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ORIGINAL PAPER

Pathogen-driven decision for implant retention in the management of infected total knee prostheses

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Abstract
Purpose In prosthetic joint infections (PJIs) of the knee, debridement with implant retention is associated with a high risk of recurrence.
Methods A single-centre cohort study was performed with extensive analysis of the literature covering 1980–2012.
Results In 21 patients (mean age 80.4 years, 19 immunosuppressed), in association with 1.5–three months of antibiotic treatment, an attempt was made to salvage the prosthesis by open (11 patients) or arthroscopic (ten patients) debridement. After a mean follow-up of seven years (range four–20 years), patients were in remission in seven cases (33 %). Remission was achieved in 0 % of all methicillin-resistant *Staphylococcus aureus* (MRSA) infections (zero/three), in 0 % (zero/three) of methicillin-resistant coagulase-negative staphylococcal infections, in 29 % (two/seven) of methicillin-sensitive *S. aureus* infections and in 75 % (three/four) of infections due to streptococci. The literature review focused on implant preserving approaches yielded 599 cases with an overall success rate of 47 % (284/599) and significantly more remissions in streptococcal vs staphylococcal knee PJIs (43/54 vs 144/324; $p<0.01$, odds ratio 4.9, 95 % confidence interval 2.4–10.9).
Conclusions In addition to established indications for explantation such as implant loosening, sinus tract or methicillin resistance, the decision for debridement and retention of knee PJIs should also depend on the pathogen. Implant preservation is futile with methicillin-resistant staphylococci, but seems to be a valid option for streptococcal PJIs.

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Introduction

Orthopaedic surgeons treat prosthetic joint infections (PJIs) choosing between four general approaches: one- or two-stage exchanges, debridements with prosthesis retention or lifelong oral antibiotic suppressive therapy [1]. The option of debridement with implant retention harbours a higher risk of infection recurrence than procedures with implant removal, especially for knee PJIs [1, 2]. Provided that the duration of infection is shorter than two to four weeks, there is no sinus tract, implant loosening or methicillin resistance among staphylococci [1, 3, 4], the debridement and irrigation approach may also be a valid alternative for elderly patients with less bone stock [5] and multiple co-morbidities, for whom anaesthesia and surgery could be harmful [1].

However, the chances of success with prosthesis retention remain controversial, with remission rates ranging between 11 [6] and 86 % [7]. Only small case series with short-term follow-ups may yield remissions of 100 % [8], and interestingly papers in medical journals [7, 9–12] show higher success rates than those published is surgical journals [3, 5, 13–15]. Many of these papers have substantial shortcomings. They mix up hip and knee arthroplasties [10, 12], reveal short minimal follow-up times of only several months [4, 11, 13, 16, 17], report less than ten cases [8, 13, 18–20] or report only specific pathogens [7, 9] such as methicillin-resistant *Staphylococcus aureus* (MRSA) [1, 3].

Another important factor frequently neglected in the choice of preservation versus non-preservation of the implant is the inherent role of the pathogen species per se. With

a few microbiological exceptions such as mycobacteria, fungi or possibly staphylococcal methicillin resistance [3, 15, 20, 21], the surgeon's approach to the management of PJIs is very often pathogen independent [1]. According to existing literature and experts' recommendations, neither the duration of concomitant antibiotic prescription nor the choice of the surgical approach rely on species identification [1]. In contrast, clinical experience suggests a much better outcome with streptococcal PJI. This impression is poorly investigated. Two papers [16, 22] suggest a high remission chance in streptococcal knee PJIs, but do not compare them directly with other pathogens. Other articles may hint at a better outcome in streptococcal disease, but do not investigate it [8, 14, 20].

In this single-centre cohort study and extensive literature review covering 1980–2012, we hypothesise that retention of total knee PJIs is futile for staphylococcal PJIs (MRSA or methicillin-sensitive *S. aureus*) [3, 9–11, 15, 20], but is a more than valid option for streptococcal PJIs [16, 22].

