



Available online at
ScienceDirect
www.sciencedirect.com

Elsevier Masson France
EM|consulte
www.em-consulte.com/en



Original article

Curative treatment of prosthetic joint infection in patients younger than 80 vs. 80 or older



Chloé Jamakorzyan^{a,b,*}, Vanina Meyssonier^{a,b}, Younes Kerroumi^a, Benoit Villain^{a,d},
 Beate Heym^{a,c}, Luc Lhotellier^{a,d}, Valérie Zeller^{a,b}, Jean-Marc Ziza^{a,b}, Simon Marmor^{a,d}

^a Centre de référence des infections ostéo-articulaires complexes, groupe hospitalier Diaconesses-Croix Saint-Simon, 125, rue d'Avron, Paris 75020, France

^b Service de médecine interne et rhumatologie, groupe hospitalier Diaconesses-Croix Saint-Simon, 125, rue d'Avron, Paris 75020, France

^c Laboratoire des centres de santé et hôpitaux d'Ile-de-France, groupe hospitalier Diaconesses-Croix Saint-Simon, 125, rue d'Avron, Paris 75020, France

^d Service de chirurgie osseuse et traumatologique, groupe hospitalier Diaconesses-Croix Saint-Simon, 125, rue d'Avron, Paris 75020, France

ARTICLE INFO

Article history:

Accepted 13 December 2018

Available online 6 February 2019

Keywords:

Arthroplasty

Prosthetic joint infection

Elderly

Octogenarians

Curative surgery

One-stage exchange arthroplasty

ABSTRACT

Objective: Prosthetic joint infection (PJI) is a serious complication of joint replacement surgery. The major pharmacological and surgical treatments required by PJI increase the risk of peri-operative complications in elderly patients. The increase in life expectancy combined with procedural advances make these treatments possible even in the oldest patients. Here, our objective was to compare the characteristics and outcomes of curative PJI treatment in patients <80 years vs. ≥80 years.

Methods: A prospective single-center design was used to compare the characteristics and outcomes of curative treatment for hip or knee PJI in patients <80 years and ≥80 years admitted in 2004–2014.

Results: Of 765 patients admitted for PJI, 590 were <80 years and 124 were ≥80 years. Medical history and comorbidities were similar in the two groups. The older group had a significantly higher proportion of patients with American Society of Anesthesiologists Scores ≥3 and with streptococcal infection (20% vs. 13%, $P < 0.05$). After complete surgical excision and prolonged antibiotic therapy, the only event whose frequency differed significantly between the two groups was PJI-related death, which was more common in the older patients (6.5% vs. 0.8%, $P < 0.05$). The 2-year survival rate after one-stage exchange arthroplasty was >90% in the ≥80 year group.

Conclusion: Patients aged 80 years or older are eligible for the same curative pharmacological and surgical PJI treatments used in their younger counterparts. Before surgery, the risk/benefit ratio of the major surgical procedure required to treat PJI must be assessed on a case-by-case basis.

© 2019 Published by Elsevier Masson SAS on behalf of Société française de rhumatologie.

1. Introduction

Infection remains a serious complication of hip and knee arthroplasty procedures. The frequency of hip or knee prosthetic joint infection (PJI) ranges across studies from 0.3% to 2% [1,2]. Patients aged 80 years or over are at increased risk for comorbidity decompensation in the event of major surgery, despite advances in surgical techniques and prophylactic treatments. When managing PJI in patients ≥80 years, the perioperative monitoring strategy must therefore be specifically designed to take into account the

age-related decline in adaptation to stress; increased morbidity and mortality; and frequent occurrence of early post-operative cognitive dysfunction, notably after prolonged anesthesia [3,4].

Osteoarthritis is the main reason for performing total hip arthroplasty (THA) or total knee arthroplasty (TKA). The main other indication of THA is proximal femoral fracture, which is more common in elderly individuals, notably women older than 80 years [5].

The number of arthroplasty procedures performed in industrialized countries such as France is increasing at a brisk pace. In France, over 200,000 arthroplasties were done in 2012 [6], and the number of THA and TKA procedures in the US is projected to reach 4 million in 2030 [7]. In France, it is estimated that one-third of the population will be 60 years of age or older by 2060 [8]. The aging of the population, combined with the increased healthy life expectancy, is translating into growing numbers of arthroplasty procedures in individuals aged 80 years or over.

