implant removal. There were 218 revision total knee arthroplasties included, with 182 two-stage revisions (83.5%) and 36 one-stage revisions (16.5%). The mean follow-up was 56.9 ± 30.8 months. At the last follow-up, 135 patients (61.9%) were classified as “complete healing,” 30 as “septic failure” (13.8%), 12 as “mechanical failure” (5.5%), 147 (67.4%) as “infection-cured,” and 41 (18.8%) as “controlled infection.”
Results: There were 27 patients (14.8%) who had septic failure, and 11 (6.1%) had mechanical failure in the two-stage group, versus three (8.3%) and one (2.8%), respectively, in the one-stage group ($P = 0.36$). There were 128 “R2” or “complex revision cases” (58.7%) and 90 “R3” or “salvage cases” (41.3%) according to the revision knee complexity classification. In multivariate analysis, the requirement of a flap (odds ratio [OR] = 0.28, [0.11 to 0.72]), revision knee complexity classification grade of R3 (OR = 0.37, [0.21 to 0.68]), and an American Society of Anesthesiologists score >2 (OR = 0.51, [0.28 to 0.93]) were associated with lower rates of infection healing.
Conclusions: Following a surgical strategy based on robust guidelines, one- or two-stage TKA revision for periprosthetic joint infection achieved satisfactory rates of complete healing and cure of infection despite 41% of very complex cases. Patients classified as R3, those requiring a flap, and those who had an American Society of Anesthesiologists score greater than 2 were at higher risk of failure.
Level of Evidence: III.

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Periprosthetic joint infections (PJIs) are dreaded complications after total knee arthroplasty (TKA), with an overall incidence of 1% in registers [1]. Revision TKAs (RTKAs) for PJI are complex interventions with major morbidity and mortality rates [2].

Historically, the two-stage approach was the gold standard for chronic PJI. This consists of two surgeries: the first is where the infected tissues are removed, the implant explanted, and a cemented spacer inserted; the second is conducted after a minimum interval of six weeks with the implantation of the new prosthesis. This two-step strategy may yield complications such as stiffness, new infection during the second-stage procedure, and poorer functional outcomes after six weeks without full weight-bearing [3,4].

Another possible approach to treat this chronic infection is the one-stage approach, which consists of changing the prosthesis in a single intervention. This strategy has gained popularity in the last few years, showing comparable failure risk to the two-stage approach and better functional outcomes in selected patient [5–7]. Nevertheless, these reported studies had either restrictive exclusion criteria, small sample sizes with heterogeneous populations, variable indications for one- or two-stage strategies, and/or heterogeneous definitions of failure, making it difficult to establish the superiority of one of the two strategies and accurately determine risk factors [8–13]. Both strategies have shown satisfactory results in the literature, with failure rates ranging from 0 to 30.0% [8–10,12]. The main challenge remains to accurately select the appropriate strategy for each patient, particularly for complex periprosthetic infections. Many parameters must be considered, such as chronicity of infection, comorbidities, soft tissue status, bone stock, extensor mechanism status, microorganism involved, and antibiotic susceptibility, making it complex to draw unequivocal guidelines. Studies in the literature often have many exclusion criteria, assessing only the cases of PJI that are not complex.

This study aimed: 1) to evaluate our practices for managing complex PJI after TKA in a referral center for bone and joint infection, 2) to compare the outcomes of a one-stage or two-stage strategy after RTKA for PJI, and 3) to find potential predictive factors for failure. The main hypothesis was that the two strategies had no significant difference in outcomes, even for complex cases.

Materials and Methods

Patients

From January 1, 2010, to September 30, 2021, 245 RTKAs for infection were prospectively enrolled into an institutional database at a referral center for bone and joint infection (Centre de Reference des Infections Osteoarticular complexes). Inclusion criteria were all RTKA for a chronic PJI, with a minimum follow-up of two years after the last surgical procedure. Exclusion criteria were transfemoral amputation, single-component revision, total femoral replacement, or definitive explantation.

The final analysis included 218 RTKAs (Figure 1). From this cohort, 182 patients underwent a two-stage revision (83.5%), whereas 36 underwent a one-stage revision (16.5%). The mean age at surgery was 68 years [range, 41 to 90], and the mean body mass index was 30.8 [range, 18.0 to 59.3] (Table 1). The mean follow-up was 56.9 months [range, 24.0 to 159.0]. From the evaluated population, 110 patients had previous surgery for PJI (50.5%), mainly patients undergoing a two-stage strategy ($P < 0.001$) (Table 1).

PJI Diagnosis

Chronic periprosthetic infection was diagnosed using the criteria established during the International Consensus Meeting in Philadelphia in 2018 (Supplementary Material 1) [14]. Table 2 details the responsible microorganisms associated with the revisions.

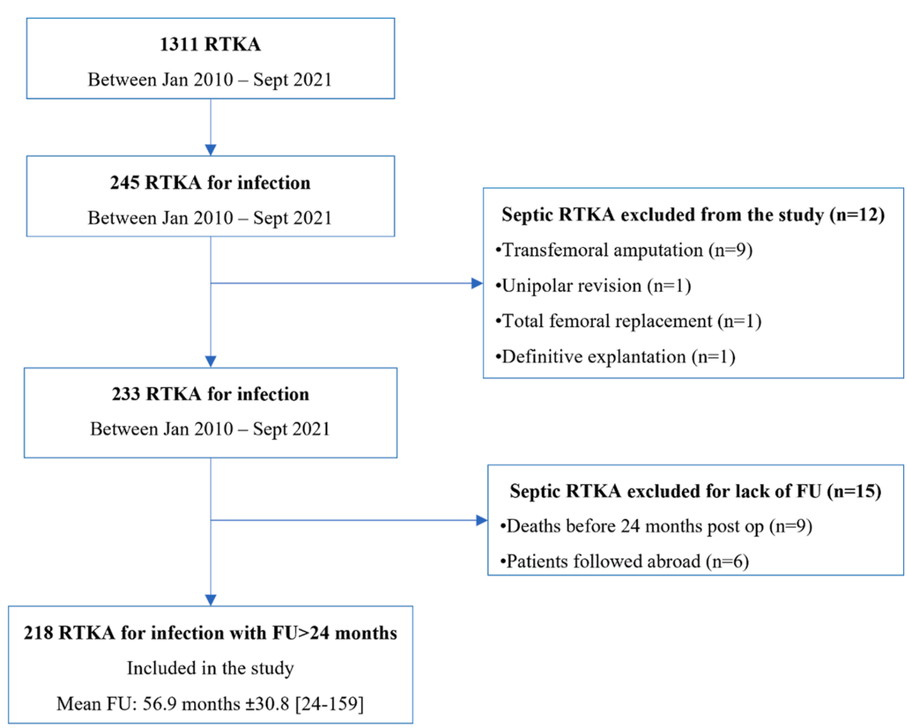

Figure 1. Flowchart. RTKA, revision total knee arthroplasty; FU, follow-up.

