A Retrospective Observational Cohort Study of Periprosthetic Hip Infection Treated by one-stage Method Including Cases With Bone Graft Reconstruction

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ABSTRACT

PURPOSE: Prosthetic joint infection (PJI) is a devastating complication that can affect hip arthroplasty. Its treatment is extremely difficult, and issues regarding the optimal treatment remain unanswered. This study intended to show the effectiveness of the one-stage treatment of PJI.

MATERIALS AND METHODS: A retrospective observational cohort study performed from July 2014- August 2018. All patients with suspected PJI were included. Major and minor criteria developed by the International Consensus on Periprosthetic Joint Infection (ICPJI) was used to define infection. Laboratory tests and image exams were performed, and all patients were followed for at least 2 years.

OUTCOMES: Success rate (2018 ICPJI definition to success) in treatment of PJI using one-stage revision method. Clinical and functional outcomes defined by Harris Hip Score (HHS).

RESULTS: Thirty-one patients were screened and 18 analyzed. 69.85 ± 9.76 years was the mean age. Mean follow-up time was 63.84 ± 18.55 months. Ten patients had acetabular defects and required bone graft reconstruction. Sixteen patients were classified as Tier 1, 1 as Tier 3D, and as 1 Tier 3E. Almost 90% of patients submitted to one-stage revision with acetabulum graft reconstruction were free of infection. The overall infection survival rate was 78.31±6.34 months. *Candida albicans* and sinus tract were statistically significant in univariate Cox's analysis. The predictor of one-stage revision surgery failure that remained final Cox's regression model was *C. albicans* (hazard ratio [HR]: 4.47).

CONCLUSION: Treatment through one-stage revision surgery associated with 6 months of antimicrobial is a viable option with acceptable results even when bone graft reconstruction is necessary. *C. albicans* was a strong predictor of failure in this cohort.

KEYWORDS: Hip, arthroplasty, replacement, total hip arthroplasty, infected arthroplasty, periprosthetic joint infection, one-stage surgical time, one-stage revision, bone graft, one-stage exchange, Xenograft, lyophilized bovine xenograft

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Introduction

The number of hip arthroplasty surgeries has grown considerably in recent years,[1,2] and periprosthetic joint infection (PJI) is a possible complication that can occur. The infection rates are estimated to be between 0.45% and 0.57% in England,[3,4] 0.2% and 1.5% in the United States,[5,6] and 1.7% in some other countries in Europe and North America.[7] It is expected that as the rates of arthroplasty surgery increase, the gross numbers of infection will increase in the following years.

Prosthetic joint infections are a significant problem[8,9] for the patient as well as for the surgeons and infectologists, and they also bring a high cost for hospitals, health plans, and public health systems.[10,11] Periprosthetic joint infection is considered one of the most expensive and devastating complications in orthopedics,[12] and its treatment is considered extremely difficult.[13] Many questions remain about the most effective treatment for PJI if the revision arthroplasty must be made in the one-stage or two-stage surgical times.[14,15]

Our study aimed to demonstrate the treatment results of the one-stage method for infected hip arthroplasty including cases in which bone graft was used, applying the guidelines developed to report outcomes after surgical treatment defined by the Workgroup of the Musculoskeletal Infection Society (MSIS).[16,17]

Materials and Methods

A retrospective observational cohort study was performed at the Orthopedic and Traumatology Service of the Santa Maria University Hospital (SOT-HUSM) at the Federal University of Santa Maria (UFSM) and at the Astrogildo de Azevedo Charity Hospital (HCAA). The research was approved by the Institutional Review Board of both hospitals (number 72074117.4.0000.5346) and followed the ethical guidelines of the 1975 Declaration of Helsinki. The inclusion time was from July 2014 to August 2018. Suspected infection was the criterion used to start the screening study. This suspicion was based on the signs and symptoms related and observed in a patient: pain, swelling, hyperemia, pruritus, local heat, sinus tract, early loosening of arthroplasty (considered loose in the first 3 years after primary arthroplasty surgery), draining of operative wound and alteration of hemogram (leucocytosis with "left deviation").

Patients considered suitable for the study fulfilled the criteria defined by the International Consensus on Periprosthetic Joint Infection (ICPJI; Table 1).[18,19] Patients who did not have musculocutaneous coverage that would allow the prosthesis to be revised in a one-stage time, as well as immunocompromised patients and patients with sepsis, were all excluded from the study, as well as those patients who did not undergo one-stage revision surgery (Figure 1—flowchart) following the recommendations of absolute contraindication to on-stage revision surgery of 2013[20] and 2018 PJI international consensus.[21] In the study, the demographic characteristic of subjects was collected. Data about the primary arthroplasty surgery were collected, as well as data about the onset and what symptoms made the patient come to the hospital. Information about previous treatments performed, and the use of antibiotics was also collected. Data about the procedure performed at our hospital were collected: type of implant used, use of bone graft, type of antibiotics used, and time of hospitalization. Laboratory examinations were also collected pre and postoperatively: hemogram, creatinine, urea, blood culture, C-reactive protein (CRP), and erythrocyte sedimentation rate (ESR). Information on intraoperative cultures was also collected (bacteria identified). Image examinations were realized pre and postoperatively. Preoperative image examination was used to classify acetabular bone defects according to the American Academy of Orthopedic Surgeons Classification (AAOS)[22]: type I—segmental defect, type II—cavitary defect with intact rim, type III—combined defect, type IV—pelvic discontinuity, and type V—arthrodesis.

Surgical technique

All patients had an epidural catheter for postoperative analgesia and underwent general anesthesia. All patients also underwent revision arthroplasty in a one-stage method, through a posterior approach by the same team of surgeons in both hospitals. First, the approach was performed with aggressive tissue debridement. In the presence of a sinus tract, methylene blue was infused, impregnating all tissue that had contact and formed the fistulous path, facilitating the debridement. All previous implants were removed after debridement. For removal of the implants, thin and long chisels were used. In some cases, it was necessary to perform a femoral osteotomy to aid in the removal of the implant and/or bone cement. This osteotomy was performed laterally on the femur, located 1.5 to 2 cm below the line of the lesser trochanter toward the diaphysis and did not exceed 1/3 of the femoral circumference. Respecting and preserving the greater trochanter and the abductor mechanism (Figure 2). Several cultures were collected: joint fluid, joint capsular tissue, peri-femoral tissue, periacetabular tissue, femoral canal tissue, and acetabular floor tissue. After debridement and culture collection, exhaustive irrigation with a physiological solution was performed, followed by irrigation of diluted iodopovidone. After debridement and irrigation, all patients were empirically started with vancomycin 2 g and cefepime 2 g intravenously, defined by the infectious disease specialists of our team. These antibiotics were maintained until the initial tissue culture results were observed in 3 days. If there is a need for change, infectologists carry it out but maintain the intravenous course. In the sequence, the surgical wound was covered, the surgical drapes were removed, the surgical team changed the surgical gowns, and a new asepsis and antisepsis was performed on patient. The surgical site was covered with new sterile drapes and new and clean surgical instruments were used. After these steps, the implant of a new prosthesis was performed therefore filling the dead spaces in the acetabulum and the femur. When the use of cemented acetabulum was chosen, 2 g of vancomycin was added to the bone cement. In some cases, when necessary, reconstruction of the acetabular bone stock was performed through the use of impacted morselized lyophilized bovine xenograft, OrthoGen® (Baumer SA, São Paulo, Brasil). In these cases, xenograft was hydrated with saline solution and 2 g of vancomycin being after morselized. At the end of the surgical procedure, exhaustive irrigation was performed with 3 L of physiological solution followed by suturing the tissue planes and closing the surgical wound, finishing filling possible remaining dead spaces. After surgery and approximately 15 days of initial intravenous antibiotic, the final results of the tissue culture were analyzed. If there was a growth of new previously unidentified germs and not covered by vancomycin and cefepime, then antibiotics were modified again by the infectious disease specialists. Antibiotics were sustained for another 15 days of intravenous administration, completing 30 days of intravenous antibiotics. After this course, all patients with clinical conditions (with healed surgical wound without signs of infection, without fever, without leucocytosis with left deviation, with CRP and ESR reduction, without complications such as deep vein thrombosis, changes in renal function markers and complications from their underlying diseases) were discharged with oral antibiotics for 5 months, performing a total of 6 months of antibiotic treatment. Oral antibiotics were