* Corresponding author at: Centre de référence des infections ostéo-articulaires complexes, groupe hospitalier Diaconesses-Croix Saint-Simon, 125, rue d'Avron, 75020 Paris, France.

E-mail address: chloejamakorzyan@gmail.com (C. Jamakorzyan).

As a corollary to this trend, the number of PJIs is increasing. The morbidity and mortality rates of the major pharmacological and surgical treatments required in PJI increase with advancing age. Nonetheless, the increase in life expectancy, together with procedural advances, can be expected to produce good outcomes even in the oldest patients.

The objective of this prospective single-center study was to compare the characteristics and outcomes of curative PJI treatments in patients <80 years vs. ≥ 80 years.

2. Methods

A prospective observational single-center study was conducted in patients admitted to a referral center for complex osteoarticular infections in Paris, France, between 2004 and 2014, for PJI after THA or TKA. The inclusion criteria were age older than 18 years and microbiologically documented PJI. Microbiological documentation was defined as recovery of a microorganism in cultures of at least two different samples of joint fluid or joint tissues. The samples could be obtained by pre-operative joint aspiration and/or intra-operative collection. Recovery of a microorganism from a single sample could be sufficient in patients with a suggestive medical history and local signs of infection. Thus, the diagnosis of PJI was based on the criteria developed by Parvizi [9].

For chronic PJI, curative treatment combined prolonged antibiotic therapy and exchange of all the prosthetic components. For acute PJI developing within 1 month after the last arthroplasty procedure or occurring abruptly due to hematogenous dissemination at a distance from the last arthroplasty procedure, curative treatment consisted in joint lavage and synovectomy, with conservation of the implants.

We divided the patients into two groups based on age < 80 years or ≥ 80 years. The following events were compared between these two groups: recurrent PJI (relapse with the same microorganism or new infection with a different microorganism), mechanical events related to the prosthesis (dislocation, loosening, fracture), and deaths due to the PJI (sepsis) or its treatment (peri-surgical complications).

Qualitative variables were described as number (%) and quantitative variables as median [interquartile range]. Recurrence-free survival and PJI-related mortality were compared between the two groups using the Kaplan–Meier method and the logrank test. R software was used for the statistical analyses.

Role for the funding source: not applicable

3. Results

Of 765 patients treated for hip or knee PJI then followed-up for at least 2 years, 51 were excluded because they did not undergo surgical treatment; among them, 66% were ≥ 80 years of age. This left 714 patients for the study, 518 with THA and 196 with TKA (Fig. 1).

Of the 714 patients, 590 were <80 years and 124 were ≥ 80 years. The only significant baseline differences between the two groups were higher prevalences in the older patients of cardiovascular comorbidities (55% vs. 29%, $P < 0.01$) and of an American Society of Anesthesiologists (ASA) Score ≥ 3 (47.5% vs. 24.0%, $P < 0.001$) and a lower body mass index (24.7 vs. 27.3, $P < 0.001$) (Table 1). The distribution of PJI types as defined by the Tsukayama classification was not significantly different between the two groups [10] (Table 2).

The most common causative microorganisms were coagulase-negative staphylococci, notably in the group <80 years, followed by *Staphylococcus aureus* and streptococci, chiefly group B strep-

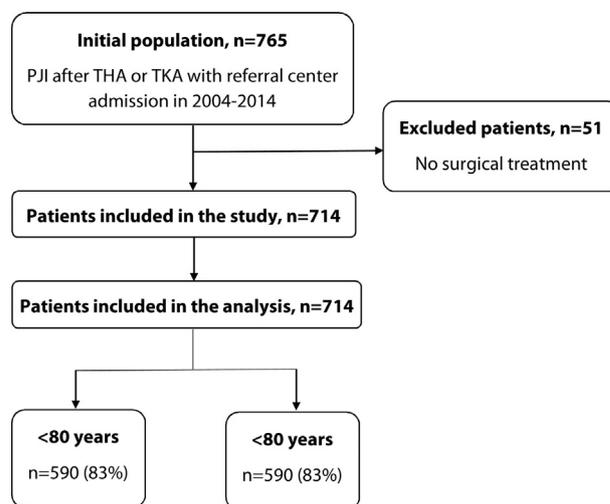


Fig. 1. Patient flow chart.