Table 1
Demographic Data.

Demographic Data	Total	Two Stage	One Stage	*P*-Value
Patients (N)	218	182 (83.5%)	36 (16.5%)	
Follow-up (months)	56.9 ± 30.8	60.1 ± 32.0	41.1 ± 17.7	<0.001[a]
mean ± SD (min-max)	(24.0 to 159.0)	(24.0 to 159.0)	(24.0 to 86.0)	
Sex (women/men)	94 (42.9%)/125 (57.1%)	79 (43.4%)/103 (56.6%)	14 (38.9%)/22 (61.1%)	0.75
Age (years)	68 ± 9.1	67 ± 9.1	69 ± 9.2	0.33
mean ± SD (min-max)	(41.0 to 90.0)	(41.0 to 89.0)	(50.0 to 90.0)	
BMI (kg/m^2)	30.8 ± 6.7	31.2 ± 7.0	28.9 ± 4.9	0.12
mean ± SD (min-max)	(18.0 to 59.3)	(18.0 to 59.3)	(19.4 to 40.1)	
Right/left knee	112 (51.4%)/106 (48.6%)	98 (53.8%)/84 (46.2%)	14 (38.9%)/22 (61.1%)	0.15
RKCC (%)				
R2	128 (58.7)	101 (55.5)	27 (75.0)	0.047[a]
R3	90 (41.3)	81 (44.5)	9 (25.0)	
ASA grade (mean)	2.44 ± 0.6	2.42 ± 0.6	2.53 ± 0.6	0.61
ASA 1 (%)	7 (3.2)	6 (3.3)	1 (2.8)	
ASA 2 (%)	114 (52.3)	98 (53.9)	16 (44.4)	
ASA 3 (%)	92 (42.2)	74 (40.6)	18 (50.0)	
ASA 4 (%)	5 (2.3)	4 (2.2)	1 (2.8)	
Diabetes (%)	64 (29.3)	59 (32.4)	5 (13.9)	0.042[a]
Comorbidities (%)	25 (11.5)	19 (11.5)	6 (16.6)	0.12
Rheumatoid arthritis (%)	7 (3.2)	7 (3.9)	0 (0.0)	
Cirrhosis (%)	5 (3.2)	4 (2.2)	1 (2.8)	
Long-term corticoids (%)	2 (0.9)	2 (1.2)	2 (0.0)	
Previous surgery for knee infection (%)	110 (50.5)	97 (53.3)	13 (36.1)	0.06
DAIR (%)	50 (22.9)	41 (22.5)	9 (25.0)	
1 stage (%)	15 (6.9)	14 (7.7)	1 (2.8)	
2 stage (%)	42 (19.3)	40 (22.0)	2 (5.5)	
Others (arthroscopic debridement) (%)	3 (1.4)	2 (1.1)	1 (2.8)	
Implants used for RTKA (%)				0.001[a]
Non constrained	42 (19.3)	39 (21.4)	3 (8.3)	
CCK	40 (18.3)	21 (11.5)	19 (52.8)	
RHK prosthesis	110 (50.5)	96 (52.8)	14 (38.9)	
Arthrodesis	26 (11.9)	26 (14.3)	0 (0.0)	
Surgical flap (%)				0.088
Local	23 (10.6)	22 (12.1)	1 (2.8)	
Free	3 (1.4)	3 (1.7)	0 (0.0)	
Spacer	176 (80.7)	176 (96.7)	0 (0.0)	
Mobile	122 (67.2)	122 (67.0)	0 (0.0)	
Non mobile	54 (29.7)	54 (29.7)	0 (0.0)	
Rank of the new prothesis (mean) (%)		2.63 ± 0.8	2.19 ± 0.6	0.001[a]
2	128 (58.7)	97 (53.3)	31 (86.1)	
3	67 (30.7)	63 (34.6)	4 (11.1)	
4	16 (7.3)	16 (8.8)	0 (0.0)	
5	6 (2.7)	5 (2.8)	1 (2.8)	
6	0 (0.0)	0 (0.0)	0 (0.0)	
7	1 (0.4)	1 (0.5)	0 (0.0)	
TTO (%)	66 (30.3)	57 (31.3)	9 (25.0)	0.58
Extensor mechanism allograft (%)	3 (1.4)	0 (0.0)	3 (8.3)	0.004[a]

BMI, body mass index; RKCC, revision knee complexity classification; ASA, American Society of Anaesthesiologists; DAIR, debridement, antibiotics, and implant retention; CCK, condylar constrained knee; RHK, rotating hinge knee; TTO, tibial tuberosity osteotomy.
[a] $P < 0.05$.

Surgical Strategy

The surgical strategy was based on the well-defined recommendations from the Philadelphia consensus and the study of Oussedik et al. [10,14,15]. The one-stage strategy was indicated if there was no sign of systemic sepsis, no additional skin coverage, no severe bone loss necessitating use of a distal femoral or proximal tibial arthroplasty implant, and no multiresistant organism [10,16]. The two-stage strategy was used if any of the contraindications of the one-stage strategy were present. For the two-stage revision, the reimplantation was performed a minimum of six weeks after the explantation [17]. Intravenous antibiotic therapy was continued for 15 days following each procedure while awaiting the final microbiological results and then adapted secondarily with an oral antibiotic if possible. Given that prosthesis infections are treated for three months, antibiotic therapy was not interrupted at six weeks to create an antibiotic

Table 2
Distribution of the Microorganisms Responsible for TKA Infections (218 TKA).

