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Original article

Above-the-knee amputation versus knee arthrodesis for revision of infected total knee arthroplasty: recurrent infection rates and functional outcomes of 43 patients at a mean follow-up of 6.7 years.

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Abstract

Introduction

In cases of repeated treatment failure of periprosthetic joint infections (PJI) of the knee, above-the-knee amputation (AKA) or knee arthrodesis can be proposed to reduce the risk of recurrent infection, especially in cases with major bone defects or irreparable damage to the extensor mechanism of the knee. Since AKA versus knee arthrodesis results have been rarely assessed for these indications, we conducted a retrospective case-control study to compare both the rates of recurrent infection and functional outcomes.

Hypothesis

Patients who underwent AKA had fewer recurrent infections than those who had arthrodesis.

Materials and Methods

Twenty patients who underwent AKA and 23 patients who had knee arthrodesis, between 2003 and 2019, were retrospectively included in this study. These two groups were comparable in age (73.8 versus 77.7 years (*P* = .31)) and sex (10 women and 10 men versus 16 women and seven men (*P* = .19)). Each group was analyzed individually and then compared in terms of survival (recurrent infection) and functional outcomes using clinical assessment scores (visual analog scale (VAS), French neuropathic pain questionnaire (DN4), Parker and Palmer mobility score and the 36-item short-form survey (SF-36)).

Results

The rate of recurrent infection was 10% (two out of 20 patients) for the AKA group and 21.75% (five out of 23 patients) for the arthrodesis group (*P* = .69).

The mean follow-up for the AKA group was 4.18 years (1.2-11.8) and 9.7 years (1.1-14.33) for the arthrodesis group (*P* = .002). The number of previous revisions (three (1.5-4) for AKA and two (2-3) for arthrodesis) and the time between the primary arthroplasty and surgical procedure were significantly greater in the AKA group (48.0 (12.0-102.0) months) than the arthrodesis group (48.0 (24.0-87.0) months) (*P* <.001).

The AKA group had significantly better clinical results for VAS (2.7 ± 2.2 vs. 3.1 ± 3.3), DN4 (1.5 ± 2.1 vs. 2.6 ± 2.9), Parker and Palmer (5.2 ± 1.7 vs. 4.6 ± 1.4), and SF-36 (30.9 ± 15.6 vs. 26.9 ± 17.0) (*P* <.001).

Conclusion

Above-the-knee amputation and knee arthrodesis showed no differences in the rate of recurrent sepsis. However, the comparison of the two groups demonstrated that patients who underwent an AKA had less pain, were more autonomous and had a better quality of life.

Level of Evidence: III; retrospective case-control

Keywords: above-the-knee amputation, knee arthrodesis, periprosthetic joint infection, septic revision surgery, sepsis

1. Introduction

Periprosthetic joint infection (PJI) is a major complication of total knee arthroplasty (TKA) occurring in around 2.1% of cases [1]. There is an international consensus regarding the different treatment modalities of knee PJI combining surgery and targeted antibiotic therapy once the causative infectious agent has been identified [2-3]. Despite recent advances, in particular after consensus conferences [2-4], some PJI are still resistant to the targeted treatment and require multiple joint procedures with poor functional outcomes. Some series in the literature report infection recurrence rates as high as 14 to 28% following revision TKA, thus resulting in severe morbidity and significant costs [4].

The two options often proposed in difficult-to-treat cases (significant bone defects, severe skin lesions, irreparable damage to the extensor mechanism of the knee) are arthrodesis (set with nailing or external fixation) [5] and above-the-knee amputation (AKA) [6-10]. These two extreme procedures are the only options to control the infection. Both arthrodesis and AKA lead to significant functional, esthetic, and psychological constraints for the patients. Few studies have assessed whether one procedure is superior to the other, both in terms of rate of recovery from infection and functional outcomes for those patients with infected TKA who failed to respond to therapy [11].

