



Comparison of Surgical Procedures in the Treatment of Hip Periprosthetic Infection

Comparaç o entre procedimentos cir rgicos no tratamento da infecç o de pr tese do quadril

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Abstract

Objective The present study aimed to compare the cure rate recovery time and Merle d'Aubign -Postel functional (MAPF) score after single-stage surgery (C1T) or two-stage surgery (C2T) to treat prosthetic infections of the hip considering sociodemographic and clinical features of the patients.

Materials and Methods The present retrospective study occurred in a single center from 2011 to 2014 with 37 studied cases including 26 treated with C1T and 11 with C2T. We compared the cure rate recovery time and MAPF score in the two groups as well as the sociodemographic and clinical features of the patients. We also considered surgical complications and the most common infectious agents.

Results The C1T group had a faster functional recovery than the C2T group but there were no significant differences in the cure rate surgical complications or MAPF score. However C1T group patients were significantly younger which may have influenced the outcomes. *Staphylococcus spp.* was the most common infectious agent (62%).

Conclusion Although C2T appears superior regarding infection cure C1T may be preferable for faster functional recovery. However it is critical to consider individual patient characteristics when choosing treatment. Further research with a larger sample size is required to confirm these results.

Keywords

- ▶ arthroplasty, replacement, hip
- ▶ prosthesis-related infections
- ▶ hip prosthesis
- ▶ recovery of function
- ▶ reoperation

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Resumo

Objetivo Comparar a taxa de cura, o tempo de recuperação e a pontuação na escala funcional de Merle d'Aubigné-Postel (EFMA) entre a cirurgia em tempo único (C1T) e a cirurgia em dois tempos (C2T) no tratamento de infecções protéticas do quadril, considerando as características sociodemográficas e clínicas dos pacientes.

Materiais e Métodos Foi realizado um estudo retrospectivo num único centro, entre 2011 e 2014, com um total de 37 casos estudados, sendo 26 tratados com C1T e 11 com C2T. Foram comparadas a taxa de cura, o tempo de recuperação e a pontuação EFMA entre os dois grupos, bem como as características sociodemográficas e clínicas dos pacientes. Foram também consideradas as complicações cirúrgicas e o agente infeccioso mais comum.

Resultados O grupo C1T teve uma recuperação funcional mais rápida do que o grupo C2T, mas não houve diferenças significativas na taxa de cura, nas complicações cirúrgicas ou na pontuação EFMA. No entanto, o grupo C1T era significativamente mais jovem, o que pode ter influenciado os resultados. *Staphylococcus spp.* foi o agente infeccioso mais comum (62%).

Conclusão Embora a C2T pareça ser superior em termos de cura de infecção, a C1T pode ser preferível para uma recuperação funcional mais rápida. No entanto, as características individuais dos pacientes devem ser consideradas na escolha do tratamento. São necessárias mais pesquisas com um tamanho de amostra maior para confirmar estes resultados.

Palavras-chave

- ▶ artroplastia de quadril
- ▶ infecções relacionadas a próteses
- ▶ próteses do quadril
- ▶ recuperação funcional
- ▶ reoperação

Introduction

Total arthroplasty-associated infection is a serious issue today. The estimated rate of postoperative infections in total arthroplasties ranges from 1 to 7%, resulting in significant monetary costs.¹

Over one million total hip arthroplasties occur every year worldwide.² Several studies point to an increase in this number due to the higher life expectancy. In addition, the risk of infection increases over time, leading to an absolute increase in the rate of periprosthetic infections.²⁻⁶

Hip prosthetic infection is the leading cause of hip revision surgery after mechanical etiologies, highlighting the need to find solutions to maximize its cure rate and reduce its repercussions regarding function, quality of life, and costs.^{5,7}

Hip prosthetic infection treatment may employ different strategies, including single-stage (C1T) and two-stage (C2T) prosthesis replacement, suppressive therapy, and definitive surgery for infectious control, such as amputation or the Girdlestone procedure.^{4,8}

However, there is no consensus on the treatment of prosthetic infection given the scarcity of controlled and randomized clinical trials directly comparing different treatment strategies, in contrast to osteomyelitis or septic arthritis, for instance.^{9,10}

However, many authors consider C2T the gold standard for treating hip prosthetic infections.¹⁰⁻¹² The first surgical stage consists of debridement, arthroplasty explantation, and placement of a polymethylmethacrylate spacer impregnated with antibiotics.^{11,13} Next, antibiotherapy is instituted for 4 to 6 weeks even though its duration is not a consensus.^{4,14}

The second surgical stage, a revision arthroplasty, occurs after normalization of the analytical parameters of infection.¹⁵ However, few studies addressed the long-term follow-up of these patients.¹¹

More recently, the success of C1T has been studied, demonstrating its superiority in terms of functional outcomes.¹² This treatment consists of infected tissues and implant excision and the immediate placement of a new prosthesis, followed by antibiotic treatment.¹⁵ Patients can begin physical recovery immediately. However, the same does not seem true for the success rate of infection cure.¹²

Some studies indicate that C1T may be the best option for more sensitive infectious agents and patients with good systemic and local conditions (no fistulization or severe tissue damage).¹⁵

The present study aimed to compare the two surgical strategies, C1T and C2T, to treat hip prosthetic infections. We analyzed the cure rate and functional recovery of these patients, considering their characteristics (e.g., gender, age, comorbidities, and previous surgeries).