Micro Organisms	Two Stage	One Stage
	n = 182, (%)	n = 36, (%)
Methicillin-susceptible S. aureus	24 (13.2)	6 (16.7)
Methicillin-resistant S. aureus	6 (3.3)	1 (2.8)
Methicillin-susceptible CNS	28 (15.4)	9 (25.0)
Methicillin-resistant CNS	27 (14.8)	5 (13.9)
Streptococcus spp	17 (9.3)	2 (5.6)
Gram-negative bacilli	10 (5.5)	1 (2.8)
Cutibacterium acnes	10 (5.5)	1 (2.8)
Others	7 (3.9)	4 (11.1)
Polymicrobial	27 (14.8)	2 (5.6)
Culture-negative infection with positive anatomopathology	26 (14.3)	5 (13.9)

TKA, total knee arthroplasty; CNS, coagulase-negative staphylococci.

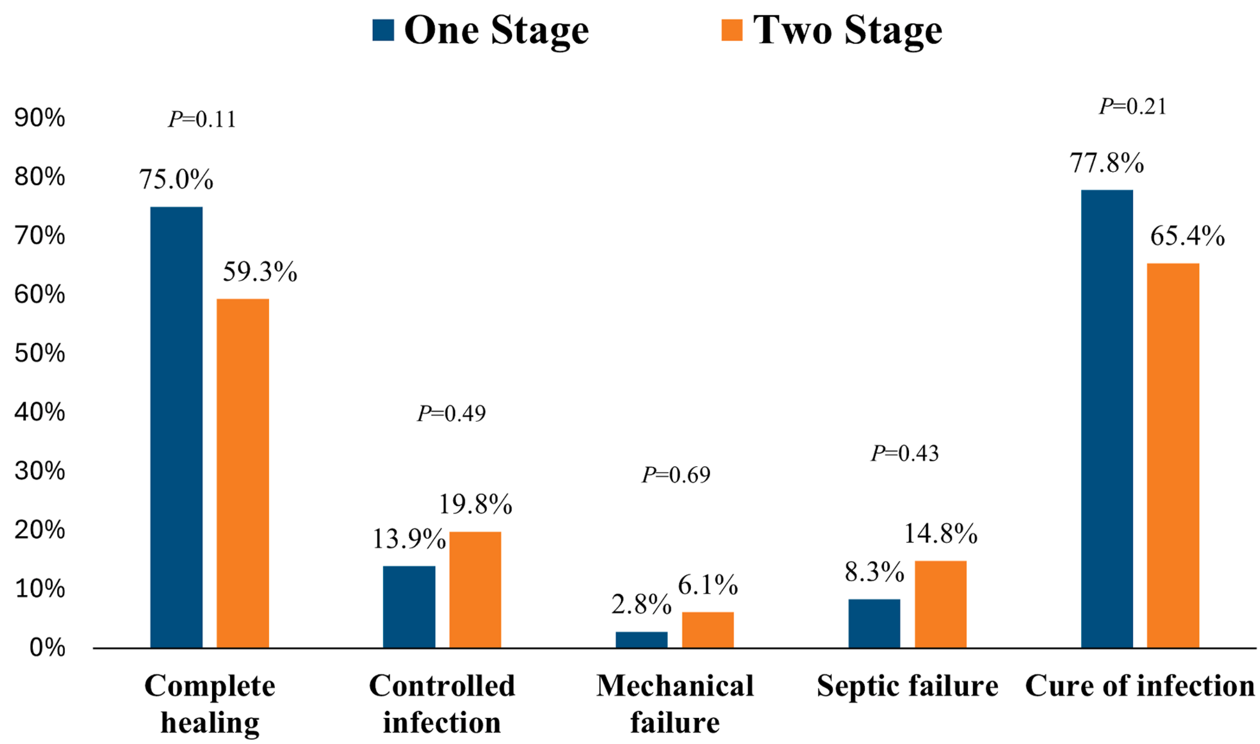

Figure 2. One- and two-stage outcomes according to the 5 overlapping groups: mechanical failure, septic failure, controlled infection, cure of infection, and complete healing.

Table 3
Outcomes, Revisions and Complications.

Outcomes, Revisions and Complications	Two Stage (%)	One Stage (%)	*P*-Value
Outcomes	n = 182	n = 36	0.36
Complete healing	108 (59.3)	27 (75.0)	0.11
Controlled infection	36 (19.8)	5 (13.9)	0.49
Mechanical failure	11 (6.1)	1 (2.8)	0.70
Septic failure	27 (14.8)	3 (8.3)	0.43
Cure of infection	119 (65.4)	28 (77.8)	0.21
Cause of RTKA for mechanical failure	11 (6.1)	1 (2.8)	0.33
Aseptic loosening	8 (4.4)	0 (0.0)	
Periprosthetic fracture	0	1 (2.8)	
Hinge fracture	1 (0.6)	0 (0.0)	
Femoral stem fracture	1 (0.6)	0 (0.0)	
Femoro patellar instability	1 (0.6)	0 (0.0)	
Surgery for septic failure	27 (14.8)	3 (8.3)	0.83
One-stage revision	7 (3.8)	0 (0.0)	
Two-stage revision	9 (4.9)	2 (5.5)	
Prosthesis removal	3 (1.6)	0 (0.0)	
Trans femoral amputation	8 (4.4)	1 (2.8)	
Reoperation for septic etiology without implant revision	29 (15.9)	4 (11.1)	1.0
DAIR	23 (12.6)	4 (11.1)	
DAIR + phagotherapy	4 (2.2)	0 (0.0)	
DAIR + stimulan	2 (1.1)	0 (0.0)	
Re-operation for mechanical etiology without implant revision	15 (8.2)	4 (11.1)	0.89
Open arthrolysis	1 (0.5)	0 (0.0)	
Arthroscopic arthrolysis	2 (1.1)	1 (2.8)	
Patellar tendon reconstruction	2 (1.1)	0 (0.0)	
Clunk resection	0 (0.0)	1 (2.8)	
TKA dislocation reduction	1 (0.5)	1 (2.8)	
Extensor mechanism allograft	2 (1.1)	0 (0.0)	
Femur fracture osteosynthesis	1 (0.5)	0 (0.0)	
MPFL reconstruction + TTO	1 (0.5)	0 (0.0)	
PE insert augmentation	2 (1.1)	0 (0.0)	
Patellar lateral facectomy	1 (0.5)	0 (0.0)	
Common fibular nerve neurolysis	0 (0.0)	1 (2.8)	
TTO fracture osteosynthesis	1 (0.5)	0 (0.0)	
Tibia fracture osteosynthesis	1 (0.5)	0 (0.0)	

RTKA, revision total knee arthroplasty; DAIR, debridement, antibiotics, and implant retention; TKA, total knee arthroplasty; MPFL, medial patello femoral ligament; TTO, tibial tuberosity osteotomy; PE, polyethylene.

