



Debridement, antibiotics and implant retention in early periprosthetic joint infection after primary total hip arthroplasty : 88 percent survival after two years follow-up

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Treatment protocols and results of debridement, antibiotics, irrigation and retention of the prosthesis (DAIR) for early prosthetic joint infection (PJI) vary in literature. The purpose of this study was to analyze the results of DAIR with a multidisciplinary designed customized antibiotic protocol for early PJI after primary total hip replacement (THR).

We retrospectively analyzed all patients with an early PJI between 2008 and 2012. When an infection was suspected, debridement of the prosthesis, and collection of intraoperative cultures, was performed. Patients were multidisciplinary discussed and treated with an appropriate antibiotic scheme for 12 weeks. Primary outcome was retention of the prosthesis after at least two years follow-up and without any signs of infection.

We identified 25 patients with early PJI. At a median follow-up time of 3.1 years (range 2.1-5.5 years), 88% had retention of the prosthesis and no signs of infection.

This study suggests that DAIR with a multidisciplinary approach and an aimed antibiotic treatment for early PJI after THR is a reasonable treatment option with 88% implant retention after two years follow-up.

Keywords : hip ; arthroplasty ; prosthetic joint infection ; debridement.

INTRODUCTION

The treatment of a prosthetic joint infection (PJI) can be challenging and may become a major problem in orthopedic implant surgery. The incidence of PJI after primary total hip replacement (THR) varies between 0.5 to 2 percent (42). Beyond the fact that the absolute number of PJI will be rising due to the increasing number of performed THRs, recent studies also suggest that the incidence of PJI is increasing (5,9,18,27,30,42). Possible reasons for an increasing PJI incidence may include changes in patient related factors (more comorbidity), changes in microbiology (increased virulence, more resistant strains), improved diagnostic methods, better registration or changes in surgery-related factors (operation time or changed surgical technique) and use of different and new definitions (5,9,18,27,30,42).

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There is no standard definition of what constitutes PJI. Clinicians define PJI on multiple sources of clinical information, none of which can be relied on as a gold standard (29). The Musculoskeletal Infection Society (MSIS) proposed a definition of PJI and their hope is that it will be adopted universally (43).

Furthermore, there are different classifications of PJI. Tsukayama *et al* (1996) classifies PJI according to duration of symptoms and time after surgery : (I) early postoperative : symptoms less than 4 weeks after surgery ; (II) late chronic : a gradual, indolent onset of symptoms ; or (III) acute hematogenous : acute onset in a previously well-functioning prosthesis (40). A similar classification describes early (< 3 months), delayed/low-grade (3-24 months), and late infection (> 24 months) (Trampuz and Zimmerli 2005) (39). The classification proposed by McPherson *et al* (2002) considers criteria other than timing such as assessment of the overall medical and immune health of the host and grading of the local wound (23).

It is widely accepted that the treatment of PJI should be a combination of surgical and antibiotic therapy (20).

Surgical options in early PJI are generally DAIR (debridement, antibiotics, irrigation and retention of the prosthesis) or one or two stage revision (20,21, 28,44). In comparison with revision arthroplasty DAIR is less complex, reduces morbidity, length of hospital stay and costs (11,19,24,31). Nevertheless, there is lack of agreement regarding what constitutes successful outcome for PJI treatment. Various criteria to define success or failure have been proposed and success rates of DAIR for PJI treatment show large variation in literature (10). Reported successful outcomes with respect to retention of the prosthesis following DAIR range from 14% to 100% (3,8,34,45).

Romano *et al* showed in a systematic review that DAIR, after treatment by a single or repeated DAIR procedure, failed in 45.9 and 52 percent of the patients respectively, at a mean follow up of 53 months. Failure was defined by the diagnosis of recurrent infection or the need for further surgery (34). Important remarks which are mentioned in their review are : the role of multiple factors that can affect the

likelihood of infection control after periprosthetic infection (for example patient comorbidities), different selection of patients and treatment indications across different centers, variation in postoperative treatment across studies (for example antibiotic therapy), the surgical technique may differ even in the same case series, and hip and knee prosthesis are considered together (34).

The goal of our study is to overcome some of these limitations and to show results and success rate of DAIR treatment in early PJI after primary THR with a multidisciplinary treatment approach and customized antibiotic regime of 12 weeks.

METHODS

We retrospectively analyzed all medical records of patients with an early, less than three months postoperatively, PJI after primary THR performed in our institution between January 2008 and January 2012. PJI was classified according to the Musculoskeletal Infection Society (MSIS) criteria (43).

