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ORIGINAL STUDY

Determinants of sucess in the treatment of prosthesic joint infection with debridement, antibiotics and implant retention

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Debridement, antibiotics and implant retention (DAIR) is an appealing alternative for the treatment of periprosthetic infections. A retrospective clinical study that included all patients with prosthetic infection treated from January 2010 to December 2015 was made. Many variables were analyzed including the patient characteristics, infection characteristics and the type of medical and surgical treatment performed. Success was defined as the healing of the infection with the preservation of the original prosthesis. Fifty patients with a mean follow-up of 38.4 months (minimum 12 months) were studied. Global success rate was 46% (23/50).

The key determinants of treatment success were shorter duration of infection (21.4vs.73.1 days ; p=0.048), exchange of mobile components (87.0%vs.29.6% ; p<0.001, OR=15.8 [IC95%3.6-68.7]) and adequate "anti-biofilm" antibiotic therapy (78.2%vs.25.9% ; p<0.001 ; OR=10.3 [IC95% 2.8-38.2]). In the 20 cases where a pre-established protocol was strictly met the treatment success rate was 85% (17/20) versus the other cases where the protocol was not met and the success rate was 20% (6/30) (p<0.001 ; OR=22.7 [IC95% 5.0-103.5]). DAIR is an effective alternative for the treatment of periprosthetic infections if some conditions are met. The short duration of infection, strict surgical debridement with exchange of mobile parts and antibiotic therapy with "anti-biofilm" regimens are essential conditions for success.

Keywords : arthroplasty replacement hip ; arthroplasty replacement knee ; infection control ; prosthesis-related infections ; debridement.

INTRODUCTION

Total joint replacement surgery is overwhelmingly successful. However, complications do occur, and infection is one of the most feared. Despite growing awareness, the socioeconomic costs of prosthetic joint infection (PJI) is rising mainly due to the increasing number of procedures performed worldwide *(1)*.

The treatment of PJI is difficult and frequently complex. The possibility of treating PJI with surgical debridement, antibiotics and implant retention (DAIR) is an appealing alternative both for the surgeon, because it is technically less demanding, and for the patient as recovery is easier and faster.

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However, results reported in the literature are highly variable, with success rates varying between 0-90% *(2,3)*. Such huge discrepancies relate to a number of factors such as correct surgical technique, antibiotic therapy and most importantly, patient selection.

The goal of this study was to determine predictive factors of success when performing a DAIR procedure. Our hypothesis was that correct patient selection and a structured surgical and medical treatment plan, can offer good results.

MATERIAL AND METHODS

This study focused on 50 patients with hip or knee PJI treated initially with DAIR procedures, in our institution between June 2010 and June 2015. PJI cases treated with implant removal as a first step were excluded from this study.

We recorded patient characteristics and site of arthroplasty (age, gender, body mass index, comorbidities such as diabetes mellitus, obesity, pharmacologic induced immunosuppression or previous history of cancer were given special attention), infection characteristics (duration of symptoms prior to surgery, local soft tissue conditions and type of microorganism isolated), surgical technique variables (exchange or not of mobile components, use or not of perfusion-aspiration systems and number of surgical debridements performed) and medical treatment used (type and duration of antibiotics).

Treatment success was defined as healing of the infection with retention of the original prosthesis (healed wound without fistula, drainage, or pain), after a minim follow up of 12 months, after discontinuation of antibiotic therapy. A more classic time-frame would be 24 months after surgery but the authors believe this definition may be greatly biased by the duration of suppressive antibiotic therapy after DAIR procedure. Treatment failure was defined as evidence of persistent infection or need for subsequent reintervention and/or implant revision *(4)*.

Results were analyzed dividing patients into two groups according to treatment success or failure, in order to correlate the different variables and the final outcome. In a secondary analysis, the patients were divided into two groups, according to whether or not their treatment respected a previously established protocol. Success rates between two groups was then compared.

We considered inadequate local soft tissues for DAIR in the presence of sinus tract or a musculocutaneous flaps was required to close the wound.

Based on literature, we considered “bacteria difficult to treat” : methicillin-resistant *Staphylococcus aureus* (MRSA), Enterococcus sp. and gram-negative microorganisms *(5-8)*.

Exchange of mobile components include replacement of polyethylene in TKR and replacement the femoral head in cemented as well as the polyethylene in cementless THR. In some cases, perfusion-aspiration system was used, consisting of one drain to instill saline, and two suction drains.