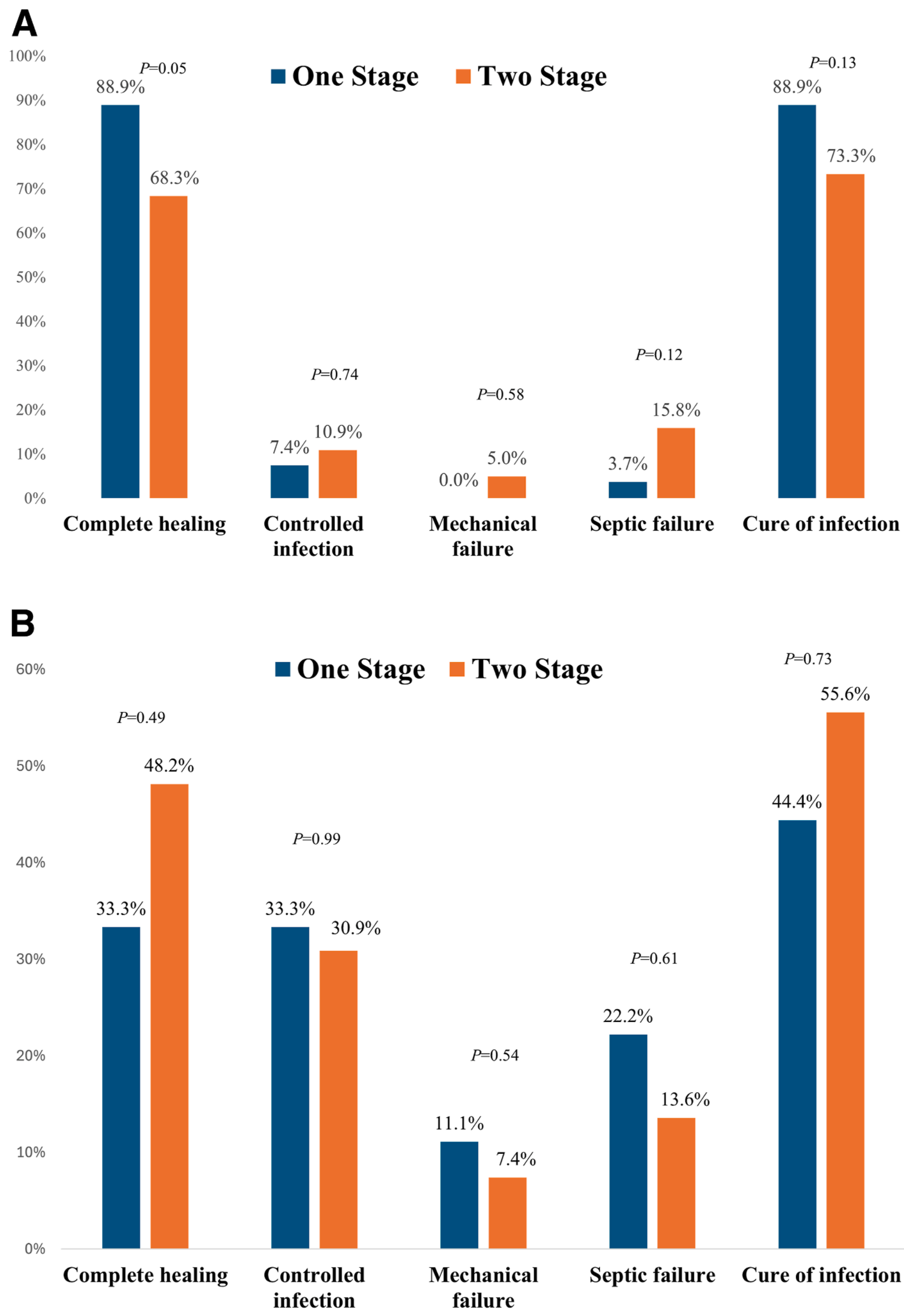

Figure 3. (A) One-stage and two-stage outcomes in the R2 population (RKCC) according to the 5 overlapping groups. (B) One-stage and two-stage outcomes in the R3 population (RKCC) according to the 5 overlapping groups. RKCC, revision knee complexity classification.

window before the second surgery. As such, the reimplantation procedure took place under effective antibiotic therapy. Nevertheless, samples were taken at the time of reimplantation. In cases of a long period between the two interventions for the two-stage strategy, antibiotic therapy was continued for three months, followed by an antibiotic window of at least 15 days before reimplantation.

The complexity of the revision surgery was assessed using the revision knee complexity classification (RKCC): R1 or “less complex revision surgery,” R2 or “complex revision surgery,” “R3 or most complex and salvage cases” [18,19]. Although a revision for “recurrent infection” is classified as R3, we chose to classify patients who have a history of debridement, antibiotics, and implant retention as R2, as we defined revision as the replacement of all implants.

Surgical Technique

All surgery protocols (one-stage or two-stage revisions) were discussed and decided during regional multidisciplinary team meetings. The choice of constraint of the new implant was assessed clinically and radiologically during preoperative planning and confirmed intraoperatively (Table 1). For two-stage revision, an antibiotic-impregnated cement spacer (PALACOS Gentamicin (Heraeus Kulzer GmbH & Co, Wehrheim, Germany)), with manually added vancomycin (one gram of vancomycin per one dose of