Demographics, perioperative data, type of treatment, causative organism, duration and type of antibiotic treatment, and complications were recorded. After the antibiotic treatment patients were discharged from clinical follow up with clear instructions (i.e. in case of wound problems (redness/pain/swelling/discharge), hip pain or fever contact our hospital). After this period patients returned to their standard care protocol. CRP values were measured only on indication.

The DAIR procedure always took place according to the following steps : First, wound margins were excised and the subcutaneous space and fascia is opened. Then three tissue samples are obtained followed by a meticulous debridement. Second, the intra-articular space is opened and three tissue samples are obtained again, followed by debridement. Exchange of modular components was not regularly performed. Third, pulsatile lavage with six liters of saline and povidone-iodine (Betadine®, 0.35% solution, during 3 minutes) was performed. Placement of gentamicin beads was decided by the individual orthopedic surgeon. Fourth, placement of a subfascial low vacuum drain and tight closure of all wound layers. In case of applied gentamicin beads (Septopal®, Biomet Europe B.V., Dordrecht, Netherlands), two weeks after the first debridement procedure, the beads were surgically removed and the DAIR procedure was repeated after obtaining at least three tissue samples again. If necessary the DAIR procedure was

repeated a third time. Vacuum assisted closure therapy was used in patients with wound healing problems, but is not part of our standard protocol (37).

None of the patients received antibiotics prior to culture. To achieve broad spectrum treatment, cefazolin, 1000 milligrams three times a day, was intravenously administered immediately after the tissue samples had been obtained and maintained until the results of tissue cultures were known, 10 to 12 days after surgery. To protect the prosthesis from biofilm formation, rifampicin 450 mg two times daily was started when the culture samples showed a rifampicin sensitive microorganism and the wound showed no leakage. During a meeting once a week, the culture results were discussed by a multidisciplinary infection team (medical microbiologist, infection disease specialist, orthopedic surgeons, pharmacist and hospital hygienist) and the appropriate antibiotic regimen was selected. Furthermore, response to, and the need for modification of treatment during antibiotic therapy was

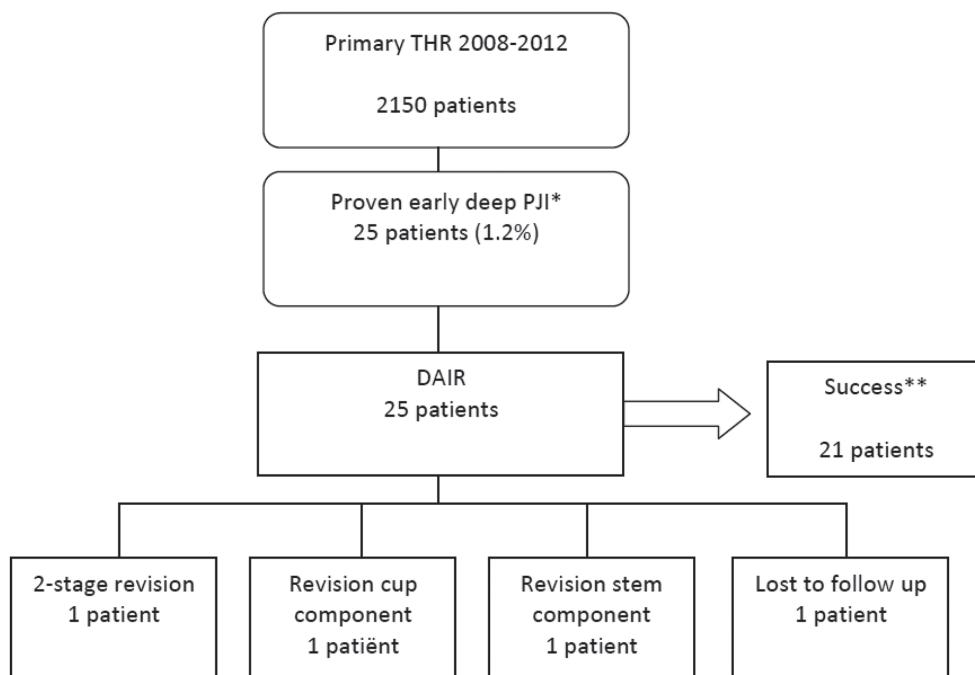
also evaluated when necessary. An initially duration of antimicrobial therapy of 12 weeks after DAIR was based on recommendations by Zimmerli (35,44,45).

