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ORIGINAL ARTICLE

Efficacy of debridement in hematogenous and early post-surgical prosthetic joint infections

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ABSTRACT

Purposes: *To review patients with a hematogenous and early post-surgical prosthetic joint infection (PJI) due to S. aureus treated with debridement and retention of the implant and to compare their clinical characteristics and outcome.*

Methods: *From January 2000 all patients with a prosthetic joint infection treated in a single-center were prospectively registered and followed-up. All potentially variables associated with outcome were recorded. For the present study, cases with a hematogenous or early post-surgical PJI due to S. aureus treated with debridement and at least 2 years of follow-up were reviewed. Cox regression model to identify factors associated with outcome were applied.*

Results: *12 hematogenous and 53 early post-surgical PJI due to S. aureus were included. Number of patients presenting with fever, leucocyte count, C-reactive protein concentration, and the number of bacteremic patients were significantly higher in hematogenous infections while the number of polymicrobial infections was lower in hematogenous than in early post-surgical infections. The global failure rate in hematogenous and early post-surgical PJI was 58.7% and 24.5%, respectively (p=0.02). The Cox regression model identified hematogenous infections (OR: 2.57, CI95%: 1.02-6.51, p=0.04) and the need of a second debridement (OR: 4.61, CI95%: 1.86-11.4, p=0.001) as independent predictors of failure.*

Conclusion: *Hematogenous infections were monomicrobial and had more severe symptoms and signs of infection than early post-surgical PJI. Hematogenous PJI due to S. aureus, using debridement with implant retention, had a worse outcome than early post-surgical infections.*

KEY WORDS: *Prosthetic joint infection,* Staphylococcus aureus*, Outcome, Debridement*

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INTRODUCTION

Late infection of prosthetic joints as a result of the hematogenous spread of an organism from a remote site with the seeding of that organism on the bone-implanted prosthesis interface is a well-documented but rare complication of prosthetic joint surgery (1). In a recent report, the incidence of hematogenous PJI was 0.11% (7 out of 6101) (2). However, the risk of prosthesis becoming infected after *Staphylococcus aureus* bacteremia is high. Murdoch et al (3) prospectively evaluated 44 patients with *S. aureus* bacteremia who had a non-infected prosthetic joint and fifteen of these patients (34%) developed a hematogenous infection. The current protocol for the management of early post-surgical and hematogenous PJI with ≤ 3 weeks of symptoms and a stable implant is an open debridement followed by a course of antibiotics with activity against surface-adhering microorganisms (4, 5). However, information about hema-

togenous infections and their outcome with conservative surgical approach is limited. Meehan et al (6) described 19 hematognous cases due to penicillin-susceptible *Streptococcus spp.* treated with debridement and antibiotics and failure was documented in 2 cases (10.5%). In contrast, previous data suggest that *S. aureus* infections are associated with a worse outcome (7-13).

The aim of our study was to review, in our database, those patients with a hematogenous and early post-surgical PJI due to *S. aureus* treated with debridement and retention of the implant and to compare their clinical characteristics and outcome.

PATIENTS AND METHODS

From January 2000 all patients with a prosthetic joint infection treated in a single-center were prospectively registered in a database and followed-up. Relevant information about demographics, co-morbidity, type of implant (hip or knee prosthesis), clinical manifestations, leukocyte count, and C-reactive protein (CRP) concentration at the moment of admission for infection, surgical treatment, isolated microorganisms, antimicrobial therapy, and outcome were recorded. Outcome was evaluated according to the following definitions: i) remission, when the patient had no symptoms of infection, the prosthesis was retained; and ii) failure, when inflammatory signs and high CRP remained during treatment or re-appeared after completing it, or when the patient developed an aseptic loosening that required the prosthesis to be substituted and deep samples taken during surgery were negative. The patient was considered to have a relapse when the microorganism isolated at the moment of failure was the same as the one isolated in the primary infection or when no microorgnism was found; and a re-infection when the microorganism was different. All activity was conducted in accordance with the Declaration of Helsinki and national and institutional standards. Approval of the Ethics Committee was not required for this study.