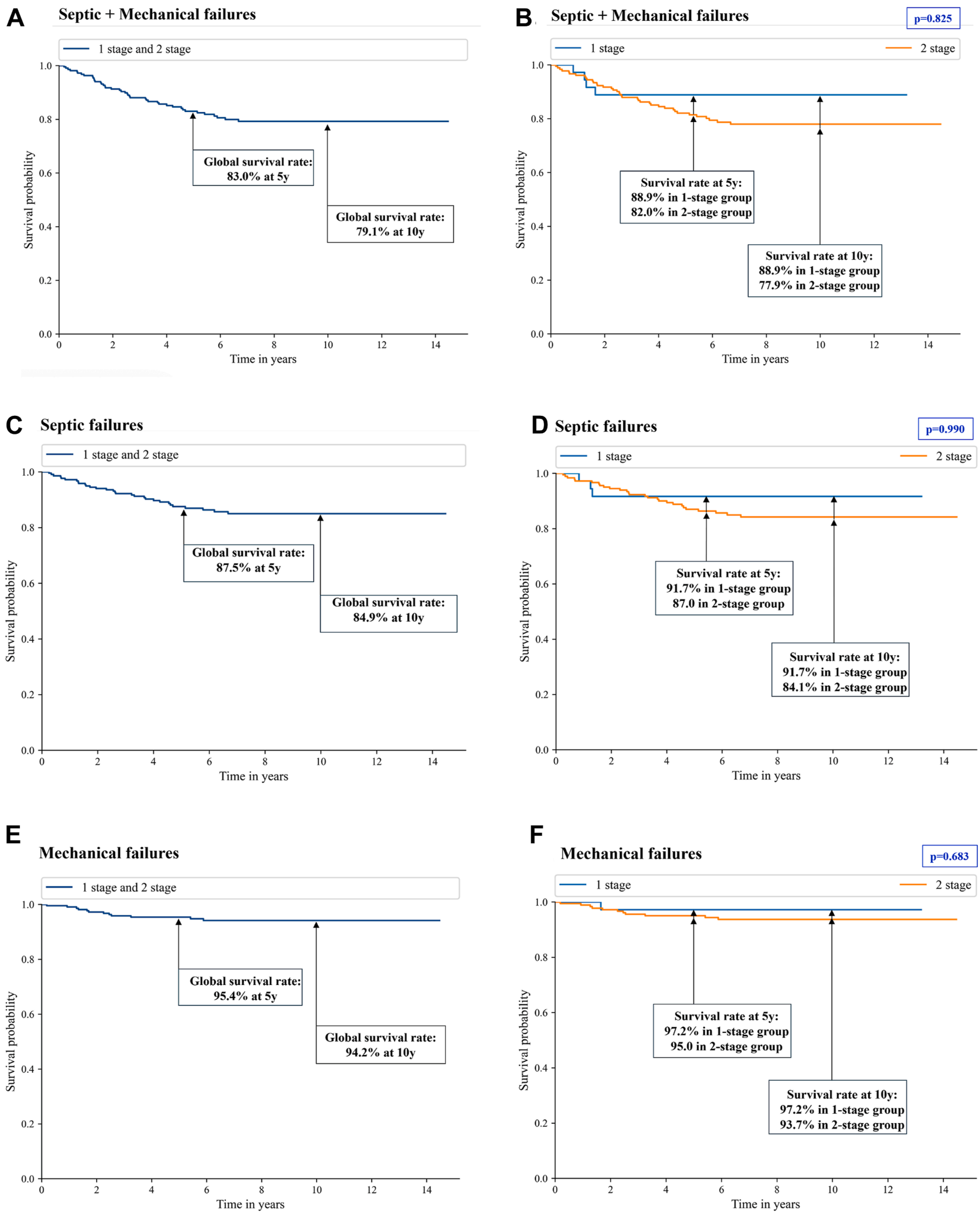

Figure 4. (A and B) Survival curves with septic and/or mechanical failures as endpoints in the whole cohort (A) and in the one- and two-stage cohorts (B). (C and D) Survival curves with septic failures as endpoints in the whole cohort (C) and in the one- and two-stage cohorts (D). (E and F) Survival curves with mechanical failures as endpoints in the whole cohort (E) and in the one- and two-stage cohorts (F).

Figure 5. Complete healing after a one-stage strategy for a patient classified R2. Case of a 68-year-old man who had a chronic Methicillin-susceptible CNS infection on his right TKA (A). He underwent a one-stage revision with the implantation of a CCK prosthesis (B). He was classified as a completely healed at a 3-year follow-up. CNS, coagulase-negative staphylococci; TKA, total knee arthroplasty; CCK, constrained condylar knee.

cement) was inserted during the first surgery. Dynamic spacers were used when possible. A static spacer was used for the following situations: severe bone loss, unhealthy soft tissue, extensor mechanism deficit, and collateral ligament insufficiency.

Outcomes Assessment

All patients had standardized follow-up, consisting of consultations at two weeks, six weeks, three months, and six months after reimplantation, and then an annual consultation. Patients treated with two-stage revision were also followed at two and four weeks after the first surgery. Radiographic evaluation was made at each consultation, with an antero-posterior view, lateral view, full long-leg X-ray, and patella skyline view.

Patients were classified into five overlapping groups: mechanical failure (revision for mechanical cause), septic failure (revision for persistent or new infection), controlled infection (no revision but suppressive antibiotic therapy), cure of infection (no revision for infection and no suppressive antibiotic therapy), and complete healing (no revision, no suppressive antibiotic therapy). Patients can be classified into one or two groups. Revision was defined as the need for a new surgery with implant replacement. Patients undergoing subsequent surgery for septic or mechanical etiology without implant removal and no suppressive antibiotic therapy at the last follow-up were classified as "complete healing." Additionally, possible complications and their assessments were also collected.

Data Analyses

Statistical analyses were performed with EasyMedStat version 3.28 (www.easymedstat.com). Continuous variables were described using means, SDs, and ranges. Categorical variables were described using counts (percentages), whereas categorical outcomes were compared using Fisher's exact and *Chi*-square tests. Normally distributed continuous variables were compared using Student *t*-tests. The survival rates were calculated using the Kaplan–Meier method, with a 95% confidence interval, based on the following endpoints: mechanical and/or septic failures. The multinomial logistic regression model was employed to investigate risk factors of failures, including classical demographic data and all the data that emerged as relevant from the univariate analysis. A *P*-value < 0.05 was considered statistically significant for all analyses.

Ethical Approval

All procedures were performed in accordance with the ethical standards of the institutional and/or national research committee, the 1964 Helsinki Declaration and its later amendments, or comparable ethical standards. Data collection and analysis were carried out in accordance with MR004 Reference Methodology from the Commission Nationale de l'Informatique et des Libertés (Ref. 2229975V0) obtained on May 6, 2023. The study was registered and filed on the Health Data Hub website.