Setting and methods

The Geneva University Hospitals that conduct a total joint arthroplasty cohort also supported this study (No. Ethics Committee 08–057). Diagnosis of PJI is based upon the presence of intraoperative pus together with clinical signs of infection (new onset of pain, fever, discharge and/or radiographic signs of prosthesis loosening). Identification of the infecting organism requires the same pathogen to be present in at least two intra-operative samples. Remission is defined as the absence of any clinical, laboratory or radiological signs of recurrence after a minimal follow-up of two years. In our institution, whenever the decision for surgical revision with implant preservation is taken, infected arthroplasties are debrided by arthroscopy or arthrotomy with synovectomy and irrigation with nine litres NaCl 0.9 %. The procedure may be repeated after two to five days if there is no substantial decrease in local and systemic inflammation after the first intervention.

A literature review searching for all English-language scientific papers in PubMed and the Internet without time restriction was performed. References of retrieved articles were hand-searched for additional information. Important requirements were a linked outcome to underlying pathogens and attempts at implant retention based on a few recommendations: duration of infection shorter than three to four weeks, absence of a sinus tract or of implant loosening [1]. Articles without detailed information regarding microbiology, outcome or treatment modalities in human cases were excluded, as were opinion papers without the author's own data or desperate isolated attempts at implant retention against international experts' guidelines [1].

Local results

A total of 21 total knee PJIs in 21 patients, treated with debridement and implant retention, within three weeks of infection onset, were retrieved between 1996 and 2006 (ten men and 11 women, mean age 80 years) (Table 1). There were no unicompartmental knee joint replacements. As opposed to the implant explantation-reimplantation approach, the debridement and irrigation approach has been individually chosen as being considered less aggressive than the standard one- or two-stage arthroplasty exchange procedure. The patients showed significant co-morbidities and immunosuppression: diabetes mellitus (n=five), obesity (three), alcoholism (two), active cancer (three), autoimmune disease requiring steroids (two) and severe undernourishment (four), as defined by a serum albumin concentration <15 mmol/L. None of the PJIs showed radiological signs of loosening, of fistula or of a sinus tract.

The mean delay between arthroplasty and first clinical signs of PJI was two years (range, nine days–12 years). Overall, two PJIs occurred after a delay of three months following prosthesis implantation. Twelve (57 %) occurred between three months and two years, and seven (33 %) occurred after two years post-arthroplasty according to the validated criteria of Zimmerli et al. [1]. All PJIs were treated with a targeted antibiotic therapy for a mean duration of nine weeks (range six–12 weeks) and underwent one to two debridements (arthrotomies in 11 patients and arthroscopies in ten patients).

After a mean active follow-up of seven years (range four–20 years), patients were in remission in only seven cases (7/21, 33 %). The 14 recurrences occurred on average after 5.4 months post-antibiotic therapy (range 0.5–17 months) and were due to the same pathogen as during the first episode. However, this low success rate differed according to the microbiological strata (Table 1). Remission was achieved in 0 % of all MRSA infections (zero/three), in 0 % (zero/three) of methicillin-resistant coagulase-negative staphylococcal infections and in 29 % (two/seven) of methicillin-sensitive *S. aureus* infections, but in 75 % (three/four) of infections due to streptococci. The difference between staphylococci and streptococci showed a trend [Fisher's exact test p=0.09, odds ratio 0.1, 95 % confidence interval (CI) 0.1–2.1], whereas the duration of antibiotic prescription (six weeks vs 12 weeks) did not influence remission chances (three/seven vs four/seven, p=1.0).

Literature review

We identified 27 articles (28 together with the present one) matching our search criteria and describing in full detail the experience of the authors with debridement and retention of infected knee PJIs (Table 2). We found seven additional papers describing this approach, but without detailed

Table 1 Prosthetic knee joint infections treated with debridement and implant retention at Geneva University Hospitals