For the present study, those cases with an acute hematogenous (n=12) or early post-surgical (n=53) PJI due to *S. aureus* treated with debridement and prosthesis retention and at least 2 years of follow-up from debridement were retrospectively reviewed and the characteristics and outcome of both cohorts were compared. Acute prosthetic joint infection due to *S. aureus* was defined by the presence of local inflammation or wound discharge of acute onset (<15 days), macroscopic evidence of extension of the infection through the capsule during open debridement, and isolation of *S. aureus* in deep samples. when the onset of symptoms was within the first 3 months after joint arthroplasty it was considered to be post-surgical infection; when the symptoms appeared suddenly after >3 months of joint arthroplasty and the function of the prosthesis was normal until the onset of infection it was considered to be an hematogenous infection.

In terms of debridement, pre-existing incisions were always used, necrotic tissue was excised and the joint was washed with 6 to 9 liters of sterile water. The components were left in situ after confirming that no signs of loosening were found at the time of surgery. In knee arthroplasties, the polyethylene component was removed and replaced with a new component and in total hip arthroplasties modular components were substituted. When systemic or local signs of infection persisted after debridement, the patient was taken back to the operating room to repeat the irrigation and debridement. A second debridement was not considered a failure when it was performed within the first 10 days after the first one.

After open debridement, a broad-spectrum intravenous antimicrobial regimen including vancomycin (1 g/12 h) plus ceftazidime (2 g/8 h) was started and maintained until obtaining definitive microbiological results. When *S. aureus* was susceptible to methicillin, vancomycin was switched to intravenous cloxacillin (2 g/4 h). The definitive oral antibiotic treatment was levofloxacin (500 mg/24 h) plus rifampin (600 mg/24 h) except in those cases with resistant strains or polymicrobial infection in which an alternative therapy was selected according to the antibiogram. Antibiotic dosages were adjusted to renal function. The protocol of our hospital recommends 7 to 10 days of intravenous antibiotic and the duration of oral therapy was decided in each case according to the clinical manifestations and CRP concentration by the infectious diseases specialist of the clinical multi-disciplinary team.

Characteristics of hematogenous and early post-surgical PJI as well as characteristics of patients in remission and with failure were compared using χ^2 test or Fisher's exact test for categorical variables and the Student's t-test for continuous variables. The cumulative probability of failure in the Kaplan-Meier curve according to the type of infection (hematogenous vs. early post-surgical), age (≤70 or >70 years), sex, co-morbidity (having or not having one or

more of the following entities: diabetes mellitus, liver cirrhosis, chronic renal failure, rheumatoid arthritis, or chronic obstructive pulmonary disease), type of prosthesis (hip or knee), primary or revision arthroplasty, and methicillin- or fluoroquinolone-resistant were assessed and compared using a log-rank test. Those variables with significantly higher cumulative probability of failure in the Kaplan-Meier curve (log-rank test) were included in a stepwise forward and backward Cox regression model. The dependent variable was clinical failure, including relapse, re-infection, or aseptic loosening during follow-up. Statistical significance was defined as a two-tailed p value <0.05. The analysis was done by the program SPSS (version 12.0; SPSS, Inc., Chicago, IL, USA).