Results

At the most recent follow-up, 135 patients (61.9%) had fully recovered (complete healing), 30 (13.8%) presented with septic failure, 12 (5.5%) with mechanical failure, 147 (67.4%) were infection-cured, and 41 (18.8%) had a controlled infection (Figure 2). In the two-stage revision group, 27 patients (14.8%) presented with septic failure and 11 (6.1%) with mechanical failure, versus three (8.3%) and one (2.8%) in the one-stage revision group, respectively ($P = 0.36$). The three patients who had septic failure in the one-stage group respected the recommendations to perform one-stage surgery. The rate of complete healing was not statistically different between one-stage (75.0%) and two-stage (59.3%) ($P = 0.11$). Both groups had no significant difference in the septic and mechanical complications (Table 3). There were 128 "R2" or "complex revision cases" (58.7%) and 90 "R3" or "most complex

Figure 6. Complete healing after a two-stage strategy with a prosthesis arthrodesis for a patient classified R3. Case of a 69-year-old woman who had a chronic *Pseudomonas aeruginosa* infection on her right TKA, with a previous failed two-stage revision and an active fistula (A). She underwent a two-stage revision, with initially a dynamic spacer (B) that had to be changed because of a knee posterior dislocation (C) to a static spacer (D). She was reimplanted 5 months later with a prosthesis-arthrodesis (E), and she is now completely healed at a 3-year follow-up. TKA, total knee arthroplasty.

cases or salvage cases" (41.3%). Within the "R3" category, 57 patients (26.1%) had a history of failed septic revision on the same knee. There were significantly more "R3" in the two-stage group versus the one-stage group (44.5 versus 25.0%, $P = 0.047$) (Table 1). The one-stage and two-stage outcomes in the R2 and R3 populations according to the RKCC are shown in Figure 3. The survival rate without septic failure was 84.9% at 10 years for the whole cohort (Figure 4).

For patients reoperated for septic causes, a new microorganism was found in 50.9% of cases; the remaining patients had a recurrent infection with the same organism (49.1%). Patients who had no prior surgery for PJI had a significantly superior rate of complete healing than those who did (70.4 versus 53.6%, $P = 0.016$). Additionally, patients classified as R3 had a significantly inferior rate of complete healing compared to the R2 category (46.7 versus 72.7%, $P < 0.001$) (Figures 5 through 7).

There was no significant difference between dynamic and static spacers in terms of complete healing (63.9 versus 51.2%, $P = 0.18$), septic failure (14.8 versus 13.0%, $P = 0.82$), or mechanical failure (5.0 versus 9.3%, $P = 0.32$).

There was no difference in terms of complete healing between one- and two-stage strategies in the population of negative-culture cases (Table 4).

Patients who required a flap had a significantly lower chance of complete healing (30.8 versus 66.2%, $P = 0.001$) and a significantly greater risk of suppressive antibiotic therapy (42.3 versus 15.6%, $P = 0.003$) than those not requiring a flap.

In multivariate analyses, the requirement of a flap (odds ratio [OR] = 0.28, [0.11 to 0.72]), RKCC grade R3 (OR = 0.37, [0.21 to 0.68]), and an American Society of Anesthesiologists (ASA) score >2 (OR = 0.51, [0.28 to 0.93]) were associated with lower rates of infection healing (Table 5). A one-stage revision (OR = 1.64, [0.70

Figure 7. Mechanical failure after a two-stage strategy for a patient classified R3. Case of a 60-year-old patient who had a chronic infection of his left TKA (A). He was initially treated with a two-stage strategy with a static spacer and a medial gastrocnemius muscle flap (B). During the second stage, a hinge prosthesis was implanted, and a tibial tubercle osteotomy was needed for exposure (C). He was reoperated on 5 years after for a femoral loosening (D) with a one-stage revision and implantation of a mega-prosthesis (E). More than 3 years after the last revision, he walks without crutches and has a full range of motion. TKA, total knee arthroplasty.

to 3.85]) was not associated with a lower rate of complete healing.

Discussion

The main findings of this study were the satisfactory rate of complete healing and infection-cured status after one- or two-stage TKA revision for PJI despite 41.3% of very complex cases, thanks to a surgical strategy based on robust guidelines. Several risk factors for a low rate of complete healing have been identified: requirement of a flap, RKCC grade R3, and ASA score greater than 2.

Both the one- and two-stage strategies give good results in RTKA for PJI, with similar rates of complete healing (75.0 versus 59.3%) and infection-cured status (77.8 versus 65.4%) for the one-stage and two-stage strategies, respectively (Table 3). However, concluding the superiority of one-stage seems inappropriate. Indeed, the indications for these two strategies are usually

Table 4
Outcomes in Culture-Negative Infections Population.

Culture-Negative Infections Population	One Stage (%)	Two Stage (%)	P-Value
Outcomes	N = 5	N = 26	>0.99
Complete healing	4 (80.0)	17 (65.4)	
Controlled infection	0 (0.0)	1 (3.9)	
Mechanical failure	0 (0.0)	4 (15.4)	
Septic failure	1 (20.0)	4 (15.4)	
Cure of infection	4 (80.0)	21 (80.8)	

different. In this study, surgeries were markedly more complex in the two-stage group (44.5 R3 versus 25.0%, $P = 0.047$) (Table 1). In addition, patients benefiting from the two-stage strategy had more polymicrobial infections (14.8 versus 5.6%) and more skin disorders (13.8 of flaps versus 2.8%) (Tables 1 and 2). This result demonstrates the relevance of the surgical indications. The surgical strategy was based on the Philadelphia consensus and the literature [10,15]. In 2015, Haddad et al. reported in their series of 28 patients for one-stage surgery an impressive reinfection rate of zero percent reinfection rate after three years of follow-up [10]. They defined very strict recommendations for one-stage revision. These indications are based on the facility or difficulty managing the infections and/or the surgical reconstruction. The necessity of knowing the infective organism causing a PJI to propose a one-stage strategy remains a matter of debate. In this study, no difference in complete healing between one- and two-stage strategies was observed in the population of negative-culture cases. Thus, it does not appear as a contraindication to a one-stage strategy. These findings are consistent with the literature [20–22].

The studies in the literature were very heterogeneous, and no consensus was reached (Tables 6 and 7). Moreover, some published studies do not report the definition of failure nor detail the surgical strategies. This study classified patients into specific groups: mechanical failure, septic failure, controlled infection, cure of infection, and complete healing. To our knowledge, this was the first series to classify the results like this and with a large sample size. In this investigation, the rate of septic failure was 8.3% for the one-stage group and 14.8% for the two-stage group, showing no statistical difference among the surgical strategies ($P = 0.43$). Similar findings were reported by Goud et al. in a systematic review, stating that there was no difference in terms of reinfection between the one-stage (12.7%) and two-stage (16.2%) approaches [31]. Moreover, these values agree with reported failure rates by Bosco et al. in a systematic review focusing on one-stage revision (12.2%) [32]. However, our study included all patients who had RTKA for infection, particularly very complex cases (41.3%).