Case no.	Delay between implantation and infection	Main pathogen	1st debridement	2nd debridement	Recurrence
1	9 days	MSSA	Arthroscopy		No
2	21 days	*Escherichia coli*	Arthrotomy		No
3	4 months	MRSA	Arthroscopy		Yes
4	4 months	MSSA	Arthroscopy		Yes
5	5 months	*Streptococcus agalactiae*	Arthrotomy		No
6	9.5 months	MRSA	Arthrotomy	Arthrotomy	Yes
7	9.5 months	*Streptococcus agalactiae*	Arthroscopy	Arthroscopy	No
8	11.5 months	MRSA	Arthrotomy	Arthrotomy	Yes
9	12 months	CoNS	Arthroscopy		Yes
10	12.5 months	CoNS	Arthrotomy		Yes
11	16 months	MSSA	Arthrotomy	Arthrotomy	Yes
12	17 months	MSSA	Arthroscopy		Yes
13	19 months	MSSA	Arthrotomy	Arthrotomy	Yes
14	19 months	MSSA	Arthroscopy	Arthroscopy	No
15	2.4 years	CoNS	Arthrotomy	Arthrotomy	Yes
16	4 years	MSSA	Arthroscopy		No
17	6 years	MSSA	Arthrotomy		Yes
18	6.4 years	*Clostridium septicum*	Arthrotomy		Yes
19	7.2 years	*Pasteurella multocida*	Arthroscopy		Yes
20	10 years	Group G *Streptococcus*	Arthrotomy		No
21	12 years	*Streptococcus milleri*	Arthroscopy		Yes

MSSA methicillin-sensitive *Staphylococcus aureus*, *MRSA* methicillin-resistant *Staphylococcus aureus*, *CoNS* coagulase-negative staphylococci

information about the proportion of knee and hip PJIs or the causative pathogen. These papers were excluded from analysis. Finally, our literature review involved 599 cases. The majority was infected with methicillin-susceptible *S. aureus* and treated with arthroscopic or open debridement (arthrotomy) in at least 274 cases. The duration of concomitant antibiotic therapy peaked around two months (Table 2). Overall remission chance averaged 47 % (284/599), but it differed in favour of streptococcal infections compared to staphylococcal PJIs [43/54 (80 %) vs 144/324 (44 %)]. This difference was highly significant (χ^2 test $p<0.01$, odds ratio 4.9, 95 % CI 2.4–10.9) (Table 3).

Discussion

Our long-term follow-up data and literature review suggest that debridement and retention of knee PJIs may be inefficient for MRSA infections [3, 15], moderately successful for methicillin-sensitive *S. aureus* infections [7, 9, 14, 23], but a valid option for streptococcal PJIs [8, 16]. The odds for succeeding with implant retention for streptococcal PJIs compared to staphylococcal infections (methicillin-susceptible *S. aureus* and coagulase-negative staphylococci included) were fivefold. This is an encouraging message for clinicians and hospital administrators. At the same time, our review underlined a non-negligible probability of implant preservation failure for patients infected with MRSA or other staphylococci.

The better outcome with streptococcal disease has been suggested, even if not fully investigated, in other single-centre studies. Meehan et al. revealed only an 11 % relapse rate with debridement and implant retention among 19 streptococcal knee PJIs [16]. Ilahi et al. reported a ubiquitous remission with implant retention among five patients, of whom four were infected due to streptococci [8]. Research groups from the USA [14, 22] and Japan [20] mentioned 100 % success rates among patients infected with streptococci, but less for those infected with staphylococci.

However, it should not be forgotten that a better success with streptococcal knee PJI is not ubiquitously displayed. There are also smaller series denying a better outcome [13] or demonstrating a worse outcome [23] of streptococcal infection as compared to *S. aureus*.

The literature is sparse when it comes to the explanation of why streptococcal infections have a better outcome than staphylococcal infections (especially methicillin-resistant infections). This might be surprising, considering that surgical debridement, viewed as the most important measure, is pathogen independent in its nature. From a theoretical point of view, methicillin-resistant infection might yield a higher

Table 2 Literature review of 1980–2012: management of infected prosthetic knee joints with debridement/retention