We performed a retrospective single-center case-control study comparing AKA and arthrodesis with intramedullary nailing as treatment for repeated TKA infections to compare both the rates of recurring infection and functional outcomes assessed using scores (visual analog scale (VAS), French neuropathic pain questionnaire (DN4), Parker and Palmer mobility score and the 36-item short-form survey (SF-36)). Our hypothesis was that patients who underwent AKA had fewer recurring infections than those who had arthrodesis.

2. Materials and methods

2.1 Patients

All patients who underwent AKA or arthrodesis for repeated TKA infections at the Regional University Hospital Center of Lille between 2003 and 2019 were included in this single-center study. TKA infection was defined according to the Musculoskeletal Infection Society (MSIS) criteria [2]. Twenty patients were enrolled in the above-the-knee group during the inclusion period, with five deaths occurring during the follow-up period. Twenty-three patients were enrolled in the arthrodesis group during the inclusion period with nine deaths occurring during the follow-up period. None of these deaths were related to the infection (Figure 1).

The principal characteristics of these two groups are summarized in Table 1. They were comparable except for two variables: the time between the primary TKA and the surgical procedure (amputation or arthrodesis) (*P* <.001) and the number of revisions performed before the amputation or arthrodesis (*P* <.001), which were higher in the AKA group.

In the AKA group, 35% of patients (7/20 patients) had sterile bacteriological specimens from the femoral resection and 35% of patients (7/20 patients) had positive polymicrobial bone resection specimens. *Staphylococcus aureus* (isolated or associated with another bacterium) was the cause of infection in seven of the 20 patients (35%) (Table 2).
In the arthrodesis group, 19/23 (82.6%) patients underwent a two-stage arthrodesis with nail fixation. Consequently, the long-term bacteriological analysis showed that 9/23 (39.1%) patients in this group had sterile specimens. Twelve of the 23 (52.8%) patients had bacteriological specimens from the operating site identifying a monomicrobial infection (Table 3).

2.2 Methods

Surgical indications were validated during a multidisciplinary team meeting at a French reference center for complex bone and joint infections (CRIOAC). AKA was indicated when a significant bone defect prevented arthrodesis and/or if there was an associated loss of soft tissue and/or if the patient requested this procedure after a reflection period and a visit to a rehabilitation center for amputees. Knee arthrodeses were performed in one or two stages and all involved fixation with an intramedullary nail. The first stage of a two-stage arthrodesis consisted of the removal of the septic TKA, bacteriological sample collection and the placement of an antibiotic-impregnated cement spacer. The patients were given concurrent empirical antibiotics therapy which was adapted to the intraoperative specimens. After an average of six weeks of targeted antibiotic therapy, a therapeutic window enabled lavage and the second stage of the procedure was performed. This second stage included the removal of the antibiotic-impregnated cement spacer, collection of new bacteriological specimens and the insertion of an arthrodesis nail. A new antibiotic therapy was administered according to the same modalities as in the first stage. The nail used was an uncemented modular Link™ nail (Link, Hamburg, Germany).
Bacteriological samples were collected for all cases, in particular from the amputation section and medullary cavity [12]. Intravenous empirical antibiotic therapy was administered immediately after surgery until the partial (D5) and final (D15) bacteriological results were received. This antibiotic therapy was then adjusted or stopped depending on whether a microorganism was found.

2.3 Assessment methods

All patients were clinically assessed by an independent observer. The different patient characteristics collected were age, age at surgery, age at primary TKA, sex, body mass index (BMI), smoking, chronic kidney disease, type of TKA, number of revisions, initial etiology, time between primary TKA and the surgical procedure, presence of staphylococcus in the collected specimens, follow-up, and postoperative neuropathic pain therapy. Recurrent sepsis was defined according to the MSIS criteria as the appearance of a new sepsis event that required a surgical procedure [2]. We screened for factors that may affect survival: age, sex, diabetes, BMI and number of revisions less or greater than three [13]. Functional scores (VAS, DN4, Parker and Palmer, SF-36) [14-16] were analyzed during the last follow-up.