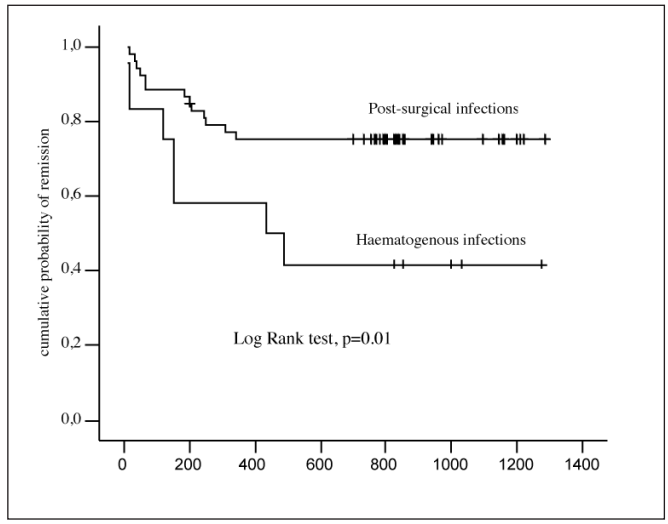

Fig. 1 - *The graph shows the Kaplan-Meier survival curve for haematogenous and early post-surgical prosthetic joint infections.*

RESULTS

During the study period 65 patients met the inclusion criteria of the study. There were 12 hematogenous and 53 early post-surgical infections. Both groups were similar in terms of age, sex, co-morbidity, days of symptoms, methicillin- or fluoroquinolone- resistant *S. aureus*, the need of a second debridement within 10 days from the first one, days on intravenous and on oral antibiotics, the type of antibiotics administered or the length of follow-up (Tab. I). Although not statistically significant, the number of knee prostheses was higher among hematogenous PJI (83 vs. 66%). The number of patients presenting with fever, leucocyte count, C-reactive protein concentration, and the number of bacteremic patients were significantly higher in hematogenous infections while the number of polymicrobial infections was lower in hematogenous than in early post-surgical infections (Tab. I). The global failure rate in hematogenous and early post-surgical PJI was 58.7% and 24.5%, respectively (p=0.02) after at least 2 years of follow-up except in 1 case of early post-surgical PJI who died after six months without evidence of failure. Failure in hematogenous infections was always due to infection relapse while in early post-surgical infections 7 failures were due to reinfection, 5 due to infection relapse, and 1 due to an aseptic loosening (Tab. I). Variables associated with failure were hematogenous infections and the need of a second debridement (Tab. II). According to Kaplan-Meier curves, both hematogenous infections (Fig. 1) and the need of a second debridement had a significantly higher cumulative probability of failure and were included in the Cox regression analysis. The analysis showed that both the need of a second debridement (OR: 4.61, CI95%: 1.86-11.4, p=0.001) and hematogenous infections (OR: 2.57, CI95%: 1.02-6.51, p=0.04) were independently associated with failure.

DISCUSSION

The aim of our study was to review the clinical characteristics of hematogenous and early post-surgical PJI due to *S. aureus* and to define their outcome when the initial surgical approach is debridement with implant retention according to a surgical and antimicrobial treatment protocol. Several authors have described a low incidence of hematogenous infections (1, 2) and as a consequence, clinical experience about the management of these infections is scarce. In streptococcal hematogenous infections, debridement and antibiotic therapy was associated with a high success rate (90%) in a series of 19 cases (6), however, in another series of 6 patients mainly due to *S. aureus* the success rate was 50% (13).

The clinical manifestations of hematogenous PJI were significantly different from early post-surgical PJI and they were close to native septic arthritis including fever, high leukocyte count, and C-reactive protein, monomicrobial and bacteremic infections. These data and the fact that hematogenous PJI were independently associated with a high risk of failure, primarily due to a higher relapse rate (58.3%)

TABLE I - CLINICAL CHARACTERISTICS OF HAEMATOGENOUS AND EARLY POST-SURGICAL PROSTHETIC JOINT INFECTIONS DUE TO *S. AUREUS*