Table 1
Main features of the study patients.

	Age < 80 years (n = 590)	Age ≥ 80 years (n = 124)	P-value
Features			
Male sex	320 (54%)	55 (44%)	< 0.05
Age (years)	67 [60.1–73.7]	83.3 [81.5–85.6]	
Body mass index, kg/m ²	27.3 [24–30.8]	24.7 [21.8–28]	< 0.001
Comorbidities			
Hypertension	286 (48.5%)	72 (58%)	NS
Cardiovascular disease	172 (29%)	68 (55%)	< 0.01
Diabetes	77 (13%)	12 (9.7%)	NS
Cancer within the past 5 years	33 (5.5%)	5 (4%)	NS
Hematological disease			
Inflammatory joint disease	41 (7%)	5 (4%)	NS
ASA Score ≥ 3	143 (24%)	59 (47.5%)	< 0.001
History of PJI	153 (26%)	22 (17.7%)	NS
Glucocorticoid and/or immunosuppressant therapy	34 (5.7%)	7 (5.5%)	NS
Site of infection			
Hip	430 (73%)	88 (71%)	NS
Knee	160 (27%)	36 (29%)	NS

ASA: American society of anesthesiologists; PJI: prosthetic joint infection; NS: non-significant.

Table 2
Presentation of the prosthetic joint infection.

	Age < 80 years (n = 590)	Age ≥ 80 years (n = 124)	P-value
Early post-operative infection	99 (17%)	25 (20%)	NS
Chronic infection	192 (32.5%)	30 (24%)	NS
Hematogenous infection (secondary)	173 (29%)	46 (37%)	NS
Unclassified infection	126 (21%)	23 (18.5%)	

NS: non-significant.

tococci and commensal oral and gastrointestinal streptococci. The older group had a nonsignificantly higher prevalence of Enterobacteriaceae (12/124, 10% vs. 33/590, 5.5%) and a significantly higher prevalence of streptococci (25/124, 20% vs. 77/590, 13%, $P < 0.05$) (Table 3).

The proportions of patients managed by one-stage and by two-stage exchange arthroplasty were similar in the two groups. Excision/lavage was used more often in the ≥ 80 year group (16/124, 13% vs. 36/590, 6%, $P = 0.01$), notably to treat early PJI (20% vs. 6%, $P < 0.05$, data not shown) (Table 4). The prolonged antibiotic

Table 3
Bacteria recovered from the prosthetic joint infections.

	Age < 80 years (n = 590)	Age ≥ 80 years (n = 124)	P-value
Gram + bacteria			
<i>Staphylococcus aureus</i>	100 (17%)	24 (19.3%)	NS
MRSA*	13 (2%)	3 (2.5%)	
<i>Staphylococcus epidermidis</i>	129 (21.9%)	17 (13.7%)	< 0.05
MRSE [†]	99 (17%)	13 (10.5%)	
Other staphylococci	65 (11%)	8 (6.5%)	
Streptococci	77 (13%)	25 (20%)	< 0.05
Enterobacteriaceae	13 (2%)	2 (1.5%)	
Gram- bacteria			
Enterobacteriaceae	33 (5.5%)	12 (10%)	NS
<i>Pseudomonas aeruginosa</i>	11 (1.8%)	2 (1.5%)	
Other organisms			
<i>Cutibacterium acnes</i>	51 (8.5%)	10 (8%)	
Other <i>Cutibacterium</i>	5 (0.8%)	0	
Other organisms	32 (5.5%)	8 (6.5%)	
> 1 organism	74 (12.5%)	16 (13%)	

MRSA: methicillin-resistant *Staphylococcus aureus*; MRSE: methicillin-resistant *Staphylococcus epidermidis*; NS: non-significant. *: MRSA : methicillin-resistant *Staphylococcus aureus*; †: MRSE : methicillin-resistant *Staphylococcus epidermidis*.

Table 4
Treatment strategies.

	Age < 80 years (n = 590)	Age ≥ 80 years (n = 124)	P-value
One-stage EA	419 (71%)	89 (72%)	NS
Two-stage EA	93 (16%)	11 (9%)	0.05
Excision/lavage/synovectomy	36 (6%)	16 (13%)	0.01
Other ^a	42 (7%)	8 (6.5%)	

EA: exchange arthroplasty; NS: non-significant.