Table 1. Definition of periprosthetic joint infection according to the International Consensus Group.

MAJOR CRITERIA (AT LEAST ONE OF THE FOLLOWING)				DECISION
Two positive cultures of the same organisms				Infected
A sinus tract with evidence of communication to the joint or visualization of the prosthesis				
MINOR CRITERIA			**SCORE**	**DECISION**
	Serum	Elevated CRP or D-Dimer	2	⩾6 infected
		Elevated ESR	1	
	Synovial	Elevated synovial WBC or LE	3	2-5 possibly infected[a]
		Positive alpha-defensin	3	
		Elevated synovial PMN (%)	2	0-1 not infected
		Elevated synovial CRP	1	
		INCONCLUSIVE PRE-OP SCORE OR DRY TAP[a]	**SCORE**	**DECISION**
Intraoperative diagnoses		Preoperative score	–	⩾6 infected
		Positive histology	3	4-5 inconclusive[b]
		Positive purulence	3	
		Single positive culture	2	⩽3 not infected
MARKER		**CHRONIC (>90 DAYS)**		**ACUTE (<90 DAYS)**
Serum CRP (mg/dL)		1.0		10
Serum D-dimer (ng/mL)		860		860[c]
Serum ESR (mm/h)		30		–
Synovial WBC count (cells/mL)		3000		10 000
Synovial PMN (%)		80		90
Synovial CRP (mg/L)		6.9		6.9
Synovial alpha-defensin (signal-to-cutoff ratio)		1.0		1.0

Source: Reprinted from Parvizi et al[19], pp. 1312 and 1313, Copyright (2018), with permission from Elsevier.
Abbreviations: CRP, C-reactive protein; ESR, erythrocyte sedimentation rate; LE, leukocyte esterase; PMN, polymorphonuclear; WBC, white blood cell.
This is an adaptation of the Musculoskeletal Infection Society Definition of PJI. New scoring based definition for periprosthetic joint infection (PJI). Proceed with caution in: adverse local tissue reaction, crystal deposition disease, slow growing organisms.
[a]For patients with inconclusive minor criteria, operative criteria can also be used to fulfill definition for PJI.
[b]Consider further molecular diagnostics such as next-generation sequencing.
[c]Further studies are needed to validate a specific threshold.

chosen by infectious disease specialists and take into account the analysis of the susceptibility of the germs identified in the tissue cultures. Patients who did not have clinical discharge conditions or in which one-stage revision failed, who needed another surgery, remained hospitalized. These patients also had their oral antimicrobial therapy also started at the end of the 30 days of intravenous antibiotics.

Medical follow-up after discharge

All patients were followed up postoperatively, at 8, 16, 24, 48, 72, and 96 weeks after the operation. In these consultations, an examination of the surgical wound and its conditions was performed, as well as collected laboratory examinations (hemogram, creatinine, urea, CRP, and ESR) and image examinations. In the postoperative radiological images obtained in the follow-up consultations, the presence of areas of acetabular radiolucency (according to the Delee and Charnley zones[23]) and femoral radiolucency (according to Gruen zones[24]) were evaluated, as well as the presence of implant movement/migration and the status of the xenograft.

Outcomes

Verify the success rate in the treatment of periprosthetic hip infections using the one-stage revision method. The 2018

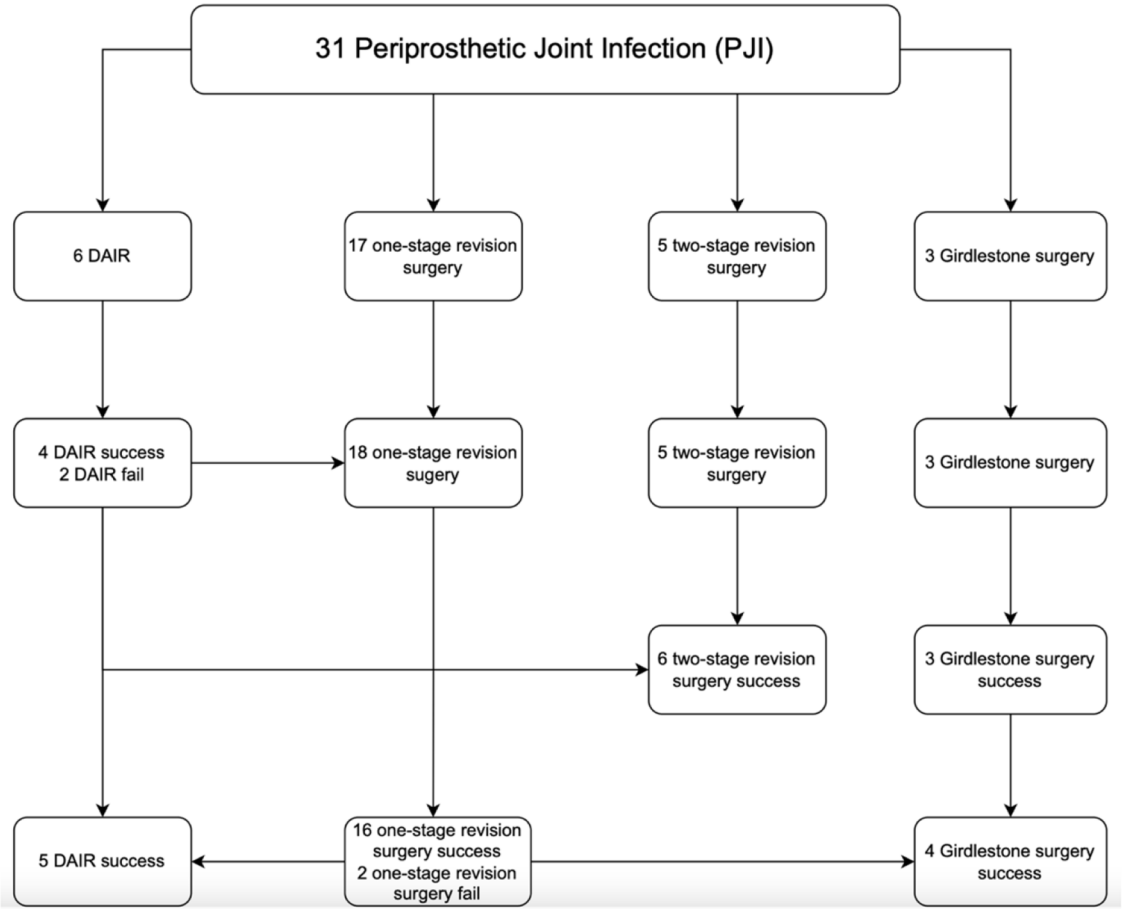

Figure 1. Flowchart.
PJI indicates periprosthetic joint infection, DAIR indicates debridement, antibiotics and implant retention.