Success was defined as retention of the primary prosthesis two years after DAIR without any antibiotic treatment and no clinical and/or anamnestic infection symptoms at the latest clinical visit (43,44).

Statistical analysis was performed with Stata 10.1. Descriptive statistics were calculated, including mean, median, frequency, and proportions.

RESULTS

Figure 1 shows a flowchart of our patients included in the study. We identified 25 early PJI's after primary THR between 2008 and 2012. Patient demographics are shown in Table I. One patient died two months postoperatively due to a myocardial infarction and was analyzed as lost to follow-up.



* PJI according to MSIS criteria (43) with two or more positive peroperative cultures with the same microorganism and < 3 months after primary THR

** retention of primary prosthesis 2 years after latest DAIR procedure, without clinical signs of infection and no antibiotic use

PJI, prosthetic joint infection; DAIR, debridement, antibiotics, irrigation and retention of the prosthesis; THR, total hip replacement

Fig. 1. — Flowchart of 25 patients with early PJI after primary THR treated with DAIR

Table I. — Patient demographics

	Number of patients	Success of treatment	Failure of treatment	Lost to follow-up
All	25	21 (88%)	3 (12%)	1
Age (years) (range)	66 (40-97)	65 (40-97)	69 (58-80)	
Sex				
Male	17	13	3	1
Female	8	8	0	
BMI (kg/m ²) (SD)	29.6 (5.5)	30.2 (5.6)	25.5 (2.5)	
ASA score (median) (range)	2 (1-4)	2 (1-4)	2	
DM	3	1	2	
RA	3	3	0	
Current smoker	3	1	2	
Type of prosthesis				
Cemented	10	9	1	
Cementless	15	12	2	1
Median start of DAIR after THR (days) (range)	14 (10-42)	17.5 (10-42)	12.0 (11-13)	
Median symptom duration until DAIR (days) (range)	10 (1-31)	11 (1-31)	2 (1-10)	
Median duration of hospital stay (days) (range)	23 (8-57)	23 (8-57)	18 (11-23)	

BMI, body mass index ; SD, standard deviation ; ASA, American Society of Anesthesiologists ; DM, diabetes mellitus ; RA, rheumatoid arthritis ; DAIR, debridement, antibiotics, irrigation and retention of the prosthesis ; THR, total hip replacement.

After a median follow-up of 3.1 (2.2 to 5.5) years, 21 out of 24 patients (88%) had retention of the primary hip prosthesis without any antibiotic treatment and no signs of infection.

Three out of 24 patients underwent exchange of the hip prosthesis. The first patient underwent a stem revision because of stem loosening noticed during the first debridement procedure. The second patient underwent a two-stage revision due to a persistent infection and the last patient warranted revision surgery because of recurrent dislocations.

The median time until patients were treated with DAIR was 14 days (range 10-42 days) after the primary THR. Median duration of symptoms until DAIR was 10 days (range 1-31 days). Twelve out of 25 patients were treated within one week after onset

of symptoms, including two patients whose treatment failed. Three patients were not treated within three weeks after onset of symptoms, but did have a successful outcome. All failures were treated with DAIR within three weeks after THR.

Surgical treatment

Table II shows the type of DAIR procedure. 13 patients underwent one DAIR procedure. 12 patients were operated more than once. One patient underwent three debridement procedures (first time only lavage with subsequently a second and third procedure for gentamicin beads placement and removal), because of persistent drainage with pus three days after the first procedure. Another patient

Table II. — DAIR treatment

	Number of patients	Success of treatment	Failure of treatment follow-up	AB duration (weeks)	Lost
Only lavage	12	11	1		
Lavage with gentamicin beads	12	9	2		1
Only lavage with femoral head replacement	1	1	0		
Number of irrigation procedures					
1	13	12	1	12 (8-15)	
2	10	7	2	12 (9-20)	1
3	2	2	0	20 (16-24)	

with abnormal wound healing after gentamicin beads placement and removal underwent a third procedure because of a muscle transplantation with lavage during the same session. These two patients who underwent three DAIR procedures had successfully outcome. Twelve patients were treated with gentamicin beads. In one patient gentamicin beads were placed, but not subsequently removed because of the clinical condition of the patient (too fragile to undergo another operation).