Materials and Methods

An observational, cross-sectional, retrospective, descriptive-analytical study was performed on subjects undergoing hip prosthesis revision surgery due to a diagnosis of prosthetic infection according to the Musculoskeletal Infection Society criteria⁷ from January 2011 to December 2014 in a tertiary reference hospital. The inclusion criterion was a periprosthetic hip infection, and the exclusion criteria were the lack of explantation of all hip prosthesis components and

placement of a hip revision prosthesis. Our institutional database identified 242 hip replacement revision surgeries. We selected 37 of the patients diagnosed with a periprosthetic hip infection. Of these, 26 underwent C1T (C1T group) and 11 underwent C2T (C2T group). Collected data included age, gender, time of evolution of the prosthetic infection, infection cure status, infection laterality, infectious agent, relevant comorbidities,¹⁶ history of previous surgeries at the infected site, surgical complications in infection treatment, time for functional status recovery, and Merle d'Aubigné-Postel functional (MAPF) score¹⁷ (recorded after 1 year of follow-up).

Data analysis used the IBM SPSS Statistics for Windows, version 22.0 (IBM Corp., Armonk, NY, USA). Graph construction used GraphPad Prism, version 6.01 (GraphPad Software, La Jolla, CA, USA). The Shapiro-Wilk test evaluated the Gaussian distribution of continuous variables from all groups. Group comparison used the following tests: t-test for independent samples, Mann-Whitney U test, two-tailed Fisher exact test, and the respective effect magnitude measures. Results were statistically significant if $p < 0.05$ at a 95% confidence interval (CI).

Results

The study included 37 surgeries for hip prosthetic infection treatment performed from 2011 to 2014. These procedures included 26 C1Ts and 11 C2Ts.

We performed a comparative analysis of the sociodemographic and clinical characteristics of the sample (► **Tables 1 and 2**). The C2T group was significantly younger than the C1T group, with a moderate effect magnitude. Our institution avoids C2T in older patients because of the negative impact on functional recovery. Outcome analysis considered this fact.

Most infections occurred on revision implants, lasted ≥ 4 weeks, and their etiological agents were resistant organisms. Most cases presented comorbidities with a Charlson index ≥ 1 .¹⁶ Only 21.6% of subjects had surgical complications during the perioperative period. There were no statistically significant differences in clinical parameters between the two groups.

There was no mortality associated with periprosthetic infection. Five patients died of unrelated causes.

The C1T group had a lower cure rate than the C2T group (► **Fig. 1**), but we did not observe a statistically significant association between the surgical procedure and cure rate.

For a Charlson index ≥ 1 , the cure rate was higher for the C2T group than for the C1T group. The opposite occurred in patients with no comorbidities (null Charlson index) (► **Fig. 2**), but there was no statistical significance.

The cure rate for primary implants was higher in the C2T group than in the C1T group, again with no statistical significance (► **Fig. 3**). In cases of revision implants, the cure rate was $\sim 70\%$.

In cases with no previous surgical procedures at the infection site, C2T had a 25% higher cure rate than C1T (► **Fig. 4A**), but without statistical significance. In cases with previous surgical procedures, the cure rate was $\sim 70\%$ in both groups (► **Fig. 4B**).

Some authors reported an increased risk of periprosthetic infection in subjects > 75 years old.¹⁸ We compared the cure rate in patients aged ≥ 75 and < 75 years old (► **Fig. 5A**), but the association was not statistically significant. The cure rate was 18% lower in the ≥ 75 -year-old group than in the < 75 -year-old group, but the fact that the C1T group was significantly younger and had a slightly lower cure rate than the C2T group may be a confounding factor. No surgical procedure showed a statistically significant advantage according to age (► **Fig. 5B-C**).

The cure rate was higher for females but with no statistical significance (► **Fig. 6**).

Functional recovery was faster for the C1T group than for the C2T group (► **Fig. 7**), with a statistically significant difference for the two age groups (< 75 and ≥ 75 years old) (► **Fig 8**).

There were no statistically significant differences in the MAPF score between C1T and C2T (► **Fig 9**).

► **Table 3** shows the infectious agents in decreasing order of frequency. Staphylococci were the most common organism, with proportions consistent with the literature.^{2,4,9,19-21} There were 3 cases (8.1%) of methicillin-resistant *Staphylococcus aureus* (MRSA) infection and 5 cases (13.5%) of methicillin-resistant *S. epidermidis* (MRSE).