^a prosthesis removal, arthrodesis, resection.

Table 5
Treatment outcomes.

	Age < 80 years (n = 590)	Age ≥ 80 years (n = 124)	P-value
Infection relapse	31 (5%)	5 (4%)	NS
New infection	54 (9%)	14 (11.3%)	NS
PJI-related death	5 (0.8%)	8 (6.5%)	< 0.05
Death unrelated to PJI	70 (12%)	29 (23.5%)	
Unexplained death	8 (1.3%)	7 (5.5%)	
Dislocation	24 (4%)	1 (0.8%)	NS
Loosening	26 (4.5%)	3 (2.5%)	NS
Periprosthetic fracture	17 (3%)	8 (6.5%)	< 0.05
Other	11 (2%)	0 (0%)	

NS: non-significant; PJI: prosthetic joint infection.

treatment, given for 6 weeks in acute PJI and 12 weeks in chronic PJI, was similar in the two groups.

The only post-operative event whose frequency differed significantly between the two groups was PJI-related death, which was more common in the older group (8/124, 6.5% vs. 5/590, 0.8%; $P < 0.05$) (Table 5). Relapses and new infections occurred with similar frequencies in the two groups. Among the mechanical events, periprosthetic fractures were more common in the older group (6.5% vs. 3.0%, $P < 0.05$).

In the older group, the 2-year survival rates without septic events were 92% after one-stage exchange arthroplasty, 66% after two-stage exchange arthroplasty, and 67% after excision/lavage. The corresponding 2-year survival rates without mechanical events were 92%, 66%, and 94%; and those without PJI-related death were 95%, 91%, and 94%, respectively. None of these survival rates differed significantly from the corresponding value in the younger group.

4. Discussion

The management of PJIs is a complex challenge that is being increasingly well standardized by international recommendations [11]. In France, the creation of referral centers for complex osteoarthritic infections has benefited the management of complex PJIs. One criterion for PJI complexity is patient vulnerability, due for instance to advanced age with or without clinically significant comorbidities. Here, we report the first data on curative PJI treatment in very elderly patients. We found a high 2-year success rate in patients ≥ 80 years, with a greater than 90% 2-year survival rate after one-stage exchange arthroplasty.

The causative microorganisms differed significantly between the two age groups, with higher prevalences of streptococci and Enterobacteriaceae in the older patients. This difference may be related to the higher prevalence of early post-operative infections by hematogenic dissemination after THA used to treat hip fractures, which were more common in the older group. Previous work also suggested an increased susceptibility in elderly patients to Gram-negative rods including Enterobacteriaceae. Thus, a study published in 2016 found that Gram-negative rods caused 67% of early post-operative PJIs in elderly institutionalized patients [12]. Conceivably, asymptomatic bacteriuria with Gram-negative rods may be more common in elderly institutionalized patients and may increase the risk of PJI [13,14]. The higher prevalence of streptococcal PJIs in elderly patients has also been reported previously [15,16]. Age-related immune-system alterations may result in greater susceptibility to streptococcal infections [17]. Consequently, prophylactic measures should be implemented to minimize the risk of infection in the very elderly. To allow early ambulation after surgery, preference should be given to prosthesis implantation via the anterior approach with full weight-bearing immediately after surgery. Other preventive measures include good oral hygiene, eradication of all foci of infection, and appropriate treatment of any chronic skin conditions that might promote skin colonization by staphylococci or streptococci. These preventive measures should be implemented not only preoperatively, but also in the long term, which requires raising awareness among primary-care physicians of the risk of PJI. A standardized geriatric evaluation involving the use of specific tools and scoring systems can be useful in the very elderly to predict the chances of survival and the risk of surgical complications [18].