Characteristics	Hematogenous PJI (n=12)	Early post-surgical PJI (n=53)	P[b]
Mean (SD) Age	74 (8.9)	70 (10.8)	0.25
Female sex	6 (50)	28 (58.2)	0.55
Co-morbidity[a]	5 (41.7)	16 (30.2)	0.32
Type of implant			
Knee	10 (83.3)	35 (66)	0.20
Hip	2 (16.7)	18 (34)	
Mean (SD) age of implant	1470 (1172.5)	24.6 (20.5)	0.001
Primary implant	9 (75)	51 (96.2)	0.04
Fever	10 (83.3)	12 (22.6)	0.0001
Leukocyte count (cells/mm^3)	11508 (3823.7)	9060.1 (3319.4)	0.02
C-reactive protein (mg/dl)	23.9 (13.7)	9.5 (11.2)	0.0001
Bacteremia	6 (50)	6 (11.3)	0.006
S. aureus resistant to (%) :			
Methicillin	1 (8.3)	4 (7.5)	0.65
Fluoroquinolones	3 (25)	7 (13.5)	0.27
Polymicrobial infection	0	15 (28.3)	0.03
Mean (SD) days of symptoms	4.7 (3.7)	5.6 (4.4)	0.53
Need of >1 debridement	2 (16.7)	8 (15.1)	0.59
Mean (SD) days on intravenous antibiotics	11 (4.6)	10.6 (6.7)	0.82
Main intravenous antibiotic:			
Cloxacillin	7 (58.3)	25 (48.1)	0.37
Vancomycin	4 (33)	25 (48.1)	0.27
Mean (SD) days on oral antibiotics	115.4 (55.3)	86.4 (46.8)	0.10
Mean (SD) days of follow-up after debridement	529.1 (448.8)	700.9 (365.3)	0.16
Mean (SD) days of follow-up after finishing antibiotics	434.5 (400)	612.4 (349.9)	0.12
Outcome (%):			
Relapse	7 (58.3)	5 (9.4)	0.001
Re-infection	0	7 (13.2)	0.22
Aseptic loosening	0	1 (1.9)	0.81
No. of deceased patients (infection-related deaths)	2 (1)	5 (0)	0.39

SD = standard deviation.
[a] Co-morbidity includes diabetes mellitus (n=11), rheumatoid arthritis (n=4), chronic renal failure (n=3), liver cirrhosis (n=3), dementia (n=3) or chronic obstructive pulmonary diseases (n=2).
[b] Chi-squared or Fisher's exact tests were used for categorical variables and Student's t-test for continuous variables.

TABLE II - CHARACTERISTICS OF PATIENTS ACCORDING TO THE OUTCOME

Characteristics	Failure [b] (n=20)	Remission (n=45)	P [c]
Mean (SD) age	69.5 (11.5)	71.4 (10.2)	0.50
Female sex	10 (50)	24 (53.3)	0.50
Co-morbidities [a]	9 (45)	12 (26.7)	0.12
Type of implant (%):			
Knee	17 (85)	28 (62.2)	0.05
Hip	3 (15)	17 (37.8)	
Primary arthroplasty (%)	19 (95)	41 (91.1)	0.50
Polymicrobial infection (%)	6 (30)	9 (20)	0.28
Type of infection (%):			
Hematogenous	7 (35)	5 (11.1)	0.02
Post-surgical	13 (65)	40 (88.9)	
S. aureus resistant to (%):			
Methicillin	0	5 (11.1)	0.62
Fluoroquinolones	3 (15)	7 (15.9)	
Mean (SD) days of symptoms	5.1 (4.3)	5.6 (4.3)	0.65
Need of >1 debridement	8 (40)	2 (4.4)	0.001
Mean (SD) days of follow-up after debridement	169.3 (141.9)	891 (204.7)	-
Mean (SD) days of follow-up after finishing antibiotics	99.3 (84.8)	793 (192.8)	-

SD = standard deviation.
[a] Co-morbidity includes diabetes mellitus (n=11), rheumatoid arthritis (n=4), chronic renal failure (n=3), liver cirrhosis (n=3), dementia (n=3) or chronic obstructive pulmonary diseases (n=2).
[b] Failure includes relapse, reinfection, and aseptic loosening.
[c] Chi-squared or Fisher's exact tests were used for categorical variables and Student's t-test for continuous variables.