We created two categories to investigate potential differences in the cure rate depending on the resistance of the

Table 1 Sociodemographic features of the patients

Variables	Total	C1T	C2T	U	p-value	r
	n = 37 (100%)	n = 26 (70.3%)	n = 11 (29.7%)			
	Median (IQR)	Median (IQR)	Median (IQR)			
Age ^a (in years)	74 (18.0)	77 (16.0)	64 (18.0)	83.0	.046	0.33
	n (%)	n (%)	n (%)		p-value ^b	ϕ
Sex						
Male	21 (56.8)	15 (57.7)	6 (54.5)		1.000	0.029
Female	16 (43.2)	11 (42.3)	5 (45.5)			

Abbreviations: ϕ , phi coefficient; C1T, single-stage prosthesis replacement; C2T, two-stage prosthesis replacement; IQR, interquartile range.

^aAt the date of the surgical treatment (for C2T, it corresponds to the age at the date of the first surgical procedure).

^bFisher exact test. Significant p-values (< 0.05) are shown in bold.

Table 2 Clinical features of the patients

Variables	Total	C1T	C2T	p-value ^a	φ
	n = 37 (100%)	n = 26 (70.3%)	n = 11 (29.7%)		
	n (%)	n (%)	n (%)		
Infection^b					
Primary implant	14 (37.8)	10 (38.5)	4 (36.4)	1.000	0.020
Revision implant	23 (62.2)	16 (61.5)	7 (63.6)		
	0 [#]				
Number of previous surgeries^c					
0	12 (32.4)	8 (30.8)	4 (36.4)	1.000	0.055
≥ 1	25 (67.6)	18 (69.2)	7 (63.6)		
	0 [#]				
Infection time^d					
< 4 weeks	6 (16.2)	6 (23.1)	0 (0.00)	0.151	0.286
≥ 4 weeks	31 (83.8)	20 (76.9)	11 (100)		
	0 [#]				
Side^e					
Left	16 (43.2)	14 (53.8)	2 (18.2)	0.071	0.329
Right	21 (56.8)	12 (46.2)	9 (81.8)		
	0 [#]				
Infectious agent (resistance)^f					
Low	13 (38.2)	10 (41.7)	3 (30.0)	0.704	0.109
High	21 (61.8)	14 (58.3)	7 (70.0)		
	3 [#]				
Comorbidities (Charlson index^g)					
0	14 (37.8)	10 (38.5)	4 (36.4)	1.000	0.020
≥ 1	23 (62.2)	16 (61.5)	7 (63.6)		
	0 [#]				
Complications^h					
Absent	29 (78.4)	21 (80.8)	8 (72.7)	0.672	0.089
Present	8 (21.6)	5 (19.2)	3 (27.3)		
	0 [#]				

Abbreviations: φ, phi coefficient; C1T, single-stage prosthesis replacement; C2T, two-stage prosthesis replacement.

Notes: ^aFisher exact test.

^bDistinguishing whether the infection occurred in a primary implant or a revision implant.

^cNumber of any previous surgical procedure at the site of infection, except primary arthroplasty surgery.

^dTime of evolution of the prosthetic infection; all infection cases had an evolution time of ≥ 3 weeks.

^eHip prosthetic infection side.

^fLow-resistant agents include those known as easier to eliminate (non-methicillin-resistant Staphylococci), while high-resistant agents include agents those known as more difficult to eradicate (methicillin-resistant Staphylococci, Gram-negative agents, and polymicrobial cases).

^gCharlson comorbidity index.

^hSurgical complications include perioperative fracture, perioperative hemorrhage, dysmetria, and neuronal injury (one case with an adverse reaction to rifampicin, consisting of erythema and anemia, was not considered a surgical complication).

[#]Missing values. Significant p values (< 0.05) are shown in bold.

infectious agent (►Fig. 10A). There was a statistically non-significant increase of ~ 5% in the cure rate for low-resistant agents. There were no statistically significant differences in the functional recovery time between the two resistance categories (►Fig. 10B).

Discussion

Most cases of hip prosthesis revision due to infection occur in males (►Table 1), consistent with previous studies.⁶ Furthermore, our study showed that, although there is no

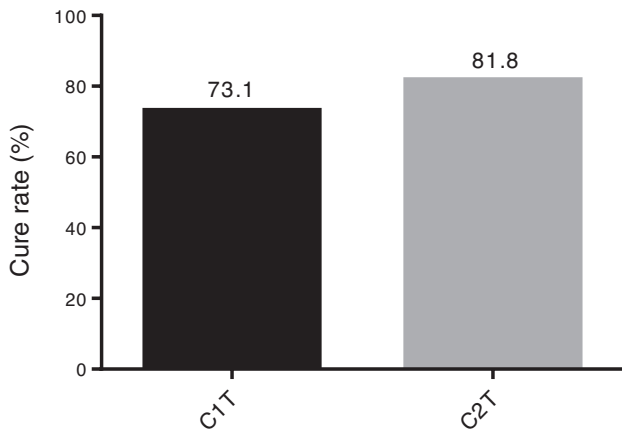


Fig. 1 Cure rate according to the surgery type for treating a prosthetic infection. $n_{C1T} = 26$; $n_{C2T} = 11$. $p = 0.695$, two-tailed Fisher exact test, $\phi = 0.093$.

statistical significance, the cure rate is lower in males and, consequently, the infection recurrence rate is higher in these subjects (►Fig. 6). These two pieces of information support the hypothesis that the male gender is a risk factor

for hip prosthetic infection,^{3,22} even though the literature is controversial.^{10,18}

During the present study, there were no deaths related to any surgery type. Previous studies in the elderly point to a hip prosthetic infection-related death rate of ~8%.²³ A larger sample is required to assess this parameter.