2.4 Statistical methods

Descriptive statistics (frequency and percentage) were used to analyze the qualitative data. The normal distributions were analyzed using the mean and standard deviation, while the non-normal distributions were analyzed using the median and interquartile range. The normality of the data was verified using the Shapiro-Wilk test and a graphical method. Comparisons between the two groups (AKA and knee arthrodeses) were done using either the Chi^2 test or Fisher exact test (when conditions of validity of the Chi^2 test were not verified) for qualitative data, a Mann-Whitney U test for continuous non-normal distribution and a *t* test for continuous normal distribution. The median follow-up time was calculated using the Kaplan-Meier estimate and findings from both groups were compared with a log-rank test. Functional scores between the groups were compared with a Mann-Whitney U test. The Fine and Gray model was used to determine the factors associated with the onset of a new sepsis event, considering death without revision as a competing risk. Bilateral tests were performed with a significance level of 5%. Statistical analyses were done using SAS software (SAS Institute version 9.4).

3. Results

3.1 Assessment of recurrent infection

In the AKA group, 2/20 (10%) patients underwent revision surgery. The revision procedures were performed early, at one and three months from the primary TKA. The rate of recurrent sepsis was 10% (no recurrence of infection in 18 patients) at a mean follow-up of 4.18 years (1.2-11.8) ± 3.97 years. The two patients who underwent a revision had abnormal wound healing (dehiscence and persistent discharge). The surgical procedure consisted of scar revision with lavage and collection of new specimens, followed by a targeted antibiotic therapy.

In the arthrodesis group, 5/23 (21.75%) patients required revision surgery. The mean time from primary TKA to revision was 70.6 months (0.5-161). The rate of recurrent infection was 21.75% (no recurrence of infection in 18 patients) at a mean follow-up of 9.7 years (1.1-14.33) ± 4.73 years. All of the five patients who underwent revision had a recurring infection according to the MSIS classification. One patient underwent a simple surgical lavage with specimen collection, one patient had a one-stage arthrodesis nail exchange, and three patients underwent a two-stage arthrodesis nail exchange (of these three patients, one relapsed and was left to heal by secondary intention by controlling fistula drainage).

There was no significant difference in recurring infection between both groups (P = .6949 95% confidence interval (CI); 0.288-6.461) (Figure 2). We did not find any factors influencing recurrent sepsis (Table 4).

3.4 Assessment of functional scores

Functional score results are summarized in Table 5. In the AKA group, the mean VAS at follow-up was 2.67/10 (min-max: 0-7). The mean DN4 score at follow-up was 1.53 (min-max: 0-6). The mean Parker and Palmer mobility score at follow-up was 5.2 (min-max: 3-7). The mean SF-36 score was 30.88 (min-max: 9.3-56.5).

In the arthrodesis group, the mean VAS at follow-up was 3.07/10 (min-max: 0-10). The mean DN4 score at follow-up was 2.64 (min-max: 0-8). The mean Parker and Palmer mobility score at follow-up was 4.64 (min-max: 3-8). The mean SF-36 score was 33.78 (min-max: 9.1-64.4).

The AKA group had significantly better VAS, DN4, Parker and Palmer, and SF-36 scores (P <.001 for all four scores) (Table 5).

4. Discussion

Our study did not show any significant differences between both procedures in terms of risk of recurrent infection. There are few series in the literature on this subject. Only Hungerer et al [17] reported no significant difference in the onset of recurrent infection between knee arthrodesis and AKA (P = .25).

Our rate of recurrent sepsis in knee arthrodesis with nail fixation was comparable to the data reported in the literature, with a rate of recurrent infection between 20 and 50% [13, 18-19]. Our study observed a rate of recurrent infection for AKA (10%) that was lower than reported in the literature (20 to 40%) [17, 20-21]. This difference could be explained by the smaller number of amputee patients in our study, the short time to follow-up, as well as the significant number of deaths in this group.