Antibiotic therapy

After the initial cefazolin period most of the patients were treated with teicoplanin, clindamycin or ciprofloxacin dependent of the culture results and the multidisciplinary meeting. 23/25 patients were treated with rifampicin (rifampicin oral, 450 milligrams twice daily, Sanofi Aventis Netherlands B.V.). In two patients cultures with a rifampicin resistant *Staphylococcus epidermidis* were found and were treated with antibiotics adapted to the susceptibility of the organism but no rifampicin was given.

The median total duration of antibiotic therapy in the group with successful outcome was 12 weeks (range 8-24 weeks). Three patients underwent antibiotic treatment shorter than 12 weeks. One patient with a moderate clinical condition experienced nausea symptoms, the reason why the antibiotic treatment was shortened. Two patients, which were discussed in our multidisciplinary team, underwent shorter antibiotic treatment, but the reason why is unclear.

The failed case with the two stage revision was in total treated for 14 weeks with antibiotics until the decision to start a two stage revision treatment.

Microbiology

In all patients intraoperative cultures were concluded as positive for infection. Two patients had negative culture samples after the first debridement with gentamicin beads placement, but positive cultures during the subsequent removal of beads two weeks later. The most frequently isolated organism was *Staphylococcus epidermidis* (Table III). Twelve infections were polymicrobial. All patients with *Staphylococcus aureus* showed successful outcome. The three patients with treatment failure showed *Staphylococcus epidermidis* (2/3), Group B Streptococcus (1/3), *Corynebacterium* (1/3) and *Enterococcus faecalis* (1/3) in their culture samples. No methicillin resistant *Staphylococcus aureus* (MRSA) was isolated.

Complications

After the DAIR procedure seven out of 25 patients experienced antibiotic related problems, most of the time gastrointestinal symptoms like nausea and vomiting. Liver toxicity ($n = 1$) and blood disorders (leukopenia, $n = 1$) were caused by rifampicin and/or teicoplanin. One patient developed an anaphylactic reaction, probably induced by teicoplanin. They were treated by switching the

Table III. — Organisms isolated intraoperatively and treatment outcome

	Number of patients	Success of treatment	Failure of treatment	Lost to follow-up
Staphylococcus epidermidis	21	18	3	
aureus	14	11	3	
warneri	7	7	0	
	1	1	0	
Streptococcus	6	4	1	1
Enterococcus faecalis	5	4	1	
Polymicrobial	12	10	2	

responsible antibiotic or by changing the dosage. None of them developed permanent injury.

One patient developed wound healing problems and vacuum assisted closure therapy was started. A plastic surgeon successfully closed the wound with a muscle transplant.

DISCUSSION

This retrospective study showed an 88% success rate of DAIR in early PJI after primary THR with a follow-up of at least two years. With respect to the literature, our 88% success percentage is favorable, since there is a lot of variety in success rates of DAIR (14-100%) (3,8,34,45).

Our relatively favorable results might be explained by the fact that for the majority of our patients (23 out of 25 patients) the time interval was within the time limits recommended by Zimmerli *et al* (44). The longer the duration of infectious symptoms, the higher the risk of DAIR treatment failure (41). Zimmerli recommends treatment of early PJI within three weeks after onset of clinical symptoms (44). Geurts *et al* mentioned that starting DAIR treatment more than four or even eight weeks post-operatively caused an increase in failure risk of 20% to 50% respectively (13). Others recommend debridement within a week after the start of symptoms (41).

The optimal duration of antibiotic treatment following DAIR is still not clear. Bernard *et al* suggest treatment of six weeks, Zimmerli *et al* recommend three months in patients with early PJI of the hip (6,44). Others stated that CRP is a valuable parameter to decide when to stop antibiotic thera-

py (15). Our study group may be small, but our results suggest that 12 weeks or even eight weeks of antibiotic treatment is satisfactory. A multidisciplinary approach is important to discuss the exact duration and, switching antibiotic therapy when necessary. This is to our opinion the strength of our treatment.

Like other studies the most common cultured microorganisms in our study were Staphylococcus epidermidis and Staphylococcus aureus (17,32,41,42). In contrast to Westberg *et al*, we identified no MRSA infections (41). Reasons for this may be the small study group, and the relatively low prevalence of MRSA in the Netherlands (12). In agreement with earlier reports, present study did not show an association between Staphylococcus aureus and higher failure rates (4,7,21,44). In contrast, an early PJI after primary THR due to Staphylococcus aureus gives probably a better prognosis because of early recognition and good treatment options in the Netherlands (lower prevalence of multiresistant strains).