First author	No. of prostheses	Main pathogen	Arthrotomy (vs arthroscopy)	Duration of antibiotic treatment	Remission	Minimal follow-up
Teeny [2]	21	MSSA	–	0.7–2 months	6 (29 %)	12 months
Bradbury [3]	19	MRSA	19 (100 %)	1.0–1.5 months	3 (16 %)	24 months
Dixon [4]	15	MSSA	0 (0 %)	3–16 months	9 (60 %)	4 months
Deirmengian [5]	31	MSSA	31 (100 %)	1.5 months	11 (35 %)	24 months
Woods [6]	27	MSSA	–	1.0–1.5 months	3 (11 %)	36 months
Aboltins [7]	7	MSSA/MRSA	7 (100 %)	12 months	6 (86 %)	12 months
Ilahi [8]	5	Streptococci	0 (0 %)	2.0–2.5 months	5 (100 %)	36 months
Barberán [9]	28	CoNS	–	1.5–3 months	19 (68 %)	12 months
Byren [10]	51	MSSA	-	18 months	38 (75 %)	3 months
Cobo [11]	46	MSSA	–	1.5–3 months	29 (63 %)	0 month
Vidil [13]	5	MSSA	0 (0 %)	3 months	2 (40 %)	6 months
Waldman [14]	16	MSSA	0 (0 %)	1.5 months	6 (38 %)	36 months
Siddiqui [15]	12	MRSA	12 (100 %)	1.5 months	4 (33 %)	24 months
Meehan [16]	13	Streptococci	–	0.5–1.2 months	12 (92 %)	4 months
Schoifet [17]	31	MRSA	31 (100 %)	2 months	7 (23 %)	7 months
Freeman [18]	6	MSSA	–	3 months	5 (83 %)	12 months
Flood [19]	2	MSSA	0 (0 %)	–	2 (100 %)	30 months
Tsumura [20]	9	MRSA	0 (0 %)	–	7 (78 %)	13 months
Burger [22]	39	MSSA	39 (100 %)	0.5–2 months	7 (18 %)	12 months
Chiu [23]	40	MRSA	40 (100 %)	1.5 months	12 (30 %)	36 months
Tattevin [25]	34	MSSA	–	–	13 (38 %)	12 months
Hartman [26]	33	MSSA	32 (97 %)	0.5–3 months	20 (61 %)	–
Rasul [27]	10	CoNS	–	1.0–1.5 months	4 (40 %)	24 months
Mont [28]	24	MSSA	24 (100 %)	1.5–3 months	20 (83 %)	48 months
Wilson [29]	31	MSSA	23 (74 %)	–	17 (55 %)	24 months
Borden [30]	11	MSSA	–	–	5 (45 %)	–
Grogan [31]	12	MSSA	5 (42 %)	–	5 (42 %)	18 months
This article	21	MSSA	11 (55 %)	1.5–3 months	7 (33 %)	24 months
Total/average	599	MSSA	274 (46 %)	2 months	284 (47 %)	19 months

MSSA methicillin-sensitive *Staphylococcus aureus*, *MRSA* methicillin-resistant *Staphylococcus aureus*, *CoNS* coagulase-negative staphylococci

recurrence risk [9], because available antimicrobial agents (e.g. vancomycin) reveal diminished bactericidal activity compared to antibiotics against sensitive microorganisms [21]. But this fact does not appear sufficient to explain the outcome differences between sensitive staphylococci and streptococci, inasmuch as physicians and surgeons use almost the same antibiotic classes for both. Here, the capacity of biofilm formation may play a role. According to our current understanding, biofilm formation is more enhanced in staphylococcal foreign body infections than in streptococcal PJIs [24]. Other, yet unexplored physiopathological mechanisms are most probably involved in this respect.

Table 3 Comparison of recurrence stratified between staphylococci and streptococci (literature review and our own cases)

	Remission of arthroplasty infection	Recurrence of arthroplasty infection[a]
Streptococci, $n=54$	43	11
Staphylococci, $n=324$	144	180

[a] Literature review of this article and references [3–5, 7–9, 13–15, 18, 20, 22, 23, 26, 28]

As a conclusion, based upon our findings, we believe that the identified pathogen (and not merely its methicillin resistance [1, 3, 5, 15]) should influence the decision for prosthesis retention in knee PJIs, besides consideration of the patient's general condition, sinus tracts, implant loosening or chronicity of the infection. We thus disregard retention in cases of knee PJI for all staphylococcal disease and feel relatively comfortable in cases of streptococcal disease. Further studies are needed to confirm this presumption or to identify other pathogens with equally better outcomes in cases of implant retention.

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Conflict of interest The authors declare that they have no conflict of interest.

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