Although there were no significant differences in epidemiological data between the two groups (Table 1), the patients in the AKA group had the most severe infections (higher number of recurrences and revisions and higher number of recurrent infections with different microorganisms postoperatively) (Table 2). This study showed a lower rate of recurrent infection in the AKA group, but the difference was minimal. While AKA may be perceived as a last resort treatment, especially when all unfavorable elements (skin, bone and infection) are present; arthrodesis remains a conservative intermediate solution that should be considered before AKA, in particular when it is performed using an intramedullary nail [22-23].

Our study showed a significant difference in functional scores between both groups, with better results in the AKA group. Amputee patients had better VAS, Parker and Palmer, DN4 and SF-36 scores. However, other studies [24-25] have shown that these two procedures often led to chronic pain, decreased functional capabilities, and consequently reduced the patients' autonomy and morale. However, some patients in the AKA group were being treated for neuropathic pain (Table 1) and had better pain and functional recuperation results than patients in the arthrodesis group. This demonstrates the need for systematic pain assessment and therapeutic pain management. AKA should therefore not be perceived as a last resort procedure with poor outcomes, but rather as an option for patients who are not responding to the treatment for their infected TKA [10, 26], and this regardless of the size of the femoral resection, the use of distal femoral implants to fit patients with a prosthesis and the ability to walk properly [27]. However, the addition of a distal implant exposes the patient to the risk of infectious or non-infectious loosening [28].

Our study had several limitations:

1) The retrospective nature of our study contributed to information bias, particularly the pre- and postoperative data. Even so, none of the patients in our series were lost to follow-up between the primary TKA and clinical reassessment, and all patients were evaluated by a single independent observer.

2) Our sample size was small. In fact, we did not find any significant differences regarding the main clinical analysis criteria, namely the recurrent sepsis. However, our results were consistent with the only current series in the literature focusing on the management of patients with repeated revisions for infected TKA from Hungerer et al [14]. Despite a larger cohort (N = 81), they did not observe any significant differences between the two groups.

3) The VAS, Parker and Palmer, DN4 and SF-36 scores used for the analysis of the clinical results were not specific to the assessment and treatment of AKA or arthrodesis. These scores were selected to give a general assessment. Furthermore, some of these scores require a whole joint, which was not the case in our series.

4) The number of deaths was significant in both groups and can be explained by the demographics of our study population; advanced age and several comorbidities, such as diabetes, chronic kidney disorder, smoking and arrhythmia. All the deaths that occurred between surgery and clinical assessment were not related to the procedure.

Methodologically, death was defined as a concurring risk to minimize its statistical impact on our study.

5. Conclusion

AKA and arthrodesis are two types of surgical procedures with serious functional and psychological consequences. The rate of recurrent sepsis was comparable for both procedures involving failed TKA due to multiple infections. The Parker and Palmer and SF-36 scores revealed that patients who underwent AKA had less mechanical and neuropathic pain than the arthrodesis group. However, since the final decision ultimately lies with the patient, surgical teams need to adapt to offer the best functional outcome while limiting the risk of recurrent infection.

Conflicts of Interest: The authors declare they have no conflicts of interest directly related to this study. Outside the scope of this study, Henri Migaud is the editor-in-chief for Orthopaedics & Traumatology: Surgery & Research and an educational and research consultant for Corin, Zimmer-Biomet, MSD and SERF. Gilles Pasquier is an educational consultant for Zimmer. Eric Senneville is a paid speaker for Zimmer and a consultant for MSD, Pfizer, Correvio, Bayer, Sanofi-Aventis, and Cepheid. Sophie Putman declares to be an educational and research consultant for Corin. The other authors declare they have no conflicts of interest regarding this manuscript or outside this study.

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Figure legends

Figure 1: Flowchart of the study comparing knee arthrodesis and above-the-knee amputation.

Figure 2: Rate of recurrent sepsis curves in knee arthrodesis versus above-the-knee amputation.