In our study, the only comorbidities whose prevalence differed between the two age groups were cardiovascular diseases, which were more common in the older group. In addition, a significantly higher proportion of the older patients had an ASA Score ≥ 3, a finding associated with higher perioperative morbidity and mortality rates. PJI-related deaths were more common in the older group ($n = 8$, 6.5% vs. $n = 5$, 0.8%; $P < 0.05$). Of the 8 patients who died of PJI-related causes, 6 had an ASA Score ≥ 3. Surgery-related deaths were slightly more common than after clean or scheduled orthopedic surgery. In a 2003 study of 90-day mortality after scheduled THA in 62,000 patients, mortality was 1% overall [19]. However, mortality in the subgroup ≥ 80 years was 3 times higher than in the group aged 65–69 years and 2 times higher than in the group aged 70–79 years. These data invite a careful assessment of the risk/benefit ratio of arthroplasty procedures in elderly patients with an ASA Score ≥ 3. However, the PJI-related mortality rate was far lower than the 10%–25% rates reported after orthopedic trauma surgery [5,20].

The only difference in surgical strategies between the two groups was significantly greater use of synovectomy-lavage in the older group, notably to treat early post-operative infections (20% vs. 6%, $P < 0.05$). Synovectomy-lavage is a less aggressive option that may therefore have been preferred in the oldest patients despite its higher failure rate, whereas one-stage exchange arthroplasty may

have been considered more often in younger patients, even in the event of early post-operative infection.

Our results demonstrate that outcomes of one-stage exchange arthroplasty are as good in patients ≥ 80 years of age as in younger patients. This primary curative strategy obviates the need for a second surgical procedure, which may be particularly hazardous in older patients at increased risk for morbidity and mortality. It expedites the recovery process, whose goal is a prompt return to function. Consequently, when making treatment decisions for PJI, the optimal surgical strategy aimed at eradicating the infection should be discussed first. This strategy must be appropriate for the patient's characteristics, regardless of age. Patients should be selected to curative surgery by an experienced medical and surgical team, based on a case-by-case evaluation of the comorbidities that may affect the surgical risk.

Perioperative monitoring is essential. The intensity of monitoring increases with patient age [3,4]. Alternatives to surgery should be considered in patients at high surgical risk and/or when the condition of the bone precludes implantation of prosthetic material. Among these alternatives, suppressive antibiotic therapy to control the infection and relieve the pain can be used in the absence of implant loosening. This treatment may improve joint function, notably in streptococcal PJIs, as streptococci are highly susceptible to oral antibiotics such as amoxicillin. In patients with only minimal symptoms, therapeutic abstinence may deserve consideration [21]. In our study, we excluded 51 patients who did not undergo surgery, including 66% who were ≥ 80 years. Exclusion of these patients may have improved the outcomes in our study. However, careful selection of patients eligible for curative treatment is essential.

Finally, although the mechanical failure rate was similar in the two groups, periprosthetic fractures were significantly more common in the patients ≥ 80 years. This difference may be ascribable to the greater bone fragility in older individuals. Of the 8 patients ≥ 80 years who experienced periprosthetic fractures, 3 had risk factors for fractures (documented osteoporotic fractures motivating bisphosphonate therapy in 2 patients and a body mass index lower than 19 kg/m^2 in 1 patient). After clean orthopedic surgery, the overall estimated risk of periprosthetic fractures of 1% to 3% was increased 5-fold in patients older than 75 years [22]. Thus, our findings are consistent with previous reports, and infection does not increase the risk of periprosthetic fracture. Nonetheless, fall prevention, measures to combat bone fragility (e.g., calcium and vitamin D supplementation and physical exercise), and the management of osteoporosis is crucial before primary or revision arthroplasty, in order to decrease the risk of periprosthetic fracture in elderly patients.

In our study, the curative treatment strategy and its outcomes were similar in the two age groups, except for a noticeably higher mortality rate among the older patients. One-stage exchange arthroplasty may be the best treatment strategy in older patients given its high 2-year success rate. Although our results are very encouraging, the risk/benefit ratio of curative surgery must be evaluated carefully on a case-by-case basis in older patients. A standardized geriatric evaluation may help to guide the treatment

decisions. Further studies are needed to confirm our findings with the goal of optimizing the treatment of elderly patients, who will constitute a growing proportion of patients with PJI.

Disclosure of interest

The authors declare that they have no competing interest.