Exclusion criteria were common in one- or two-stage TKA review studies (Tables 6 and 7). Singer et al. reported a low failure rate of one-stage revision (4.8%), excluding MRSA- and MRSE-caused infections [11]. Furthermore, Pellegrini et al. reported a failure rate of 0% for a one-stage strategy but excluded infections caused by multiresistant organisms [12]. In another approach, Petis et al. excluded all patients who had previous PJI treatment [13]. In this study, no restrictive exclusion criteria were applied. In addition, the fact that this study was carried out in a regional reference center increases the number of complex cases (41.3% of "R3" or "most complex cases or salvage cases" according to RKCC classification [18,19]). Thus, this allows the extrapolation of these results to any patient attending PJI from a TKA.

Several predictive factors of poor outcomes or failure after one- or two-stage TKA revision have been reported in the literature. In this study, patients who had a history of previous septic procedures on the same TKA had significantly ($P = 0.016$) poorer outcomes (53.6%) of complete healing than those who did not (70.4%). These findings are consistent with the literature. Abdelaziz et al. reported that a history of a previous septic revision was associated with a significantly increased risk of further surgery requiring cone revision ($P < 0.001$) [26]. Patients who had a history of prior PJI treated with two-stage revision also tended to have more static spacers (74.1 versus 25.9%, $P < 0.001$). The more considerable bone loss in these cases may explain this finding. Furthermore, there was no difference in healing or failure between static and dynamic spacers, which is consistent with the literature [33].

Inadequate glycemic control is associated with a greater risk of infection after primary TKA [34]. In this study, diabetes was not significantly associated with a lower risk of healing in multivariate analysis. However, our anesthetic team made diabetes control and good glycated hemoglobin mandatory at the time of surgery.

Patients who required a flap had a significantly lower probability of complete healing in multivariate analysis (OR = 0.28, $P < 0.01$), consistent with the literature. McCulloch et al. reviewed 30 patients who had gastrocnemius flaps for PJI and showed a failure rate of 52% at the last follow-up [35]. Similar results were reported by Tetreault et al. in a retrospective study [36]. The need for a flap indicates the objective of a limb salvage strategy and, therefore, a higher failure rate in treating PJI.

Identifying risk factors for failure, independent of the one- or two-stage surgical strategy, is of major interest to the orthopaedic community. This knowledge is crucial not only for providing accurate patient information but also for evaluating the indications for combined suppressive antibiotic therapy [37].

This study has several potential limitations. This study was monocentric and retrospective. Nevertheless, the collected outcomes were objective and easily found in the patient's medical files. The database was collected prospectively, and the minimum 2-year follow-up ensures that most complications or revisions will have been identified. The monocentric characteristic allowed for a standardized protocol to manage the PJI after TKA with similar criteria for every patient. Then, the patients were not randomized between one- and two-stage procedures. However, the indications for these strategies were different. Using well-defined indications and recommendations appears more logical in extrapolating the results to current practice. Additionally, patients are very different, even within the same surgical strategy group, because of various organisms, bone loss, skin problems, etc. This is an inherent problem in studies of bone infections.

This monocentric, retrospective study has a large sample size, no restrictive exclusion criteria, and well-defined failure groups. Moreover, the surgical strategy criteria (between one and two stages) were clearly defined and based on solid recommendations.

Table 5
Predictive Factors for Complete Healing (Multivariable Analysis).

Predictive Factors	Odds Ratio	P-Value
ASA score > 2	0.51 (0.28 to 0.93)	0.03[a]
One-stage revision	1.64 (0.70 to 3.85)	0.26
RKCC		
R3	0.37 (0.21 to 0.68)	<0.01[a]
Flap	0.28 (0.11 to 0.72)	<0.01[a]

ASA, American Society of Anesthesiologists; RKCC, revision knee complexity classification.
[a] $P < 0.05$.

Table 6
Publications Reporting Results of Failure Rate of One-Stage Septic Exchange After TKA Since 2010 With Minimum 2-Years Follow-Up.

Author	Year	Sample Size	Follow-Up (years)		Mean Age at Revision	Definition of Failure	Risk Factors for Failure	Failure Rate (%)	Exclusion Criteria	Criteria for One-Stage Revision	Journal
			Mean	Range							
Whiteside et al. [23]	2011	18	5.2	2.2 to 6.2	69 ± 6 (58 to 84)	-	-	1 (5.5)	All bacteria but MRSA	-	Clin Ortho
Singer et al. [11]	2012	63	3	2 to 5	70 ± 10.5 (31 to 89)	Subsequent revision for recurrent infection	Duration of the original infection	3 (4.8)	MRSA and MRSE	- Known microorganism with an ATB susceptibility profile - Wounds that could be closed during surgery - Infection caused by MRSA et MRSE	Clin Ortho
Tibrewal et al. [24]	2014	50	10.5	2 to 24	66 (42 to 84)	Subsequent revision for any cause Subsequent revision for recurrent infection	-	10 (20.0) 1 (2.0)	-	- Bacteriologically proven infection - Identified organism - Available culture and sensitivities - Intact soft-tissue cover of the knee.	BJJ
Haddad et al. [10]	2015	28	6.5	3 to 9	65 (45 to 87)	Infection at last FU according to Musculoskeletal Infection Society definition of PJI	-	0.0	MRSA and MRSE	- No bone loss - No major soft tissue defect - Nonimmunosuppressed host - Isolation of a single low virulent organism preoperatively sensitive to bactericidal antibiotics	Clin Ortho
Zahar et al. [25]	2016	70	10	9 to 11	70 (60 to 81)	Revision surgery for infection or any other cause	-	5 (7.0)	- Culture-negative preoperative aspiration - Known allergy to local antibiotics or bone cement - Prosthesis other that rotating hinge - Cases in which radical debridement was impossible as a result of the involvement of important anatomical structures	- Diagnostic of PJI with preoperative known causative organism - No known allergy to local antibiotics or bone cement	Clin Ortho
Leta et al. [9]	2019	72	5.1	0.01 to 21.9	69 (9.5)	Subsequent revision for any cause/subsequent revision for septic cause	_	15 (20.8)/10 (13.9)	Unipolar revision	_	JBJS Rev
Abdelaziz et al. [26]	2019	72	4.2 ± 1.6	2 to 7.3	70 ± 8.2	Septic failure: patients with local or systemic symptoms of infection, needing further surgery as a result of persistent PJI or due to reinfection with new pathogens/patients who died after generalized sepsis Aseptic failure: if any procedure in which a component exchange was performed for reasons unrelated to PJI or sepsis	History of previous septic revision	8 (11.1) for septic failure and 7 (10.0) for mechanic failure	- Previous multiple failed one-stage procedures - Intraoperative findings such as the extension degree of bone and soft tissue infection including the involvement of neurovascular structures	- Known causative organism	JoA
Holland et al. [27]	2019	25	3	2 to 8.5	72 ± 7.4	Recurrence of infection	-	1 (4.0)	- Life-threatening sepsis requiring urgent joint washout and debridement	- No life-threatening sepsis requiring urgent joint washout and debridement	J Knee Surg
Pellegrini et al. [12]	2021	20	6.2	2 to 10	67 ± 10.2	-	-	0.0	- Multiresistant microorganisms	- Known organisms with known sensitivity.	Expert Rev Anti