Table 1: Comparison of epidemiological data of the AKA and arthrodesis groups

Factors	AKA Group N = 20	Arthrodesis Group N = 23	*P*
Age (years)	73.8 (54-97) ± 13.8	77.7 (55-92) ± 11.6	.31
Age at surgery (years)	70.0 (43-93) ± 13.3	68.0 (53-81) ± 11.1	.59
Age at TKA (years)	63.3 (36-90) ± 14.5	60.7 (34-76) ± 13.7	.55
Body mass index	30.8 (20.4-40) ± 8.9	28.4 (20-42) ± 5.4	.31
Sex F/M	10/10	16/7	.19
Smoking	14 (70%)	16 (69.6%)	.98
Chronic kidney disease	15 (75%)	17 (73.8%)	.94
Side L/R	12/8	12/11	.61
Diabetes	13 (65%)	12 (52.2%)	.40
Staphylococcus	15 (75%)	16 (69.6%)	.69
Time between TKA and treatment (months)	48.0 (12.0-102.0)	48.0 (24.0-87.0)	<.001
Number of revisions	3.0 (1.5-4.0)	2.0 (2.0-3.0)	<.001
Follow-up (months)	50.2	116.34	.002
Type of TKA before procedure			NC
Posterior-stabilized	3 (15%)	13 (56%)	
Semi-constrained	2 (10%)	8 (35%)	
Hinged	11 (55%)	2 (9%)	
Arthrodesis	4 (20%)		
Initial etiology			NC
Primary osteoarthritis	12 (60%)	18 (78%)	
Posttraumatic arthritis	5 (25%)	4 (18%)	
Septic arthritis	1 (10%)		
Tumor pathology	3 (15%)		
Rheumatoid arthritis		1 (4%)	
Neuropathic pain treatment at last follow-up (N = 15 AKA; N = 14 Arthrodeses)	80% (12/15)	71.4% (11/14)	.17

AKA: above-the-knee amputation; TKA: total knee arthroplasty; F: female; M: male; NC: not calculable because the number of patients was too low.

Table 2: Microbiological data for the above-the-knee amputation group

Patients	Microorganisms before AKA	Microorganisms found on the femoral resection after AKA
1	MRSE MSSA *Corynebacterium* spp.	*Pseudomonas aeruginosa*
2	*Enterobacter cloacae* ESBL	Sterile
3	MSSA	Sterile
4	MRSE	Sterile
5	*Streptococcus agalactiae* MSSA *Corynebacterium* spp.	MSSA *Streptococcus agalactiae*
6	*Enterobacter cloacae* *Pseudomonas mendocina* MSSE *Corynebacterium* spp.	MSSA
7	CoNS	MSSA
8	*Enterobacterium ESBL: Enterobacter cloacae*	*Enterococcus faecium*–MSSE
9	*Streptococcus* MRSA MRSE	MRSA
10	*Pseudomonas aeruginosa* MRSA MSSE	Sterile
11	MRSA *Escherichia coli*	MRSE *Enterococcus faecalis*
12	*Escherichia coli*	Sterile
13	*Streptococcus mitis* *Gemella* spp. *Enterococcus faecalis* *Prevotella* spp. *Bacteroides uniformis*	*Enterococcus faecalis*
14	MSSA	Sterile
15	MSSA *Enterobacter cloacae*	MSSA *Streptococcus agalactiae*
16	*Enterobacterium ESBL: Enterobacter cloacae*	*Enterobacter cloacae*
17	MSSA *Klebsiella pneumoniae* *Granulicatella adiacens* MSSA MRSE	*Enterobacter cloacae* *Bacillus cereus*
18	MSSA	Sterile
19	*Enterococcus casseliflavus* *Corynebacterium urealyticum*	*Enterococcus casseliflavus* *Corynebacterium urealyticum*
20	*Staphylococcus haemolyticus* *Enterococcus faecium*	*Citrobacter koseri* *Streptococcus agalactiae*