than in early post-surgical PJI (9.4%), suggest that *S. aureus* causing hematogenous infections are more virulent and/or they have a higher ability to survive (e.g., biofilm production). In fact, post-surgical strains are directly inoculated into the joint during surgery while hematogenous strains are able to penetrate deep tissue through non- or minimally disrupted barrier (mucosa, skin), evade the immune system to achieve blood stream and finally they invade the joint colonizing the prosthetic surface. Recently, Byren et al (8) found that acute late infections (>90 days after joint arthroplasty) had a higher failure rate (30%) than post-surgical infections (11%). Although they attributed this finding to the fact that the majority of patients were debrided with arthroscopy, this data supports our findings. In the future, it would be of interest to study the characteristics of strains isolated in different types of prosthetic joint infection.

The current recommendation for the duration of antibiotic treatment in acute prosthetic joint infections treated without removing the implant is 2 to 4 weeks of intravenous therapy followed by oral regimen for 3 months in hip infections and 6 in knee infections (5, 14). The duration of intravenous and oral antibiotic treatment in our patients was shorter, however, the success rate in early post-surgical PJI was similar to that reported in other series (15-19) in which the number of patients with *S. aureus* infection was low and patients with bacteremia or hematogenous infection were not included. Recently, Byren et al (8) analyzed 112 patients treated with DAIR (debridement, antibiotics, and implant retention) using the following protocol: 6 weeks of intravenous beta-lactam or glycopeptide followed by oral regimen including rifampin for a minimum of 12 months. In spite of the prolonged treatment, 12 patients failed after

stopping antibiotics (60%) while 8 during therapy (40%). Although the global failure rate was 17.8% (20 out of 112), in *S. aureus* infections it was 27.6% (13 out of 47) which was very similar to ours in early post-surgical PJI (24.5%). Our results support those previously presented by Berdal et al (20) in 29 patients with acute post-surgical infections (18 due to *S. aureus*) treated with 3 to 7 days of intravenous antibiotics and 3 months of oral rifampin regimen with a failure rate of 17%. Although it is possible that longer antibiotic treatment could be necessary for hematogenous PJI, our clinical experience shows that a conservative surgical approach is associated with a worse outcome in these cases. In the future, it will be necessary to evaluate the efficacy of new antistaphylococcal agents with potent activity against biofilms (21).

The limitation of our study was the low number of hematogenous PJI studied, however, this is one of the largest series, it is from a single center, and it is homogeneous in terms of the etiology (*S. aureus*) and the surgical and antibiotic treatment. This allowed us to compare the effectiveness of this therapeutic approach in hematogenous and early post-surgical PJI. Another limitation of our study was that macroscopic and biochemical characteristics of synovial fluid (glucose, differential leukocyte count, and protein concentration) as well as previous infections in other sources were not registered and they were not evaluated. However, this limitation did not hamper the analysis of clinical outcome.

In conclusion, hematogenous infections were mono-microbial and had severe symptoms and signs of infection when compared with early post-surgical PJI. Hematogenous PJI, using debridement with implant retention, had a worse outcome than early post-surgical infections.