ICPJI definition was used to define treatment success (Tier Classification and a minimum of 2 years of follow-up were carried out). Tiers 3A, 3C, 3E, 3F, and 4A were considered failures related to PJI.[16,17] For the clinical and functional outcomes results of patients, the translated and validated Harris Hip Score (HHS) was used. A total score below 70 points is considered a poor result, 70 to 80 reasonable, 80 to 90 good, and 90 to 100 excellent.[25]

Statistical analysis

Data were analyzed with SPSS 18.0 (SPSS Inc., IBM Corporation, Armonk, NY, USA). The Kolmogorov–Smirnov test was applied to test normality. Variables with normal distribution are given as mean and standard deviation and non-normal variables are given as median and interquartile range. Qualitative variables are reported as frequencies. The 95% confidence interval was used to demonstrate the age difference between genders. The outcome variable was one-stage revision surgery failure, and a univariate analysis was performed using Cox's proportional hazard regression model. All variables with a P value 0.10 were included in a Cox's proportional hazard regression model. The best model was selected based on the likelihood ratio. Kaplan–Meier survival analyses and graphs were generated to evaluate survival time until failure. In the radiographic assessment of patients, inter and intraobserver validation was performed using the Kappa test. All radiographs were evaluated twice at 2 different times, by 2 blinded authors. Interobserver reliability of 1.0 ($P < .001$) and intraobserver reliability of 0.870 ($P < .001$) was achieved. A 2-tailed P value $< .05$ was considered significant.

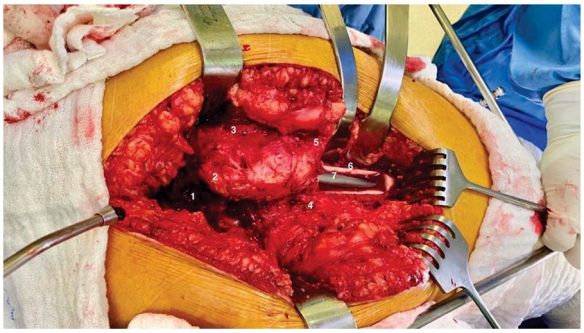

Figure 2. Femoral osteotomy: (1) acetabulum; (2) top of the greater trochanter; (3) gluteus medius and minimus muscles; (4) distal insertion of the gluteus maximus; (5) vastus lateralis muscle; (6) lateral osteotomy performed on the femur, located 1.5-2 cm below the line of the lesser trochanter toward the diaphysis and did not exceed 1/3 of the femoral circumference; (7) cementless femoral component.

Table 2. Population characteristics.

CHARACTERISTICS	
Age [years] (mean [SD] [CI]	69.83 (9.76) (64.98-74.69)
GRAM-negative	82 (0) (0)
GRAM-positive	68.86 (8.91) (63.71-74)
GRAM-negative e-positive	70.33 (14.57) (34.14-106.53)
Time from first arthroplasty to revision surgery [months] (mean [SD] [CI])	45.06 (45.18) (22.6-67.53)
GRAM-negative	0.46 (0)
GRAM-positive	53.78 (47.07) (26.60-80.96)
GRAM-negative e-positive	19.23 (20.54) (-31.80-70.27)
Intrahospital stay [weeks] (median [IQR])	6 (6-9.5)
Comorbidity (n, %)	
Systemic arterial hypertension	13 (72)
Ischemic heart disease	3 (17)
Diabetes	13 (72)
Ischemic cerebrovascular accident	2 (11)
Kidney disease	1 (6)
Lung disease (COPD)	1 (6)
Social factors (n, %)	
Alcoholism	1 (6)
Smoking	5 (28)

Abbreviations: CI, confidence interval; COPD, chronic obstructive pulmonary disease; IQR, interquartile range; SD, standard deviation.

Results

Thirty-one subjects were initially screened, and according to the inclusion and exclusion criteria, 18 subjects were analyzed (Figure 1—flowchart). The mean age at the time of revision arthroplasty surgery was 69.85 ± 9.76 years (mean ± standard deviation): 70.17 ± 10.46 (63.52-76.81) years (95% confidence interval) for female and 69.17 ± 9.07 (59.65-78.68) years for male. Around 67% (12) of the subjects were female. The average follow-up time was 63.84 ± 18.55 (range: 34.73-88.84) months. The characteristics of this population are displayed in Table 2. The mean time from the first arthroplasty surgery until the revision surgery was 45.06 ± 45.18 months, ranging from 0.46 to 114.14 months.

At the time of hospital admission, 7 patients (39%) had 2 symptoms that could suggest infection. Four (22%) had 1 single symptom, 3 (17%) had 3, 2 patients (11%) had 4 symptoms, and 2 (11%) had 5 symptoms that could suggest infection. These were considered to be complaints that could suggest infection: hyperemia, skin rash, pruritus, swelling, and a sinus tract (possibly with communication with a joint). Six (33%) patients presented positive 3-phase bone scintigraphy before revision surgery and 5 (28%) negative ones. Five (28%) patients did not undergo the examination because it was an infection that occurred in the first 2 years after primary arthroplasty. Two patients (11%) did not undergo the examination for financial reasons. Of all patients, only 3 (17%) had a positive blood culture before surgery. Two (11%) patients had leucocytosis increased, and only one of these presented a high number of band neutrophils ("left shift") in the hemogram. The preoperative average leukocyte of the subjects was 7765.72 ± 3038.75 cells/mm^3 and 2 ± 2.40 % was the number of band neutrophils. The mean values of CRP before the revision surgery were 5.02 ± 5.72 mg/dL and 38.17 ± 24.86 mm/hr was the mean values to the ESR. More details on the patients' preoperative laboratory exams are shown in Table 3.

The definitive diagnosis of periprosthetic infection was confirmed according to the criteria of the ICPJI in all patients.[18,19] Six (33%) patients had the presence of 2 major criteria (2 positive periprosthetic cultures with identical organisms and a sinus tract communicating with the joint). Twelve patients (67%) had only one major criterion (2 positive periprosthetic cultures with identical organisms). No diagnosis

Table 3. Results of laboratory exams throughout treatment.