Although age can be a confounding factor, the difference in the cure rate between the two types of surgery (►Fig. 1) was consistent with the literature. A retrospective study of 92 patients compared C1T and C2T and showed cure rates of 56.8 and 94.5%, respectively.⁸ A meta-analysis indicated an additional 3% risk of reinfection for C1T.¹⁰ However, another broader and more recent meta-analysis suggests similar cure rates for both types of surgery, ~92%.²⁴ However, the reliability of these data is questionable since no randomized clinical trial directly compared the effectiveness of these procedures.²⁴

One study described an increased risk of periprosthetic infection for Charlson indices ≥ 1 .¹⁸ However, no study compared the two procedures considering comorbidities. Our study favors C2T in patients with one or multiple comorbidities and C1T in subjects without comorbidities (►Fig. 2).

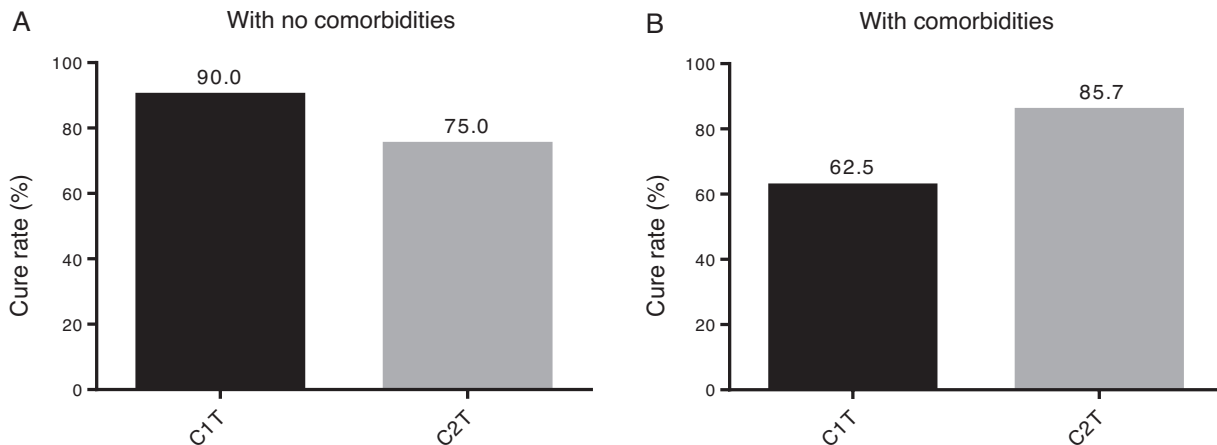


Fig. 2 (A) Cure rate in the group with no comorbidities (Charlson index = 0) for each type of surgery to treat prosthetic infection. $n_{C1T} = 10$; $n_{C2T} = 4$. $p = 0.505$, two-tailed Fisher exact test, $\phi = 0.194$. (B) Cure rate in the group with comorbidities (Charlson index ≥ 1) for each type of surgery to treat prosthetic infection. $n_{C1T} = 16$; $n_{C2T} = 7$. $p = 0.366$, two-tailed Fisher exact test, $\phi = 0.232$.

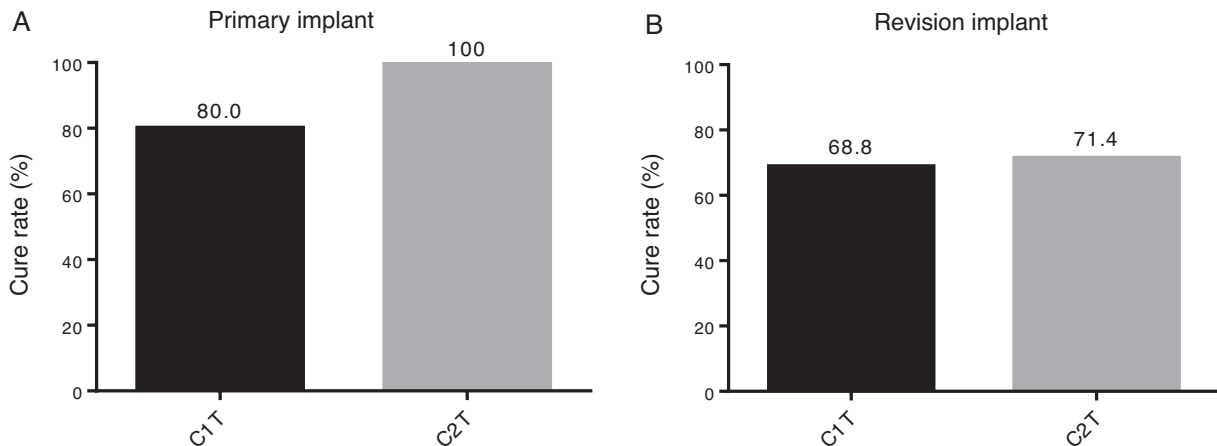


Fig. 3 (A) Cure rate in the primary implant group for each type of surgery to treat prosthetic infection. $n_{C1T} = 10$; $n_{C2T} = 4$. $p = 1.000$, two-tailed Fisher exact test, $\phi = 0.258$. (B) Cure rate in the revision implant group for each type of surgery to treat prosthetic infections. $n_{C1T} = 16$; $n_{C2T} = 7$. $p = 1.000$, two-tailed Fisher exact test, $\phi = 0.027$.