Every study has limitations. We know that our used definition of success is debatable and definitions differ between studies (34). Therefore it is important to have an international consensus definition of treatment success after PJI treatment to make a better comparison between different DAIR protocols and outcome results. Recently Diaz-Ledezma *et al* published a consensus definition (10). They define a successfully treated PJI as (1) infection eradication, characterized by a healed wound without fistula, drainage, or pain, and no infection recurrence caused by the same organism strain ; (2) no subsequent surgical intervention for infection after re-implantation surgery ; and (3) no occurrence of PJI related mortality (10). When we use that consen-

sus definition our success is still 88%. However, our follow-up time of two years is relatively short. This may have over-estimated our success rate. Other studies report longer follow-up times up to 5 to 10 years (3,8,34,41,45).

The amount of DAIR procedures for a successful outcome in early PJI remains debatable. We used a maximum of three debridement procedures. Although surgical intervention needs to be individualized for each patient, it is unlikely that multiple DAIR procedures can serve a patient well in the long run. If several attempts at DAIR fail to control infection in a patient, consideration should be given to resection arthroplasty (21,33). Mont *et al* found it reasonable to perform multiple debridements in their series of 24 acute total knee replacement (TKR) infections (25). On the other hand, failure of a single DAIR procedure is recommended to be a consideration for resection arthroplasty (36). According to a consensus during the International Consensus Meeting on Periprosthetic Joint Infection August 2013, failure of two irrigation and debridement procedures is a consideration for resection arthroplasty (14). Our study results showed no clear difference in outcome between one, two or three debridement procedures, but suggest that one or two or even three debridement procedures are justified to gain a successful outcome.

Our surgical procedure was not the same for every patient. In the first place different orthopedic surgeons performed the debridement procedure. Furthermore exchange of modular components was not regularly performed. According to recent data it is advisable to exchange modular components if possible (14).

Also the use of gentamicin beads in this study was not protocolized and therefore based on the surgeon's preference. Gentamicin beads were placed when there was macroscopic a high suspicion of infection. There is still no conclusive evidence or recommendation for the use of non resorbable devices, such as gentamicin beads, and resorbable devices, such as gentamicin sponges (14,16,17). Although initial reports of some studies have been encouraging, there are no randomized controlled studies to demonstrate that the use of these materials enhances the successful outcome of surgical in-

tervention (38). Kuiper *et al* recently showed that use of gentamicin sponges in a DAIR treatment protocol might result in an acceptable successful outcome of 74% with a follow-up of more than two years (16). The use of resorbable material is not without problems. Besides the cost, which depending on material can be substantial, local reaction to the resorbable material has been described. Calcium sulphate pellets have been shown to increase wound exudates (22,26). A recent MSIS international consensus meeting stated that there is currently no conclusive evidence that the use of antibiotic-impregnated resorbable material improves the outcome of surgical intervention for PJI (14).

Negative-pressure wound therapy (NPWT) may have potential value as an adjunct to the management of posttraumatic musculoskeletal infections and wound healing problems (37). However, its use in PJI is still not clear, it may lead to an increased risk of colonization of gram-positive cocci (e.g., *Staphylococcus aureus*) (37). In our study only one patient underwent NPWT with a successfully outcome, good wound healing and no *Staphylococcus aureus* colonization.

This is a retrospective study, limiting quality and level of evidence. According to literature it is difficult to compare outcomes and to determine which PJI treatment strategy (DIAR, one stage or two stage revision) is the best (8,28,29,34). Reasons for this are that there are no published high quality studies (i.e. randomized clinical trials) to address optimal selection of a specific surgical procedure, and the optimal duration of antibiotic treatment is unclear (1,6,9,15,28,41,46). Furthermore the available data in literature consist of single-center non-comparative cohort studies and a decision analysis based on these cohort studies which are comparable to our study (1,17,34,41,46).

Another limitation of our study is our small study group. Therefore it is difficult to compare subgroups and identify potential risk factors associated with success or treatment failure. Furthermore we have focused on retention of the prosthesis and included no results concerning functional outcome and quality of life, which are also important outcome parameters to consider (2). There were also no CRP-values available at final follow-up.

In conclusion, our results support that customized DAIR treatment with multidisciplinary decided antibiotic therapy can be successful for treatment of early PJI after primary THR. We think that it is important to treat early PJI without delay after onset of symptoms, and to use a multidisciplinary approach in order to optimize treatment results. Good quality studies with high level of evidence and clear definitions are still needed in this challenging orthopedic problem.

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