EXAM	PREOPERATIVE	1WEEK	2WEEKS	3WEEKS	4WEEKS	8WEEKS	16WEEKS	24WEEKS	48WEEKS	72WEEKS	96WEEKS
	MEAN ± STANDARD DEVIATION										
Leukocyte	7765.72 ± 3038.75	8929.44 ± 3447.92	9082.78 ± 3906.48	6972.35 ± 2776.01	7470.59 ± 3227.72	6628.19 ± 930.12	5797.73 ± 1766.00	5965.33 ± 2487.65	6256.43 ± 1024.89	6016.77 ± 830.64	6345.78 ± 1353.62
Neutrophils (% of leukocyte)	56.21 ± 16.96	62.64 ± 19.20	62.33 ± 10.37	56.36 ± 8.05	55.911 ± 11.15	56.13 ± 11.50	53.11 ± 9.42	53.71 ± 9.39	55.66 ± 7.56	51.41 ± 7.70	51.48 ± 9.58
Band neutrophils (% of leukocyte)	2.0 ± 2.4	6.22 ± 15.37	2.56 ± 3.63	2.53 ± 3.50	2.12 ± 3.22	2.69 ± 6.59	1.0 ± 1.25	0.53 ± 0.74	0.64 ± 0.93	0.85 ± 1.07	0.89 ± 1.05
Lymphocytes (% of leukocyte)	28.42 ± 13.63	18.74 ± 8.12	21.06 ± 8.65	23.64 ± 8.19	22.82 ± 7.99	24.51 ± 10.07	28.00 ± 11.31	24.37 ± 6.36	22.26 ± 8.57	24.21 ± 9.16	23.52 ± 11.40
Platelets (cells/mm^3)	264 611.11 ± 78 182.40	260 444.44 ± 57 757.32	343 222.22 ± 83 058.84	371 352.94 ± 113 131.53	283 941.18 ± 68 965.09	239 062.50 ± 46 401.82	261 066.67 ± 48 819.59	245 133.33 ± 25 447.05	240 142.86 ± 32 891.10	247 846.15 ± 50 578.07	258 888.89 ± 47 157.83
Creatinine (mg/dL)	1.15 ± 1.09	090 ± 0.29	0.86 ± 0.30	0.89 ± 0.26	1.05 ± 0.35	1.02 ± 0.33	0.95 ± 0.23	0.98 ± 0.19	0.97 ± 0.23	0.88 ± 0.25	0.90 ± 0.31
Urea (mg/dL)	37.83 ± 9.72	33.06 ± 12.92	34.94 ± 12.47	39.18 ± 0.26	44.71 ± 18.64	41.50 ± 10.60	32.71 ± 7.57	35.76 ± 7.29	35.07 ± 6.04	35.88 ± 5.19	33.78 ± 4.18

was made through minor criteria in our study. Fourteen (78%) patients had culture results for GRAM-positive bacteria, 3 (17%) for polymicrobial flora (GRAM-negative and -positive) and only one (5%) patient for GRAM-negative bacteria. Of the patients with polymicrobial flora, one had identified a fungus, a *C. albicans*. More information on the bacteria identified, the antibiotics administered intravenously in the third and fourth weeks, as well as those administered orally, are shown in Table 4.

Radiographic analysis before surgery is shown in Table 5. Ten (56%) patients had acetabular defects: 5 (50%) were classified as type II (cavitary defect with intact rim) according to AAOS,[22] 4 (40%) were type III (combined defect), and 1 (10%) was type I (segmental defect). Patients classified as type I and III defects demanded acetabular reconstruction using tantalum augmentation, and all these patients with acetabular defect required the use of a bovine lyophilized xenograft during the revision surgery. Figures 3 to 5 show a patient with acetabular defect reconstructed using lyophilized bovine xenograft and tantalum augmentation. The OrthoGen xenograft is available in 10 × 20 × 30 mm size pieces, weighing 40 g per piece. The graft average used ranged from 320 to 400 g. The lyophilized bovine xenograft was hydrated in a saline solution containing 2 g of vancomycin. After hydration, it was morselized and impacted on the acetabular floor, which was prepared by reaming, creating a bleeding, and viable host bed to receive it. After surgical treatment, alterations in CRP and ESR values were observed (Figure 6).

All patients complete a minimum of 2 years of follow-up. According to the Tier classification proposed by MSIS,[16,17] 16 (89%) of all patients were classified as Tier 1 (infection control with no continued antibiotic therapy), 1 (6%) patient as Tier 3D (need for reoperation due to infection ⩽1 year from initiation of PJI treatment. A debridement, antibiotics, and implant retention debridement, antibiotics and implant retention (DAIR) were performed) and another 1 (6%) as Tier 3E (need for reoperation, being carried out a resection arthroplasty). Considering only the 10 patients who required the use of grafts for reconstruction of the acetabular defect, 9 (90%) were classified as Tier 1 and 1 (10%) as Tier 3D. This patient after DAIR was free of infection. So, after this patient's DAIR and at the end of at 2 years of follow-up, we have 100% of infection eradication in patients where the bone graft was used to reconstruct acetabular defects. But considering the 2018 ICPJI definition to report treatment success (Tier classification and a minimum of 1 year of follow-up were carried out),[16,17] we have an overall success rate of 90% in one-stage revision surgery in patients who require lyophilized bovine xenograft reconstruction. And we have 1 (10%) failure in a patient who required acetabular reconstruction, not related to PJI.

The patient classified as Tier 3E, who did not use a bone graft, and who needed to perform resection arthroplasty, was a 60-year-old diabetic woman, who was also hypertensive and had an ischemic stroke sequel. This patient started PJI 2 days

Table 4. Characteristics of the bacteria identified and the antibiotics administered.

CHARACTERISTICS	N, %	INTRAVENOUS ANTIBIOTICS THIRD AND FOURTH WEEKS	ORAL ANTIBIOTICS
Staphylococcus aureus or coagulase-negative staphylococci	14 (78)		
Methicillin-susceptible	12 (67)	Ceftriaxone	Ciprofloxacin, clindamycin
Methicillin-resistant	2 (11)	Vancomycin. When allergy daptomycin	Ciprofloxacin, trimethoprim–sulfamethoxazole
Streptococcus species (except Streptococcus agalactiae)	3 (17)	Ceftriaxone	Amoxicillin
Enterococcus species (penicillin-susceptible) and Streptococcus agalactiae	1 (6)	Piperacillin/tazobactam, ampicillin/sulbactam	Amoxicillin
Enterobacteriaceae (quinolone-susceptible)	4 (22)	Cefepime	Ciprofloxacin
Nonfermenters (e.g., *Pseudomonas aeruginosa*)	2 (11)	Cefepime	Ciprofloxacin
Anaerobes	0	–	–
Fungal	1 (6)	Fluconazole	Fluconazole

after the primary arthroplasty surgery. She did not present with a sinus tract but presented hyperemia, swelling, pruritus, and persistent drainage of the operative wound. The same 2 bacteria (one GRAM-positive and the other GRAM-negative) were identified in this patient in at least 2 tissue samples in the first DAIRs where there was the exchange of head and liner. The presence of *C. albicans* hyphal in one cultured tissue was also identified, but the entire medical staff, both orthopedists and infectologists, believed this to be contamination of the samples. Owing to the nonimprovement of the patient health status after 2 consecutive DAIRs (both with exchange of head and liner) performed with 5 days interval, one-stage revision surgery was performed with new tissue collection for culture. Without the improvement of the patient health status in 8 days, with the surgical wound still draining, resection arthroplasty was indicated, as well as the collection of new tissues for culture. In these new tissues culture, the same GRAM-negative and -positive bacteria growth was detected. However, there was the growth of *C. albicans* in 3 different tissue samples. Treatment for fungal infection was initiated, but the antimicrobial treatment was not abandoned. After 5 days, the patient's health improved and at the end of the period, healing was achieved. The patient did not wish to undergo surgery to implant a new prosthesis.