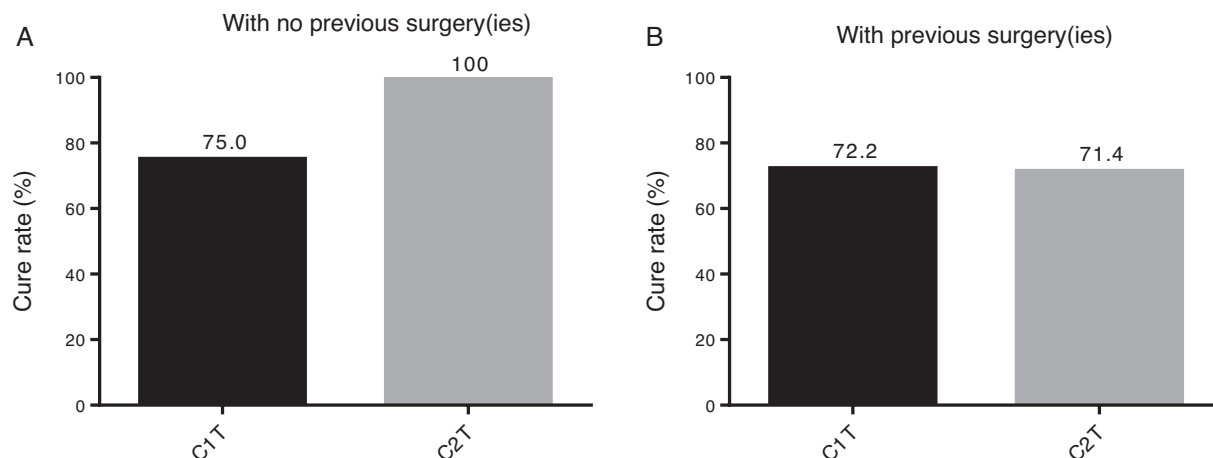


Fig. 4 (A) Cure rate in the group without previous surgeries at the infection site except primary arthroplasty (e.g., osteotomy, surgical debridement for any reason, partial or total prosthesis replacement due to infection or another reason) for each type of surgery to treat prosthetic infection. $n_{C1T} = 8$; $n_{C2T} = 4$. $p = 0.515$, two-tailed Fisher exact test, $\phi = 0.316$. (B) Cure rate in the group with previous surgery(ies) at the infection site for each type of surgery to treat the prosthetic infection. $n_{C1T} = 18$; $n_{C2T} = 7$. $p = 1.000$, two-tailed Fisher exact test, $\phi = 0.008$.