AKA: above-the-knee amputation; MRSE: methicillin-resistant *Staphylococcus epidermidis*; MSSA: methicillin-susceptible *Staphylococcus aureus*; ESBL: extended-spectrum beta-lactamases; CoNS: coagulase-negative *Staphylococcus* species, MRSA: methicillin-resistant *Staphylococcus aureus,* MSSE: methicillin-susceptible *Staphylococcus* *epidermidis.*

Table 3: Microbiological data for the arthrodesis group

Patients	Microorganisms found during 1st stage	Microorganisms found during 2nd stage
1	*Enterococcus faecalis*	/
2	MSSA	MSSA
3	MRSE	*Pseudomonas aeruginosa*
4	*Pseudomonas aeruginosa*	Sterile
5	MSSA *Streptococcus* spp.	CoNS
6	MSSA	Sterile
7	CoNS	CoNS
8	*Streptococcus* spp.	/
9	CoNS *Enterococcus* spp.	*Enterococcus* MRSA-MSSE
10	MRSA	Sterile
11	CoNS	CoNS
12	*Streptococcus agalactiae*	Sterile
13	*Fusobacterium* spp.	Sterile
14	*Pseudomonas aeruginosa*	/
15	*Staphylococcus warneri* MSSE	Sterile
16	MSSA	/
17	MSSA	Sterile
18	CoNS	MRSE
19	MSSA	Sterile
20	MSSA	Sterile
21	MSSA	MSSA
22	*Escherichia coli*	MRSE
23	*Streptococcus spp.*	Streptococcus

MRSE: methicillin-resistant *Staphylococcus epidermidis*; MSSA: methicillin-susceptible *Staphylococcus aureus*; ESBL: extended-spectrum beta-lactamases; CoNS: coagulase-negative *Staphylococcus* species*;* MRSA: methicillin-resistant *Staphylococcus aureus;* MSSE: methicillin-susceptible *Staphylococcus epidermidis.*

/ : Patient who underwent a one-stage surgical procedure.

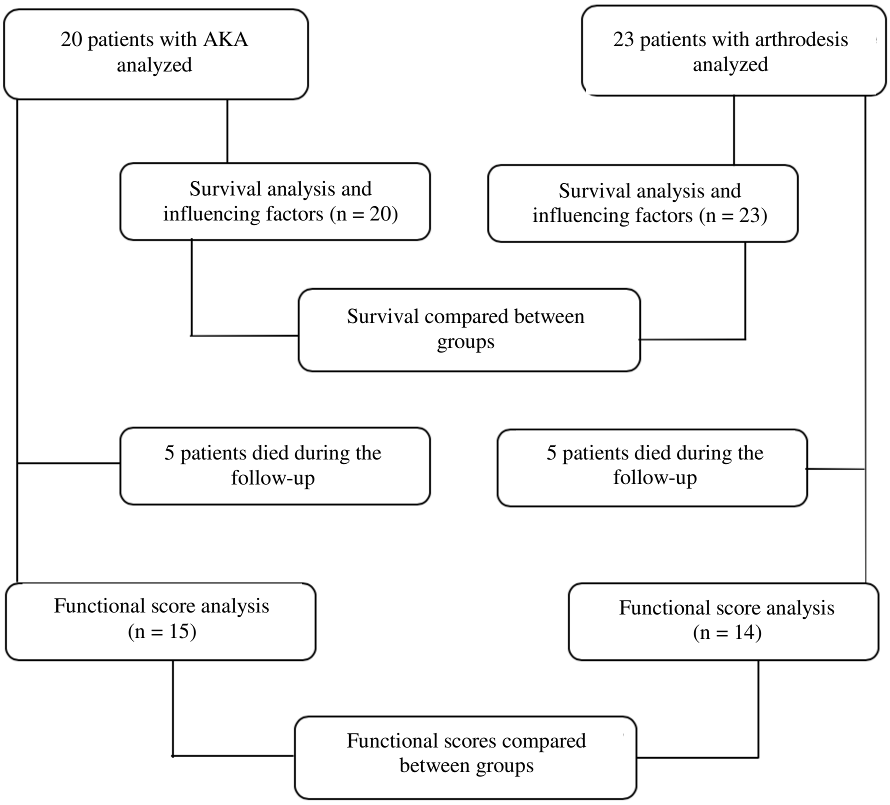
Table 4: Factors influencing recurrent sepsis