The patients presented preoperatively an average of 56.19 ± 17.64 of the HHS, being this value considered a poor clinical and functional assessment. In the 96 week postoperatively follow-up, the average of HHS presented was 82.55 ± 11.49, being considered a good clinical and functional outcome.

Survival of one-stage revision surgery in our study was analyzed using Kaplan–Meier curves, yielding an overall survival of 78.31 ± 6.34 (65.89-90.74) (mean $\pm$ standard error [95% confidence interval]) months (89%). The cumulative risk of failure of one-stage revision surgery found in our study was 0.09 ± 0.03 (-0.3 to 0.47) months (12%). Survival and hazard

Table 5. Characteristics of the implant and radiography prior to revision surgery.

CHARACTERISTICS	N, %
Acetabular component	
Cemented	11 (61)
Cementless	7 (39)
Femoral component	
Cemented	13 (72)
Cementless	5 (28)
Acetabular component radiolucency	
Yes	13 (72)
No	5 (28)
Femoral component radiolucency	
Yes	10 (56)
No	8 (44)
Presence of acetabular component movement	
Yes	10 (56)
No	8 (44)
Presence of femoral component movement	
Yes	4 (22)
No	14 (78)

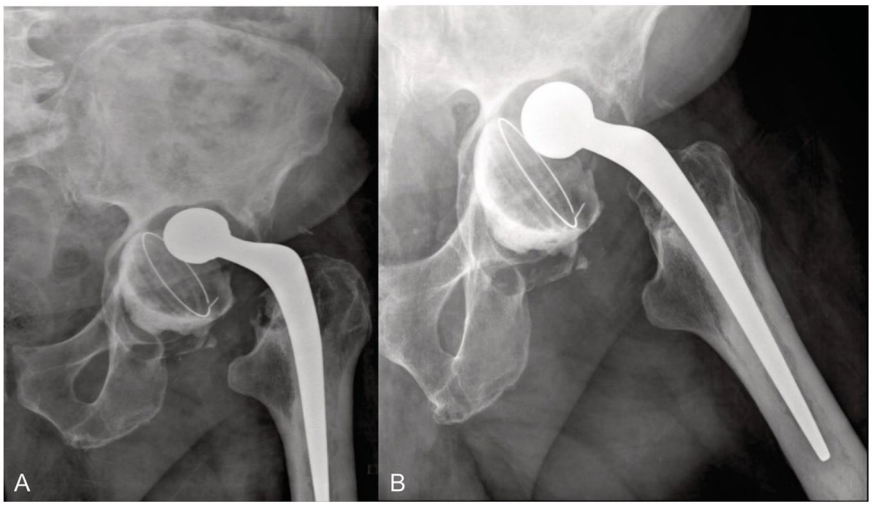

Figure 3. Preoperative image exams: a left hip X-ray demonstrating a loose cemented acetabular component medially migrated, as well as the dislocation of the arthroplasty with ascension of the greater trochanter and femur. An acetabular defect classified as type III (combined defect: cavitary and segmental defect) according to AAOS.[22] (A) anteroposterior X-ray and (B) profile/sagittal X-ray.
AAOS indicates American Academy of Orthopedic Surgeons Classification.

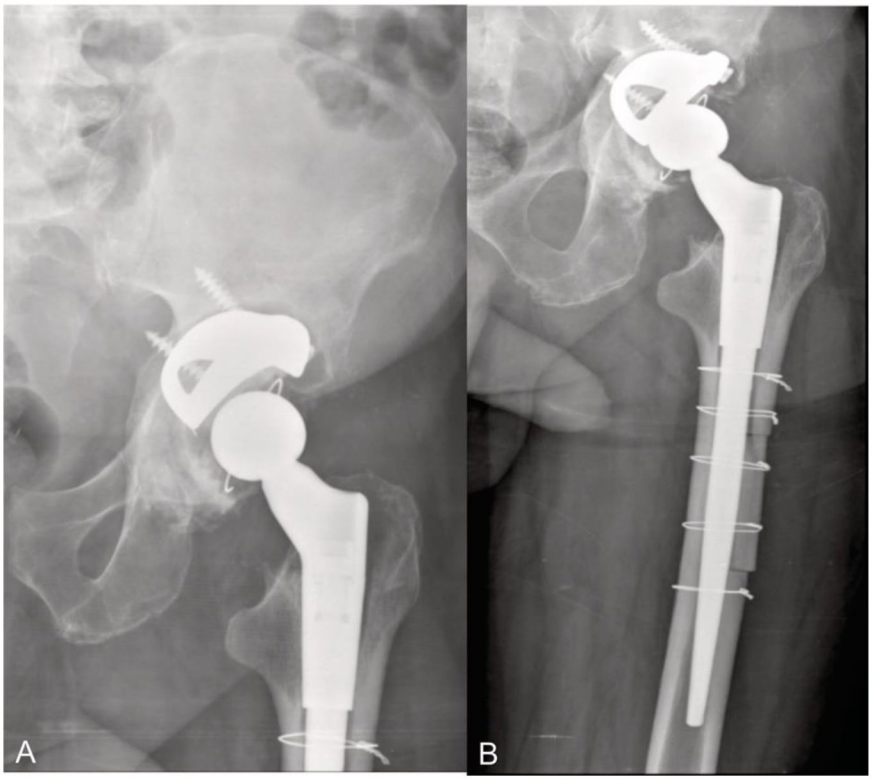

Figure 4. Immediate postoperative image exams: (A) demonstrating the reconstruction of the acetabular defect with a tantalum augmentation for the segmental defect and the lyophilized bovine xerograph morselized and impacted on the acetabular floor reconstructing the patient's bone stock. The acetabular reconstruction performed made it possible to restore the patient hip center of rotation to its original location and (B) demonstrates the revision using a long cementless distal fixation femoral component, as well as the osteotomy performed in the lateral region of the femur 1.5-2 cm below the line of the lesser trochanter.

functional graphs are shown in Figure 7. The crude HR of one-stage revision surgery failure using Cox's regression analyses is shown in Table 6. *C. albicans* and sinus tract were statistically significant, as found using univariate Cox's analysis. The predictor of one-stage revision surgery failure that remained in the final Cox's proportional hazard regression model was *C. albicans* (HR: 4.47). *C. albicans* was a strong predictor of failure in this cohort.