Antibiotic therapy was considered adequate (i.e. antibiofilm) if it : 1) included rifampicin in staphylococci infection, ciprofloxacin in gram-negative infections or both in polymicrobial infections ; 2) minimum duration of 3 months in THR and 6 months in TKR. If any of these criteria were not fulfilled (regardless the reason) antibiotic regime was considered inadequate.

Finally, compliance to the previously established protocol includes all of the following conditions : 1) duration of symptoms before surgery under < 4 weeks ; 2) adequate local soft tissues conditions ; 3) exchange of mobile components during surgery and ; 4) adequate antibiotic therapy.

Statistical analysis was performed using Statistical Package for Social Sciences (SPSS), version 23, IBM®. A descriptive analysis was performed for all variables studied. For continuous variables, normal distribution was tested using Shapiro-Wilk and Kolmogorov-Smirnov tests. Chi-square, t-student and Mann-Whitney tests were used compare both groups (treatment success vs failure) according to type of variable. When chi-square or t-student test showed statistical significance, odd-ratio and effect size was calculated respectively. A p value of less than 0.05 was considered to be significant.

RESULTS

Overall treatment success rate was 46% (23/50) with a mean follow up of 38.4 months after discontinuation of antibiotic therapy. In the other 27 cases, there was persistence or relapse of infection, with most cases requiring implant removal.

Patient characteristics are described in Table 1. There were no significant differences regarding age, gender, type of arthroplasty, type of infection (acute postoperative *versus* acute hematogenous) comorbidities and even microorganism distribution including proportion of "difficult to treat bacteria" between the two groups. A more complete characterization of the distribution of isolated microorganisms can be found in table 3.

Table 2 describes the correlation between studied variables and treatment outcome. The variables that showed statistical significance for determining treatment success were : shorter duration of symptoms prior to surgery (21.4 *vs*. 73.1 days ; p=0.048 ; g=0.53) ; exchange of mobile components (87% *vs*. 29,6% ; p<0.001 ; OR 15.8 [IC 95% 3.6-68.7]) and adequate antibiotic therapy (78.2% *vs*. 25.9% ; p<0.001 ; OR=10.3 [IC 95% 2.8-38.2]).

Table 1. — Clinical and demographic variables

	Treatment success	**Treatment failure**	***P* value**
	n=23	*n=27*	
Age*	66.6 (39-84)	65.3 (21-87)	0.73
Gender (female)	14 (61%)	17 (63%)	0.88
Ratio Hip:Knee	9:14	15:12	0.25
Obesity (BMI>30)	9 (39%)	10 (37%)	0.86
Diabetes mellitus	4 (17.4%)	4 (14.8%)	0.84
Immunosuppression	2 (8.7%)	5 (18.5%)	0.32
Bacteria "difficult to treat"	14 (60.9%)	14 (51.8%)	0.30
Acute Hematogenous / Acute Postoperative	4/19 (17.4%)	5/22 (18.5%)	1.00

* mean in years (minimum-maximum) ; BMI- Body Mass Index.

Table 2. — Correlation between analysed variables and final outcome

	Treatment success	**Treatment failure**	**P value**
	n=23	*n=27*	
Symptoms Duration (days)	21 (5-62)	73 (3-600)	0.048
Inadequate local soft tissues	0 (0%)	2 (7.4%)	0.18
Exchange mobile components	20 (87.0%)	8 (29.6%)	<0.0001
Perfusion-aspiration system	3 (13.0%)	9 (33.3%)	0.09
Surgical debridement ³2	6 (26.1%)	13 (48.1%)	0.11
Adequate antibiotic therapy	18 (78.2%)	7 (25.9%)	<0.0001
Compliance protocol	17 (73.9%)	3 (11.1%)	<0.0001

Table 3. — Distribution of microorganisms

	Overall	Treatment Success (n=23)	Treatment failure (*n*=27)
Polimicrobial	8	4	4
Number of isolated microorganisms	60	30	30
Gram positive	47	23	24
Staphylococcus aureus	23	10	13
MRSA	6	3	3
MSSA	17	7	10
Coagulase-negative staphylococci	11	7	4
Other Gram positive	13	6	7
Enterococcus spp.	9	4	5
Streptococcus spp.	3	2	1
Corynebacterium spp.	1	0	1
Gram negative	13	7	6
Enterobacteriaceae	7	5	2
Escherichia coli	1	1	0
Proteus spp.	3	2	1
Serratia marcescens	1	1	0
Providencia stuartii	2	1	1
Pseudomonas spp.	5	2	3
Acinetobacter baumani	1	0	1

Compliance to pre-established protocol as a whole was the major determinant of success (73.9% *vs.* 11.1% ; p<0.001 ; OR=22.7 [IC 95% 5.0-103.5]). When analyzing only the patients for whom the protocol was fully respected, the treatment success rate was 85% (17/20). On the other hand, the treatment success rate in the patients who did not comply to the protocol was only 20% (6/30).