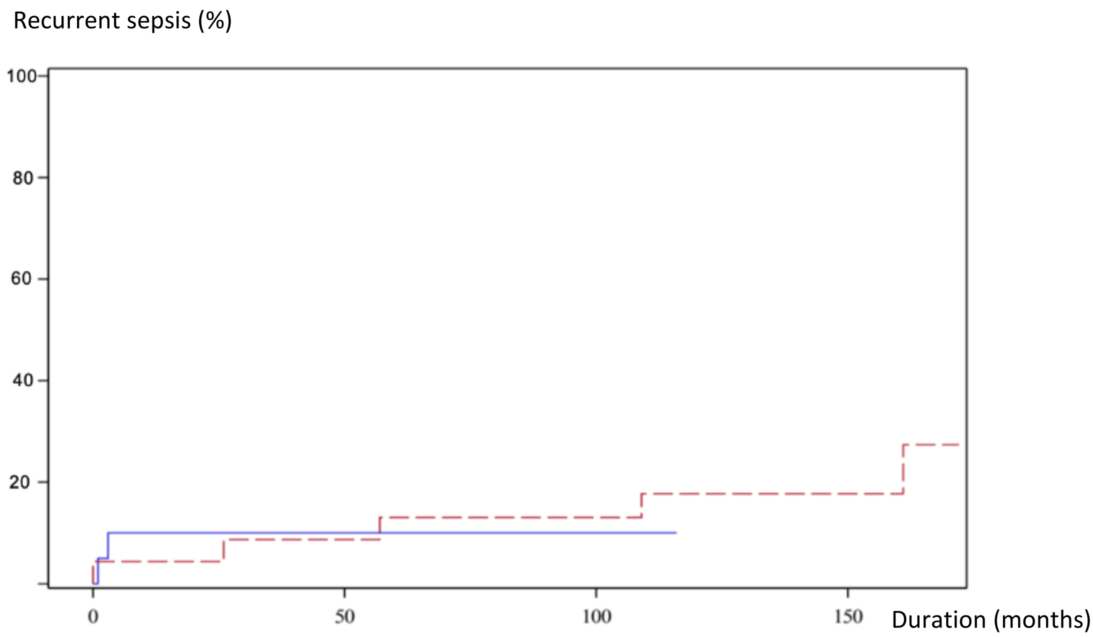
Factors	*P*	Confidence interval
Sex	.7549	(0.189-3.349)
Age	.8680	(0.953-1.041)
Body mass index	.44	(0.950-1.126)
Diabetes	.2768	(0.538-8.720)
Number of revisions	.7969	(0.197-3.476)

Table 5: Functional Scores

Score: Median (Q1–Q3)	AKA (N = 15)	Arthrodesis (N = 14)	*P*
VAS	2.0 (1–5)	3.0 (0–6)	<.001
DN4 [14]	1.0 (0.0–2.2)	2.0 (0.0–3.0)	<.001
Parker and Palmer mobility score [15]	5.0 (3.0–7.0)	5.0 (3.0–5.0)	<.001
SF-36 [16]	33.6 (14.7–44.7)	22.0 (14.7–39.8)	<.001

AKA: Above-the-knee amputation; VAS: Visual analog scale; DN4: French neuropathic pain questionnaire; SF-36: Short-form questionnaire


20 patients with AKA analyzed
23 patients with arthrodesis analyzed
Survival analysis and influencing factors (n = 20)
Survival analysis and influencing factors (n = 23)
Survival compared between groups
5 patients died during the follow-up
5 patients died during the follow-up
Functional score analysis (n = 15)
Functional score analysis (n = 14)
Functional scores compared between groups


Recurrent sepsis (%)
100
80
60
40
20
0
50
100
150
Duration (months)