In the radiograph follow-up of patients, no migration/movement of the acetabular components was observed. Only 2

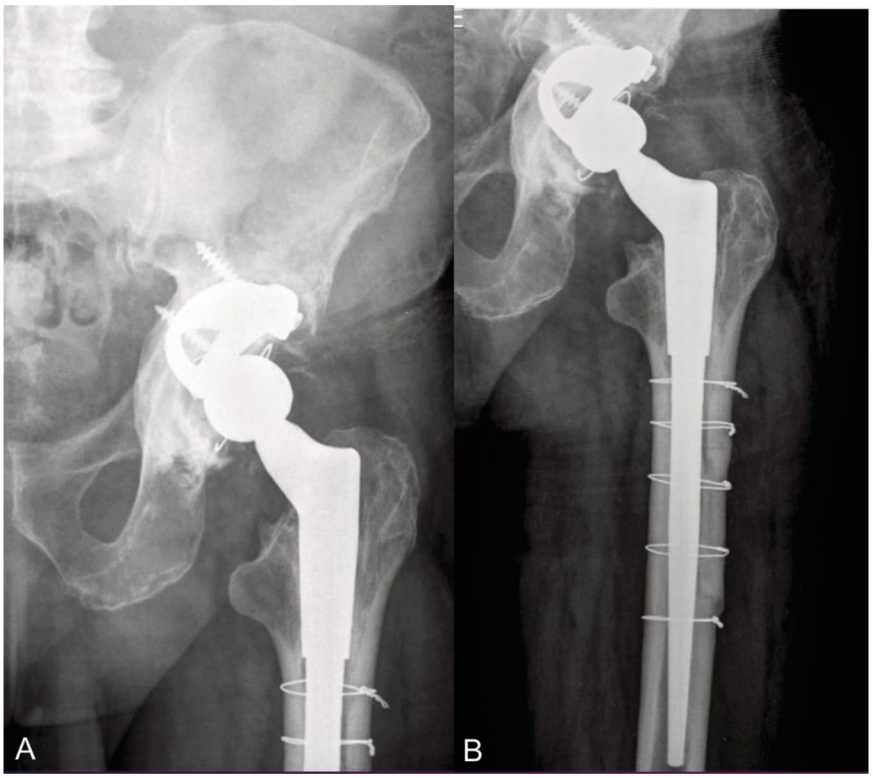

Figure 5. Sixty-four months postoperative image exams: (A) demonstrating the total osseointegration of the lyophilized bovine xenograft with the host bone. No radiolucency lines and no acetabular movement/migration are observed and (B) demonstrating that the osteotomy is completely consolidated and the long cementless distal fixation femoral component shows no movement/migration.

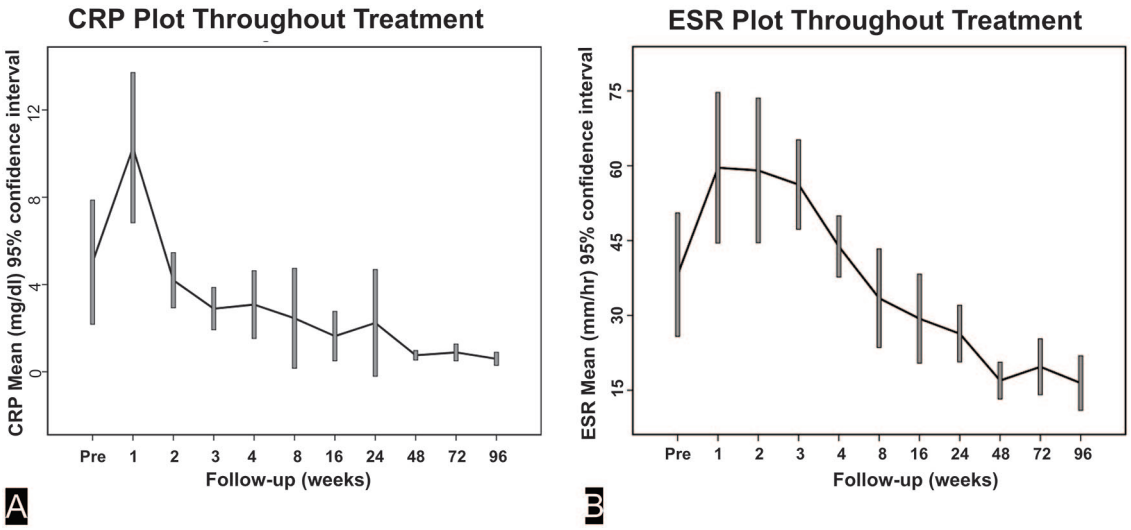

Figure 6. CRP and ESR values throughout the treatment: (A) the graph demonstrated CRP levels along with the treatment in the follow-up times. The first postoperative week and the other averages in the subsequent times: first to second week a decreased of 6.077 ± 1.362 mg/dL of CRP value, first to third week 7.379 ± 1.620 mg/dL, first to fourth 7.192 ± 1.290 mg/dL, first to eighth 7.820 ± 1.516 mg/dL, first to 16th 8.638 ± 1.387 mg/dL, first to 24th 8.0321 ± 1.697 mg/dL, first to 48th 9.515 ± 1.567 mg/dL, first to 72nd 9.385 ± 1.485 mg/dL, and first to the 96th week a decrease of 9.677 ± 1.552 mg/dL of CRP and (B) decrease in ESR values was observed only after the third week of follow-up: third to fourth week a decrease means of 12.412 ± 4.691 mm/hr, third to eighth week 22.798 ± 5.806 mm/hr, third to 16th 26.902 ± 6.069 mm/hr, third to 24th 29.902 ± 4.857 mm/hr, third to 48th 39.307 ± 4.445 mm/hr, third to 72nd 36.550 ± 5.449 mm/hr and third to the 96th a decrease means of 39.807 ± 5.406 mm/hr ESR value.
CRP indicates C-reactive protein; ESR, erythrocyte sedimentation rate.

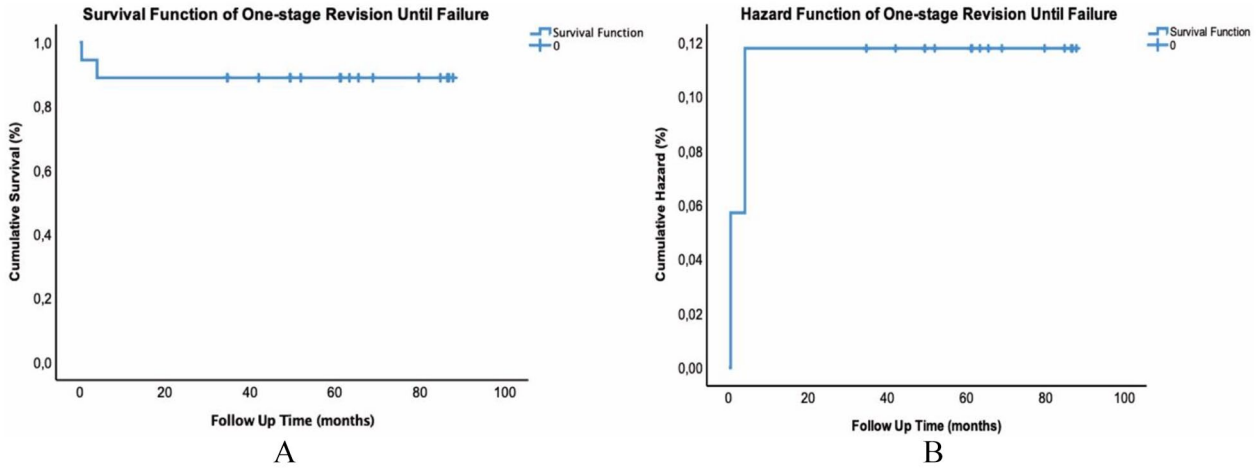

Figure 7. Kaplan–Meier curves for survival e cumulative risk: (A) an overall survival of 78.31 ± 6.34 (65.89-90.74) (mean ± standard error [95% confidence interval]) months (89%) and (B) the cumulative risk of failure of one-stage revision surgery found in our study was 0.09 ± 0.03 (−0.3 to 0.47) months (12%).

patients had lines of radiolucency, both after 1 year of one-stage revision. In one of the patients, the radiolucency line was observed in the lateral portion of Delee and Charnley's[23] zone I. The other patient presented in almost all zone III. No progression of these lines was observed during the entire follow-up period of these patients. Likewise, no lines of radiolucency and/or migration/movement of the femoral components were observed. However, in 3 cases, after 5 years of evolution, the presence of stress shielding in Gruen et al's[24] zones 6 and 7 was evidenced. In all patients who underwent acetabular reconstruction with lyophilized bovine graft, there was osseointegration of the graft to the host bone and no radiological changes were observed.