DISCUSSION

As the number of arthroplasties performed worldwide continues to rise, periprosthetic joint infections are unfortunately becoming more and more a relatively frequent complication in joint replacement practice, which all surgeons must know how to handle. Treatment is often complex, and traditionally associated with high costs, suboptimal functional outcome and a significant impact on patients quality of life and even mortality *[9, 10]*.

The main difficulty in treating these patients is the presence of bacterial biofilm that forms at the surface of the implants. Bacterial biofilms possess physical, physiological, and/or adaptive resistance mechanisms against the host immune system and most antibiotics *(11)*. As such, one or two stage revision surgery with implant removal (thus removing biofilm), is generally considered the most reliable treatment alternative for PJI *(12,13)*. Still, debridement, antibiotics and implant retention can be a valid alternative in selected cases.

However, results reported in the literature present enormous variability with success rates as low as 0% and as high as 90% *(2,3)*. As described above, many variables influence the final outcome, some like comorbidities and the bacteria virulence cannot be controlled by the surgeon *(5,14,15)*. Others, like correct selection of patients, rigorous surgical debridement and adequate antibiotic therapy are under direct control of the medical team *(16-18)*.

The findings of this study corroborate some principles often highlighted in the literature. Short duration of symptoms seems to be a major criterion when selecting whether or not to perform a DAIR. Many have recommended duration of symptoms shorter than 3-4 weeks as the ideal timeline *(6,14,15,19)* and our results show a similar pattern. It is important to stress that duration of symptoms is not synonymous with "age of the prosthesis". DAIR seems to be an equally valid alternative in cases of acute hematogenic infections as in cases of acute postoperative infections also in our cohort *(5,20)*.

A rigorous, systematic and aggressive surgical debridement is naturally an important prognostic factor, which is nevertheless very difficult to assess. The major technical aspect that influences success rate was the exchange of mobile components, which raised 15 times the probability of success. This finding is very much in line with current literature *(21,22)*. Recently, Grammatopoulos *et al.* reported a success rate almost 5 times superior when modular components were exchanged, and also a significant raise in implant survival *(23)*. The main goal of surgery is to decrease bacterial load as drastically as possible. Taking this into account it is easy to understand that exchange of mobile components increases access to the joint allowing a more efficient debridement and removing biofilm of those components. Our results do not show an advantage in using classic perfusion-aspiration systems.

Despite best surgical efforts, a residual bacteria load will remain, that requires adequate antibiotic therapy. Tornero *et al.* *(16)* reported that an incorrect antibiotic selection is the most important predictive factor to late failure of surgical debridements in acute infections. Although, it is beyond the scope of this study, it is important to highlight the importance of rifampicin in staphylococci infections *(16,20)* and ciprofloxacin in gram-negative infections *(17,24)*. The ideal duration of antibiotic therapy is still in discussion, however, it is still recommended a period of 3 months after hip infections and 6 months after knee infections *(25)*. Our results confirm that correct "antibiofilm" therapy is associated with significantly better outcomes.

This study has some limitations, we have a small sample, not allowing for conclusions to be made about the importance of local soft tissue conditions or the impact of repeated debridements. The topic of repeated debridement is very controversial. Some authors report highest failure rates, while other advocate for its routine use *(23,26,27)*. Another limitation is the absence of a medical and surgical protocol approach for a significant proportion of patients treated over the study period.

It has been consistently demonstrated that the adoption of evidence-based treatment leads to a significant improvement of results when compared to an *ad hoc* approach *(28,29)*. Our results confirm that treatment according to a previously established medical and surgical protocol was the main prognostic factor of success, with a probability of healing about 20 times higher.

CONCLUSION

To assure the best chance of success in treating PJI with a DAIR procedure, it is essential to carefully select patients with : 1) a stable prosthesis with no radiological signs of loosening ; 2) good local soft tissue conditions and no sinus tract ; 3) short duration of symptoms, ideally less than four weeks. Furthermore, surgical procedure must be rigorous with systematic and thorough debridement including mobile components exchange and copious lavage. After surgery, correct and prolonged antibiotic therapy including antibiofilm drug(s) whenever possible is also critical.

In our experience, compliance with these simple principles led to a cure rate of infection at two years of 85% *(30)*, which is at the favorable end of the spectrum described in the literature. The findings of the present study demonstrate that neglecting the principles of care mentioned earlier greatly reduces the likelihood of a favorable outcome in the treatment of PJI with implant retention.

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