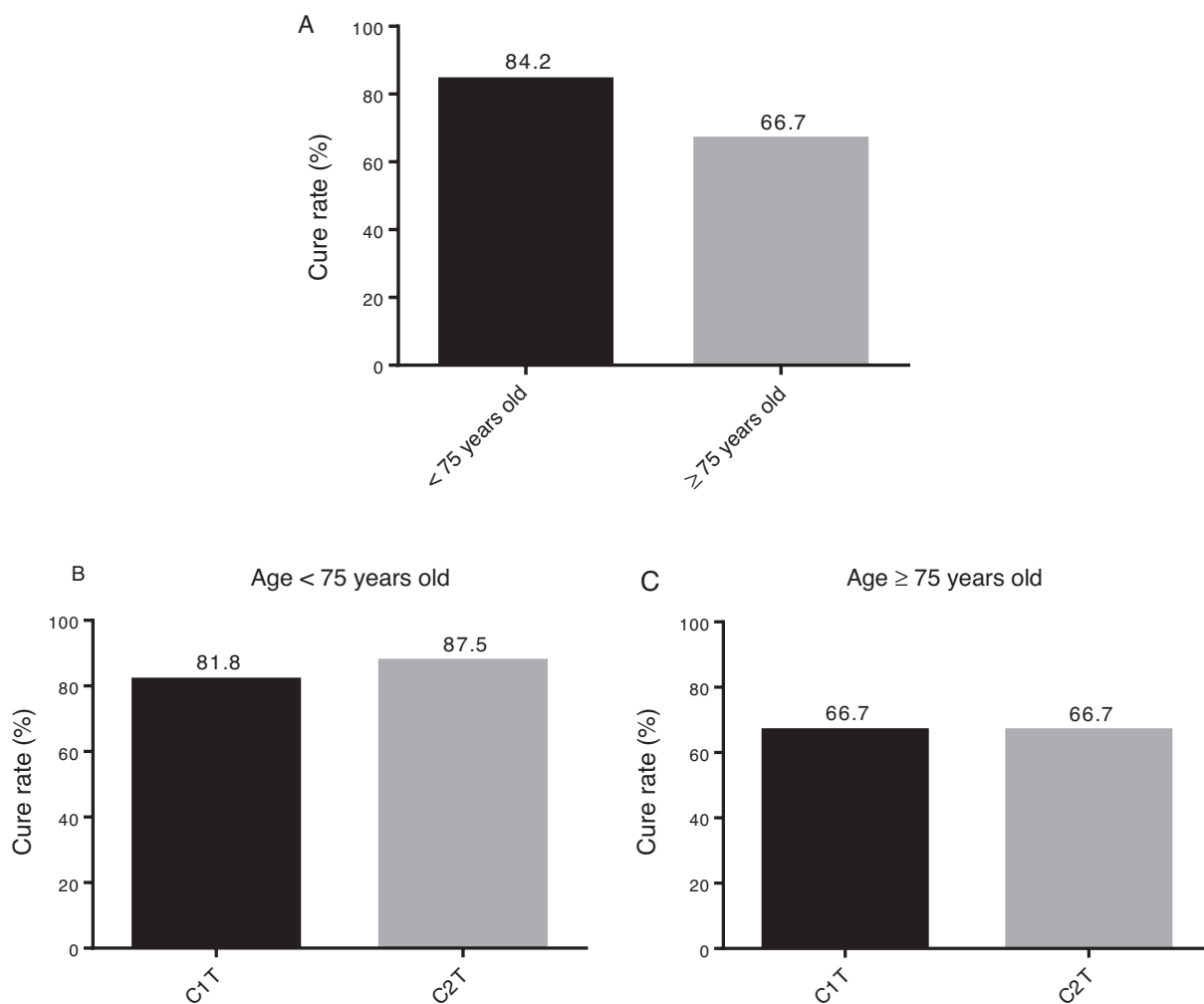


Fig. 5 (A) Cure rate in patients aged < 75 years old versus ≥ 75 years old. $n_{<75 \text{ years}} = 19$, $n_{\geq 75 \text{ years}} = 18$. $p = 0.269$; two-tailed Fisher exact test, $\phi = 0.204$. (B) Cure rate in patients aged < 75 years old for each type of surgery to treat prosthetic infection. $n_{C1T} = 11$; $n_{C2T} = 8$. $p = 1.000$, two-tailed Fisher exact test, $\phi = 0.077$. (C) Cure rate in patients aged ≥ 75 years old for each type of surgery to treat prosthetic infection. $n_{C1T} = 15$; $n_{C2T} = 3$. $p = 1.000$, two-tailed Fisher exact test, $\phi < 0.001$.

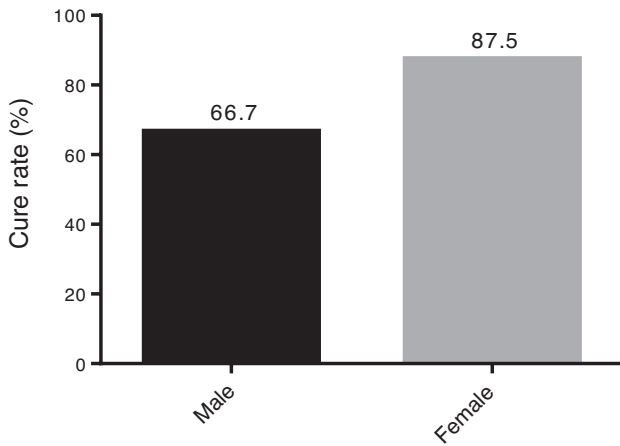


Fig. 6 Cure rate in male versus female patients. $n_{\text{male}}=21$, $n_{\text{female}}=16$. $p=0.248$, two-tailed Fisher exact test, $\phi=0.241$.

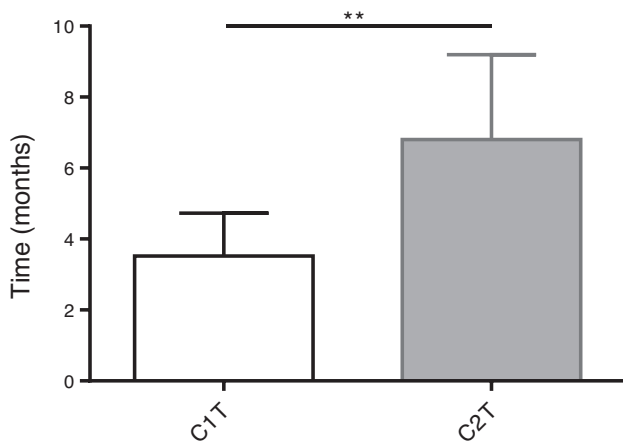


Fig. 7 Comparison of functional recovery time in months in the C1T group ($n_{\text{C1T}}=21$; $M=3.52$, $\sigma=1.21$) and in the C2T group ($n_{\text{C2T}}=10$; $M=6.80$, $\sigma=2.39$), $t(11)=4.08$, $p=0.002$, $d=1.73$. Error bars indicate σ . $**p < 0.01$.