Complications during and after treatment were observed in some patients. In the transoperative period, in one patient when removing a cementless femoral component, there was a fracture of the greater trochanter, requiring steel wire cerclage. Another intraoperative complication observed in one patient with a bone defect in the acetabular floor was that after reaming to reach a suitable host bone bed for the xenograft, there was no more bone stock. In this case, a metallic mesh was used, which was fixed with screws on the acetabular walls and then the xenograft was impacted on the acetabular floor. After surgery, one patient had deep vein thrombosis. Another presented pruritus and redness of the skin after administration of vancomycin needing antibiotic change, and 2 patients developed acute renal failure which improved after clinical management.

Discussion

Our study found the final healing of 90% of patients in whom revision of infected arthroplasty was done by the one-stage method and where the acetabular defect was reconstructed with the use of a lyophilized bovine xenograft. Likewise, we found an overall success rate of 89% of patients. Tissue culture identifying *C. albicans* in PJI increases the risk of one-stage revision surgery failure in 4.47 times.

Some authors still show fear regarding one-stage revision of an infected arthroplasty.[12,26-28] As well as those authors who believe that in surgeries in which the use of graft is necessary or if the microorganism involved in the infection is not identified[28-31] one-stage revision should not be indicated. Therefore, and based on the 2013 PJI international consensus,[20] which postulates that the non-identification of the microorganism as a relative contraindication to the method, we performed surgeries without having prior knowledge of the microorganisms. At this time, when we started performing one-stage revision arthroplasty in the institution, there was also little knowledge regarding the analysis of synovial fluid referenced for the diagnosis of PJI before the surgical treatment. Therefore, it had an unclear utility, with uncertainty thresholds that still needed to be defined.[32,33] Very different from what is observed and known today, in which there is a validation of the criteria for the analysis of synovial fluid.[19] The international consensus of PJI published in 2018[21] maintained that not identifying the infectious microorganism is a relative and not an absolute contraindication to one-stage revision surgery. Castellani et al,[34] Bori et al[35] and Lange et al[36] recently, indirectly, questioned the need to identify the microorganism preoperatively to perform the one-stage method. It is believed, and the literature supports that the success of the one-stage revision is closely related to aggressive debridement[29,37,38] and the closing and filing out of dead spaces.[39,40] Even with this fear of some authors, in Europe, such a surgical approach is widely used.[2,41] A systematic review published in 2012,[42] an international consensus of PJI in 2013,[20] the Clinical Practice Guidelines by the Infectious Diseases Society of America (IDSA) in 2013,[43] a recent systematic review and meta-analysis published in 2015,[14] a pooled individual participant data analysis in 2018[44] and the second international consensus of PJI in 2018[21] showed that no

Table 6. Multivariate analysis of risk factors for one-stage revision surgery failure.

VARIABLES	CRUDE HR (95% CI)	CRUDE *P* VALUE	ADJUSTED HR (95% CI)	ADJUSTED *P* VALUE
Age	1.02 (0.876-1.182)	.818	–	–
Blood culture before surgery	6.12 (0.38-99.31)	.202	–	–
C. albicans	16.49 (1.031-263.757)	.048	4.47 (0.279-71.808)	.029
Culture results				
Gram positive	Reference		–	–
Gram-negative	30.14 (0.00-349 694 569)	.682	–	–
Gram-positive and -negative	1.00 (0.00-1.20E)	1.00	–	–
Sex				
Female	Reference		–	–
Male	39.44 (0.00-7 819 042.99)	.555	–	–
Previous antibiotic use	0.04 (0.00-7 884 228.0)	.743	–	–
Previous diseases				
Systemic arterial hypertension	34.22 (0.00-14 513 356.2)	.593	–	–
Ischemic heart disease	6.12 (0.38-99.31)	.202	–	–
Diabetes	398.37 (0.00-4.750E)	.471	–	–
Ischemic cerebrovascular accident	7.75 (0.484-123.88)	.148	–	–
Kidney disease	0.06 (0.00-1.46E)	.819	–	–
Lung disease (COPD)	2.91 (0.181-46.675)	.451	–	–
Three-phase bone scintigraphy	6.91 (0.81-591.432)	.394	–	–
Social factors				
Smoking	0.03 (0.00-12 396.74)	.593	–	–
Alcoholism	0.05 (0.00-1.39E)	.846	–	–
Symptoms that suggest infection				
Sinus tract	203.30 (0.00-143 614 283)	.032	135 461.00 (0.00-2.437E)	.958
Persistent drainage	90.92 (0.001-9 801 678.03)	.446	–	–
Hyperemia	128.06 (0.001-24 972 255.8)	.435	–	–
Pruritus	1 059 959.59 (0.00-8.157E)	.947	–	–
Swelling	134.03 (0.001-2697.8)	.435	–	–
Material used in revision surgery				
Cemented acetabular component	Reference		–	–
Cementless acetabular component	5.72 (0.352-92.688)	.220	–	–
Cemented femoral component	Reference		–	–
Cementless femoral component	24.19 (0.00-4.612E)	.743	–	–
Lyophilized bovine xenograft	0.84 (0.053-13.495)	.904	–	–
Tantalum augmentation	2.10 (0.131-33.562)	.601	–	–

Abbreviations: CI, confidence interval; COPD, chronic obstructive pulmonary disease; HR, hazard ratio.

difference exists in the reinfection rate when comparing the one-stage with two-stage revision surgery. Therefore, according to these important publications, the gold standard treatment for PJI is yet not known. Using the one-stage method without prior knowledge of the microorganism, we achieved a success rate of 89% of patients free of infection. Our results are comparable to the results achieved using the two-stage surgical revision reported in systematic reviews.[14,42] In the 2012 systematic review it was observed that 89.9% of the patients were free of infection[42] and in the 2015 review 92.1%.[14]

The use of bone grafts in the one-stage revision of PJI for patients with bone loss is not a consensus. The need to use a graft in a revision arthroplasty surgery when performed by the one-stage method is considered a relative contraindication of the one-stage surgical technique.[20,21,43] In most cases, it is done only in the second revision of a two-stage surgery procedure,[45-47] with an infection-free survival rate close to 92%.[48] The use of an avascular bone graft in the one-stage revision would increase the chance of infection, being this graft become a sequestrum, according to some authors.[28,49-52] However, when loaded with antibiotics, it has a drug carrier effect directly on the site of infection and at the same time, a barrier preventing bacterial spread.[9,31,40] Few articles have reported the use of a bone graft in a one-stage revision of PJI. Rudelli et al[53] reported infection eradication rates of 93.2%, Winkler et al[31] 92% and Loty et al[54] 91.2%. These articles show elevated rates of cure comparable to results studied in systemic reviews[14,42] where no gold standard method was found for the treatment of PJI and no bone graft was used. The 2012 review[42] reported 89.9% infection eradication by the two-stage revision and 91.4% by the one-stage revision method; in the 2015 review,[14] 92.1% was found for the two-stage method and 91.8% for the one-stage. Our study shows an initial infection-free survival rate of 90%. At the end of 6 months of antimicrobial treatment and a minimum 2 years of follow-up, the infection-free survival rate was 90% of the cases when the antibiotics impregnated graft was used.