(*continued on next page*)

Table 6 (*continued*)

Author	Year	Sample Size	Follow-Up (years)		Mean Age at Revision	Definition of Failure	Risk Factors for Failure	Failure Rate (%)	Exclusion Criteria	Criteria for One-Stage Revision	Journal
			Mean	Range							
										- No diabetes, immunosuppression - Healthy soft tissue with minimal or moderate bone loss	Infect Ther
Ji et al. [28]	2023	132	4.5	2 to 7.1	68 (40 to 86)	Recurrence of an infection in the same knee. Mechanical failure as the loss of function of the prosthesis and/or unfavorable relationships between the prosthetic components and adjacent bone and soft tissue attachments	-	6.8 reinfection 2.3 mechanical failure 9.1 global	- Prosthesis other than CCK	-	J Knee Surg

TKA, total knee arthroplasty; MRSA, methicillin-resistant *Staphylococcus Aureus*; MRSE, methicillin-resistant *Staphylococcus epidermidis*; CCK, constrained condylar knee; ATB, antibiotics; PJI, periprosthetic joint infection.

Conclusions

Both one- and two-stage TKA revisions for PJI achieved satisfactory rates of complete healing and cure of infection despite 41% of very complex cases. A surgical strategy based on robust guidelines is mandatory to manage these PJIs. Patients classified as R3 according to the RKCC classification, those requiring a flap, and those who have an ASA score of 3 or 4 were at higher risk of failure. These patients may be considered potential candidates for suppressive antibiotic therapy.

CRediT authorship contribution statement

Jean Baltzer: Writing – original draft, Methodology, Formal analysis, Data curation, Conceptualization. **Timothy Lording:** Writing – review & editing, Validation, Methodology. **Tomas Pineda:** Writing – review & editing, Validation, Methodology, Formal analysis, Data curation. **Tristan Ferry:** Writing – review & editing, Validation, Methodology. **Elvire Servien:** Writing – review & editing, Validation, Methodology. **Sébastien Lustig:** Writing – review & editing, Validation, Supervision, Methodology, Conceptualization. **Cécile Batailler:** Writing – review & editing, Validation, Supervision, Methodology, Formal analysis, Conceptualization.

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Table 7
Publications Reporting Failure Rate of Two-Stage Septic TKA Revisions With Long Follow-Up or a Larger Study Cohort Since 2010.

Author	Year	Sample Size	Follow-Up		Mean Age at Revision	Definition of Failure	Main Risk Factors	Failure Rate (%)	Exclusion Criteria	Notes	Journal
			Mean	Range							
Mahmud et al. [29]	2012	253	4 (median)	1 to 17	70 ± 10	Additional surgery for either septic or aseptic reasons Septic failure: pain and/or a loose prosthesis with an increased CRP and a positive culture report from joint aspiration, and/or an abnormal cell count, and/or intraoperative histology consistent with infection.	-	Total failure = 33/253 = 13.0 Septic failure = 6.3 Aseptic failure = 6.7	-		Clin Ortho
Lindberg Larsen et al. [8]	2016	215	3.2 (median)	2.2 to 4.2	69 ± 10	- Surgically related death 90 days postoperatively - Re-revision due to infection - Not reaching the second stage		65/215 (30.0)	-	-	Acta Orthop.
Triantafyllopoulos et al. [30]	2017	239	11	2 to 18.2	65	Infection recurrence	- Women - Heart disease - Psychiatric disorders	9.2	-	Patients with negative culture were excluded from failure analysis	JoA
Leta et al. [9]	2019	243	5.1	0.01 to 21.9	69 (9.7)	Subsequent revision for any cause/Subsequent revision for septic cause	-	36 (14.8)/10 (11.5)	Unipolar revision	-	JBJS Rev
Petis et al. [13]	2019	245	14	2 to 25	68 (33 to 91)	Revision for reinfection	- BMI >30 - Previous revision surgery - McPherson C	41/245 (16.7)	- Any prior treatment for PJI - Follow-up < 2 years	381 cases excluded due to previous PJI treatment	JBJSAm

CRP, C-reactive protein; PJI, periprosthetic joint infection.

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Appendix

Supplementary Material 1

The Criteria Established During the International Consensus Meeting in Philadelphia in 2018 Were Used to Perform the Diagnosis of the Periprosthetic Infection.

Major Criteria (At Least One of the Following)	Decision
Two positive growths of the same organism using standard culture methods Sinus tract with evidence of communication to the joint or visualization of the prosthesis	Infected

Minor Criteria	Threshold		Score	Decision
	Acute[a]	Chronic		
Serum CRP (milligrams/liter) or D-Dimer (micrograms/liter)	100 unknown	10 86	2	Combined preoperative and postoperative score: ≥6 ***infected*** 3 to 5 inconclusive[c] <3 not infected
Elevated serum ESR (millimeters/hour)	No role	30	1	
Elevated synovial WBC (cells/ microliter) or Leukocyte esterase or Positive alpha-defensin (signal/ cutoff)	10,000 ++ 1.0	3,000 ++ 1.0	3	
Elevated synovial PMN (%)	90	70	2	
Single positive culture			2	
Positive histology			3	
Positive intraoperative purulence[b]			3	

CRP, C-reactive protein.

[a] This criteria were never validated on acute infections.

[b] No role in suspected adverse local tissue reaction.

[c] Consider further molecular diagnostics such as next-generation sequencing.