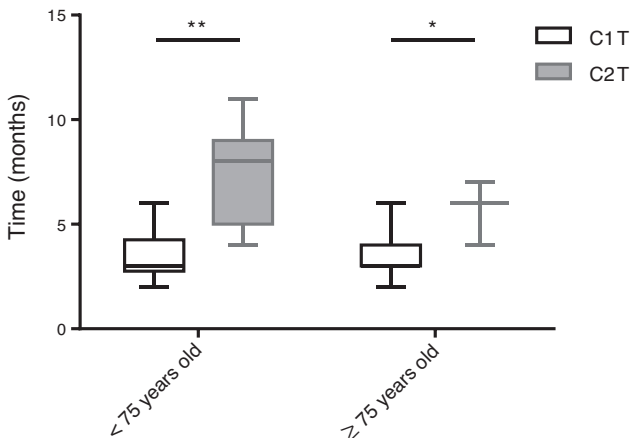


Fig. 8 Comparison of functional recovery time in months in patients aged <75 years old (C1T group: $n_{\text{C1T}}=10$; median = 3.00; interquartile range (IQR) = 1.50; C2T group: $n_{\text{C2T}}=7$; median = 8.00; IQR = 4.00; $U=6.00$; $p=0.004$; $r=0.69$ and ≥ 75 years old (C1T group: $n_{\text{C1T}}=11$; median = 3.00; IQR = 1.00; C2T group: $n_{\text{C2T}}=3$; median = 6.00; IQR not calculable; $U=4.00$; $p=0.046$; $r=0.53$). Bars represent the maximum and minimum values. $*p < 0.05$; $**p < 0.01$.

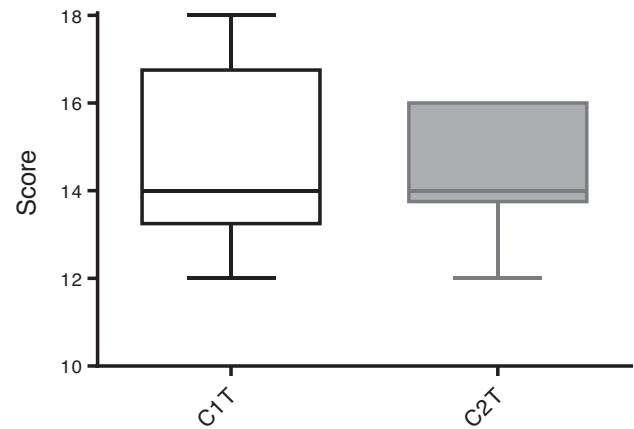


Fig. 9 Merle d'Aubigné-Postel functional (MAPF) score in the C1T group ($n=20$; median = 14.0, IQR = 4.00) and in the C2T group ($n=10$; median = 14.0; IQR = 2.00); $U=92.5$; $p=0.729$; $r=0.063$. Cases with no score record were excluded ($n=7$). Bars represent the maximum and minimum values.

Table 3 Infection-related organisms

Organism	n (%)
<i>Staphylococcus aureus</i>	12 (32.4)
Coagulase-negative <i>Staphylococci</i>	11 (29.7)
Polymicrobial infections ^a	7 (18.9)
Gram-negative agents	4 (10.8)
Unidentified organism	3 (8.1)
Total	37 (100)

Note: ^aIncluding all cases with two or more infectious agents identified, except two cases (*Staphylococcus stimularis* + *S. capitis* and *S. lugdunensis* + *S. capitis*) included in the coagulase-negative *Staphylococci* category.

► **Table 2** shows that most patients were operated on at the site of infection in addition to primary arthroplasty. These patients seemed to present a higher infection risk (► **Figs. 3** and **4**), as, in addition to the risk associated with each surgery, these procedures damage the microvasculature and lead to fibrosis, weakening the local immune response, which may exacerbate an indolent, previously insignificant infection.¹² C2T appeared beneficial in patients who, in addition to primary arthroplasty, have never undergone surgery in the same location. However, there was no superiority associated with any surgery in patients with a previous surgical history at the infected site.

Our data could not find a clear benefit in either type of surgery depending on age (► **Figs. 5** and **6**). Moreover, there was a significant difference between the two groups (► **Table 1**). Some authors argue that age is a risk factor for prosthetic infection, but data is contradictory.^{23,25}

► **Fig. 7** shows that C2T resulted in a statistically significant higher functional recovery time than C1T. However, ► **Fig. 8** reveals that the difference in recovery time between the 2 groups is lower for subjects ≥ 75 years old. In addition to the greater confidence in the statistical difference, the effect magnitude is higher for ages <75 years