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REFERENCES

1. Ainscow DA, Denham RA. The risk of haematogenous infection in total joint replacements. J Bone Joint Surg Br. 1984;66(4):580-582.
2. Uckay I, Lubbeke A, Emonet S, et al. Low incidence of haematogenous seeding to total hip and knee prostheses in patients with remote infections. J Infect. 2009;59(5):337-345.
3. Murdoch DR, Roberts SA, Fowler JV, et al. Infection of orthopedic prostheses after Staphylococcus aureus bacteremia. Clin Infect Dis. 2001;32(4):647-649.
4. Barberan J. Management of infections of osteoarticular prosthesis. Clin Microbiol Infect. 2006;12 (Suppl 3):93-101.
5. Zimmerli W, Trampuz A, Ochsner PE. Prosthetic-joint infections. N Engl J Med. 2004;351(16):1645-1654.
6. Meehan AM, Osmon DR, Duffy MC, Hanssen AD, Keating MR. Outcome of penicillin-susceptible streptococcal prosthetic joint infection treated with debridement and retention of the prosthesis. Clin Infect Dis. 2003;36(7):845-849.
7. Brandt CM, Sistrunk WW, Duffy MC, et al. Staphylococcus aureus prosthetic joint infection treated with debridement and prosthesis retention. Clin Infect Dis. 1997;24(5):914-919.
8. Byren I, Bejon P, Atkins BL, et al. One hundred and twelve infected arthroplasties treated with 'DAIR' (debridement, antibiotics and implant retention): antibiotic duration and outcome. J Antimicrob Chemother. 2009;63(6):1264-1271.
9. Deirmengian C, Greenbaum J, Lotke PA, Booth RE, Lonner JH. Limited success with open debridement and retention of components in the treatment of acute Staphylococcus aureus infections after total knee arthroplasty. J Arthroplasty. 2003;18(7 suppl 1):22-26.
10. Marculescu CE, Berbari EF, Hanssen AD, et al. Outcome of prosthetic joint infections treated with debridement and retention of components. Clin Infect Dis. 2006;42(4):471-478.

11. Morrey BF, Westholm F, Schoifet S, Rand JA, Bryan RS. Long-term results of various treatment options for infected total knee arthroplasty. Clin Orthop Relat Res. 1989;248:120-8.
12. Salgado CD, Dash S, Cantey JR, Marculescu CE. Higher risk of failure of methicillin-resistant Staphylococcus aureus prosthetic joint infections. Clin Orthop Relat Res. 2007;461:48-53.
13. 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 Am. 1996;78(4):512-23.
14. Betsch BY, Eggli S, Siebenrock KA, Tauber MG, Muhlemann K. Treatment of joint prosthesis infection in accordance with current recommendations improves outcome. Clin Infect Dis. 2008;46(8):1221-1226.
15. Barberan J, Aguilar L, Carroquino G, et al. Conservative treatment of staphylococcal prosthetic joint infections in elderly patients. Am J Med. 2006;119(11):993.e7-10.
16. Choong PF, Dowsey MM, Carr D, Daffy J, Stanley P. Risk factors associated with acute hip prosthetic joint infections and outcome of treatment with a rifampinbased regimen. Acta Orthop. 2007;78(6):755-765.
17. Laffer RR, Graber P, Ochsner PE, Zimmerli W. Outcome of prosthetic knee-associated infection: evaluation of 40 consecutive episodes at a single centre. Clin Microbiol Infect. 2006;12(5):433-439.
18. Soriano A, Garcia S, Bori G, et al. Treatment of acute postsurgical infection of joint arthroplasty. Clin Microbiol Infect. 2006;12(12):930-933.
19. Zimmerli W, Widmer AF, Blatter M, Frei R, Ochsner PE. Role of rifampin for treatment of orthopedic implant-related staphylococcal infections: a randomized controlled trial. JAMA. 1998;279(19):1537-1541.
20. Berdal JE, Skramm I, Mowinckel P, Gulbrandsen P, Bjornholt JV. Use of rifampicin and ciprofloxacin combination therapy after surgical debridement in the treatment of early manifestation prosthetic joint infections. Clin Microbiol Infect. 2005;11(10):843-845.
21. John AK, Baldoni D, Haschke M, et al. Efficacy of Daptomycin in Implant-Associated Infection Due to Methicillin-Resistant Staphylococcus aureus: Importance of Combination with Rifampin. Antimicrob Agents Chemother. 2009;53(7):2719-2724.