References

- [1] Josefsson G, Kolmert L. Prophylaxis with systematic antibiotics versus gentamicin bone cement in total hip arthroplasty: a ten-year survey of 1688 hips. *Clin Orthop Relat Res* 1993;292:210–4.
- [2] Del Pozo JL, Patel R. Clinical practice. Infection associated with prosthetic joints. *N Engl J Med* 2009;361:787–94.
- [3] Turrentine FE, Wang H, Simpson VB, et al. Surgical risk factors, morbidity, and mortality in elderly patients. *J Am Coll Surg* 2006;203:865–77.
- [4] Moller JT, Cluitmans P, Rasmussen LS, et al. Long-term post-operative cognitive dysfunction in the elderly ISPOCD1 study. ISPOCD investigators. International study of post-operative cognitive dysfunction. *Lancet* 1998;351:857–61.
- [5] Matisson L, Bojan A, Enocson A. Epidemiology, treatment and mortality of trochanteric and subtrochanteric hip fractures: data from the Swedish fracture register. *BMC Musculoskelet Disord* 2018;19:369.
- [6] Pabinger C, Lhotaller H, Portner N, et al. Projections of hip arthroplasty in OECD countries up to 2050. *Hip Int* 2018;28:498–506.
- [7] Kurtz S, Ong K, Lau E, et al. Projections of primary and revision hip and knee arthroplasty in the United States from 2005 to 2030. *J Bone Joint Surg Am* 2007;89:780–5.
- [8] Blanpain N, Chardon O, et al. Projections de population à l'horizon 2060. *Division Enquêtes et études démographiques, Insee* 2010.
- [9] Parvizi J, Zmistowski B, Berbari EF, et al. New definition for periprosthetic joint infection: from the Workgroup of the Musculoskeletal Infection Society. *Clin Orthop Relat Res* 2011;469:2992–4.
- [10] Tsukayama DT, Estrada R, Gustilo RB. Infection after total hip arthroplasty. A study of the treatment of one hundred and six infections. *J Bone Joint Surg* 1996;78:512–23.
- [11] Osmon DR, Berbari EF, Berendt AR, et al. Diagnosis and management of prosthetic joint infection: clinical practice guidelines by the infectious diseases society of America. *Clin Infect Dis* 2013;56:1–25.
- [12] Gallardo-Calero I, Larrainzar-Coghen T, Rodriguez-Pardo D, et al. Increased infection risk after hip hemiarthroplasty in institutionalized patients with proximal femur fracture. *Injury* 2016;47:872–6.
- [13] Sousa R, Muñoz-Mahamud E, Quayle J, et al. Is asymptomatic bacteriuria a risk factor for prosthetic joint infection? *Clin Infect Dis* 2014;59:41–7.
- [14] Cordero-Ampuero J, de Dios M. What are the risk factors for infection in hemiarthroplasties and 345 total hip arthroplasties? *Clin Orthop Relat Res* 2010;468:3268–77.
- [15] Schwartz B, Schuchat A, Oxtoby MJ, et al. Invasive group B streptococcal disease in adults. *JAMA* 1991;266:1112–5.
- [16] Trivalle C, Martin E, Martel P, et al. Group B streptococcal bacteraemia in the elderly. *J Med Microbiol* 1998;47:649–52.
- [17] Edwards MS, Rench MA, Palazzi DL, et al. Group B streptococcal colonization and serotype-specific immunity in healthy elderly persons. *Clin Infect Dis* 2005;40:352–7.
- [18] Aubrun F, Gazon M, Schoeffler M, et al. Evaluation of perioperative risk in elderly patients. *Minerva Anesthesiol* 2012;78:605–18.
- [19] Mahomed NN, Barrett JA, Katz JN, et al. Rates and outcomes of primary and revision total hip replacement in the United States medicare population. *J Bone Joint Surg Am* 2003;85:27–32.
- [20] Rikkinen T, Poole K, Sirola J, et al. Long-term effects of functional impairment on fracture risk and mortality in postmenopausal women. *Osteoporos Int* 2018;29:2111–20.
- [21] Prendki V, Zeller V, Passeron D, et al. Outcome of patients over 80 years of age on prolonged suppressive antibiotic therapy for at least 6 months for prosthetic joint infection. *Int J Infect Dis* 2014;29:184–920.
- [22] Hou Z, Bowen TR, Smith WR. Periprosthetic femoral fractures associated with hip arthroplasty. *Orthopedics* 2010;33:908.