In revision total hip arthroplasty surgery reconstruction of the acetabular bone stock is one of the most important steps of the surgical procedure[55] and grafts are the main choice. Autologous bone is the gold standard, however the small amount available per donor site make it difficult to use in surgeries where a large amount is required.[56,57] Allografts, another kind of graft, are other viable option,[58] but there is a risk of transmitting diseases, tumors and even inducing an unwanted immune response.[56,58,59] In our country (Brasil), the use of allografts is difficult, as few hospitals have a bone bank. The cost of maintenance and the cost of creating them are extremely elevated, which is impractical for many hospitals, such as our hospitals.[60] As an option in our patients, we used lyophilized bovine graft (OrthoGen), which has osteoconductive properties[56,57,60] and has structural and chemical similarity to human bone.[60-62] Several studies have demonstrated the good clinical results and safety for use in humans,[62-64] as well as the absence of an immune or inflammatory reaction of this xenograft.[60,65] Artificial bone grafts substitutes are not the reality of public hospitals in our country, even though they are an excellent option for the reconstruction of bone defects.[60]

The goal of antimicrobial treatment is to prevent bacterial adherence to the implant and tissues, to act against slow microbial growth and to act against biofilm formation.[2,66] These objectives require the use of bactericidal antibiotics, which results in prolonged oral or intravenous use.[2,43,66] It is agreed that the initial management is through the intravenous administration, aiming a minimum inhibitory concentration in the shortest possible time.[20,43] Nevertheless, there are divergences in this treatment time. The IDSA[43] guideline states that an ideal intravenous pathogen-specific administration should be maintained between 4 to 6 weeks after surgery independent on the type of surgical approach. Rudelli et al[53] performed a one-stage revision surgery with the use of bone graft and also recommended the use of for 4 weeks of intravenous antibiotic therapy. To IDSA[43] the intravenous treatment should be followed by oral antibiotic therapy to complete a total of 12 weeks of treatment. This time of intravenous and oral antibiotic therapy is also recommended by the international consensus of PJI.[20] Rudelli et al[53] advocated 5 months of oral therapy. Darley et al[67] and Stockley et al[68] advocated a shorter course of 2 weeks of intravenous antibiotics followed by 8 weeks of oral treatment with similar infection eradication results. Bernard et al[69] recommend 1 week of intravenous antibiotic administration followed by 5 weeks of oral therapy. They affirm that their results are equal to the results obtained with 12 weeks of treatment. Recently, a randomized, multicenter study showed that patients who continue antibiotic therapy for 12 weeks have a much lower rate of reinfection. Even though this study was carried out on patients undergoing two-stage revision surgery, it can be transposed to patients who undergo a one-stage revision[70]; therefore, we can expect that longer periods of antibiotic treatment in patients who underwent one-stage revision surgery will bring higher rates infection eradication. The suppressive antimicrobial therapy, a period greater than 12 weeks of treatment with antibiotics is not a consensus but is not prohibited by the IDSA guideline.[43] They advocate long courses of antimicrobial for rapidly growing mycobacteria.[71,72] The 2013[20] and the 2018 international consensus of PJI[73] also does not advocate suppressive therapy but does not advocate against it, and several authors use suppressive therapy for longer than 12 weeks. So, in summary, the last consensus[73] brings the important conclusion that no randomized study exists that guides the duration of antibiotic therapy, regardless of the type of surgery chosen. Thus, this point remains undefined in the literature and as the consensus postulates the treatment is universal. So, we find this possibility in the literature to practice what was proposed in our article, because nothing scientifically proven exists against as well as nothing exists in favor. In our

hospital, we followed the recommendation by the IDSA,[43] the international consensus of PJI[20,73] and Rudelli et al[53] and used 4 weeks of intravenous antibiotics. However, we believe it is essential to have a more prolonged suppressive therapy. We extended the treatment until the patient completes a total of 6 months of antibiotics (4 weeks of intravenous therapy and 20 weeks of oral therapy) as Rudelli et al[53] advocated.

Our study has several limitations. This is not a randomized trial, nor a prospective cohort study, but a retrospective cohort. The sample is very small. Our group of patients revised by one-stage surgical method without graft as well as those revised by one-stage with reconstruction using graft are small, so statistical comparisons are not possible. We also do not have control groups, as patients who underwent two-stage revision surgery, patients who underwent DAIR, and patients who underwent two-stage revision surgery with reconstruction using graft. Therefore, our findings are only descriptive regarding our sample and not comparative. However, it also has strengths. It is a study that reports in detail all the adopted protocol, the surgical technique, the treatment with antibiotics, as well as how the follow-up was done until the eradication of infection was achieved. It is one of the few studies (the second) in a developing country in Latin America that report acceptable and highs rates of infection eradication using the one-stage method to treat the periprosthetic infection. Even so, it shows similar findings to international studies published by developed countries. It is also the only study in South America, to date, that used the criteria developed by the International Consensus Group on Joint Infection Periprosthetic to diagnose infection and to report outcomes after surgical treatment as defined by the MSIS.[16] Therefore, it is an important publication on the treatment of hip prosthesis infection with a one-stage procedure, which may stimulate other hospitals to perform it.

Conclusion

One-stage revision of infected hip arthroplasty associated or not with acetabular reconstruction using grafts combined with an antibiotic therapy for 6 months offers excellent short-term success in patients with PJI. The reconstruction of the acetabular bone stock with an impacted graft hydrated in vancomycin not only stabilized the reconstructed joint but also seemed to have served as a carrier of the antibiotic directly to the site of infection, both necessary conditions for the eradication of PJI. When identifying a periprosthetic fungal infection, especially *C. albicans*, the chance of failure of one-stage revision surgery increases by 4.5 times. The authors believe that this technique offers a reliable alternative to two-stage revision surgery, with the advantage of acetabular bone stock reconstruction when necessary and clinically comparable results. Long-term results of this technique need to be studied.

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Author Contributions

RIU, LMFK, HMC, LSP, JAL and TAR data collection, writing the paper, revising the paper. HMC and LSP Infectious treatment of the patient. RIU and TAR performed surgeries. RIU, LMFK, JAL and TAR data analysis. TAR and LMFK orientation.

Consent for Publication

All authors have reviewed the final version of this article before its submission and authorize submission and publication if approved.

Ethics Approval and Consent to Participate

The research was approved by the Institutional Review Board (number 72074117.4.0000.5346) and followed the ethical guidelines of the 1975 Declaration of Helsinki.

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Availability of Data and Material

The data sets used and/or analyzed during this study are available in Mendeley Data repository: 10.17632/mvzby6y72f.8

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