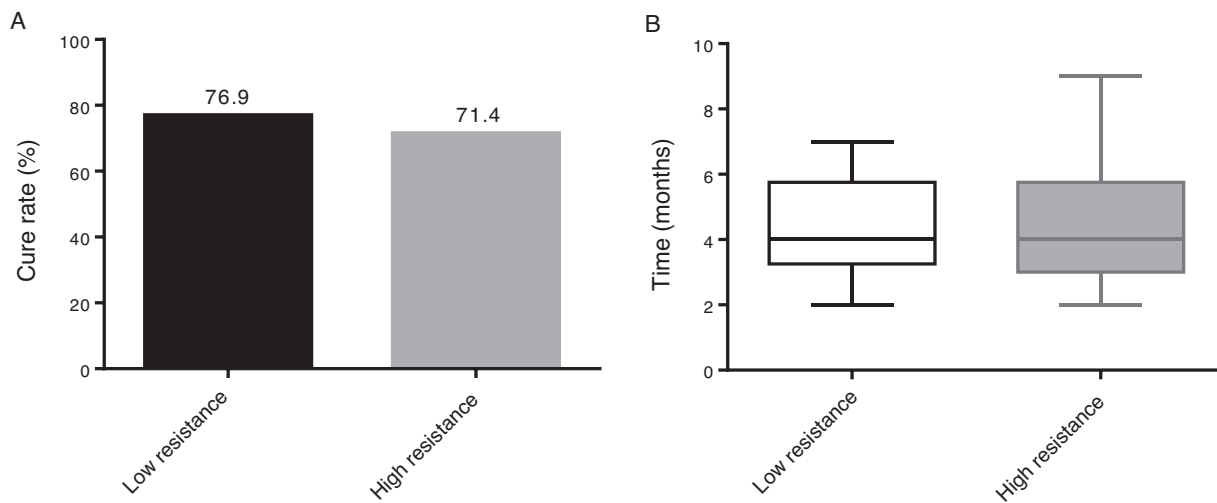


Fig. 10 (A) Cure rate in cases of infection caused by low-resistant agents (non-methicillin-resistant *Staphylococci*, $n = 13$) versus high-resistant agents (methicillin-resistant *Staphylococci*, Gram-negative, and polymicrobial agents, $n = 21$); $p = 1.000$; two-tailed Fisher exact test; $\phi = 0.061$. Cases with no organism detection ($n = 3$) were excluded from the analysis. (B) Functional recovery time in months in cases of infection caused by low-resistant ($n = 12$; median = 4.00; IQR = 2.50) versus high-resistant agents ($n = 16$; median = 4.00, IQR = 2.75); $U = 91.5$; $p = 0.832$; $r = 0.004$. Cases with no recovery time record ($n = 6$) or no organism detection ($n = 3$) were excluded. Bars represent the maximum and minimum values.

old. These data seem to suggest a weakening of the effect of C2T on the recovery time in older subjects (that is, ≥ 75 years old). Therefore, there is an apparent advantage in considering the functional recovery time as a treatment choice criterion (C1T versus C2T), especially for ages < 75 years old.

The present study detected no differences in the final functional activity level according to the MAPF score. Other studies reported average scores of 13.1 to 15.4 points after C2T and 13.8 points after C1T.^{13,21,26,27} However, none of the studies directly compared the scores between the two types of surgery.

Surgical complications increase the risk of periprosthetic infection. One study related intraoperative fracture in knee arthroplasty with an increased risk of infection.²⁸ Other studies indicated that intraoperative hemorrhage or hematoma is associated with a greater risk of periprosthetic infection.^{3,4} Our data (► **Table 2**) showed an 8% increase in the C2T group compared with the C1T group in the rate of surgical complications, without statistical significance. Therefore, we cannot make an association between the type of surgery and the rate of surgical complications, as previously suggested.²⁹ However, another study proposed that the risk of complications in C2T will be approximately two times higher than in C1T, with the risk of surgical complications at each C2T stage similar to C1T.¹²

Some authors proposed that Gram-negative agents, multi-drug-resistant organisms, and polymicrobial infections lead to worse outcomes.^{10,30} However, other studies showed that antimicrobial susceptibility testing results cannot predict the outcome of periprosthetic infection.⁹ Therefore, our data do not allow conclusions on the outcome of severe infections.

There was a selection bias since the decision on the type of surgery was not random. The exclusion of patients who did not complete the second stage of surgery probably resulted in a bias favoring C2T.

The nature of the present study does not allow us to determine whether the cases with no infectious agent detection were due to early antibiotic therapy.

The infection diagnostic criteria used (proposed by the American Musculoskeletal Infection Society⁷) do not ensure the avoidance of false-negative and false-positive results. As such, some infection cases included may have corresponded to the simple aseptic detachment of the prosthesis and contamination in the microbiological tests (most frequently by coagulase-negative *Staphylococci*), whereas some cases of true infection may have been excluded.^{9,15}

Data regarding functional recovery time are independent of the infection cure, which could be a confounding factor. Furthermore, the pain threshold may vary between younger and older subjects for sociocultural reasons. It is also possible that the functional recovery of younger patients will take longer as they will achieve a higher range of mobility than older subjects. Moreover, there were no preoperative MAPF scores.

Conclusion

Our study shows an advantage in the recovery time in subjects undergoing C1T. However, we cannot draw reliable conclusions comparing the cure rate after C1T and C2T. More studies with a larger sample size (ideally, 3,500 patients¹⁰) are required, considering risk factors and potential confounder factors.

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Conflict of Interests

The authors have no conflict of interests to declare.

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