Failure of the surgical treatment in 115 infected hip arthroplasties-analysis of a 12-year prosthetic joint cohort study (1999-2010)

ABSTRACT

Background: Infection after total or partial hip arthroplasty (HA) leads to significant long-term morbidity and high healthcare cost. We evaluated reasons for treatment failure of different surgical modalities in a 12-year prosthetic hip joint infection cohort study.

Method: All patients hospitalized at our institution with infected HA were included either retrospectively (1999-2007) or prospectively (2008-2010). HA infection was defined as growth of the same microorganism in ≥2 tissues or synovial fluid culture, visible purulence, sinus tract or acute inflammation on tissue histopathology. Outcome analysis was performed at outpatient visits, followed by contacting patients, their relatives and/or treating physicians afterwards.

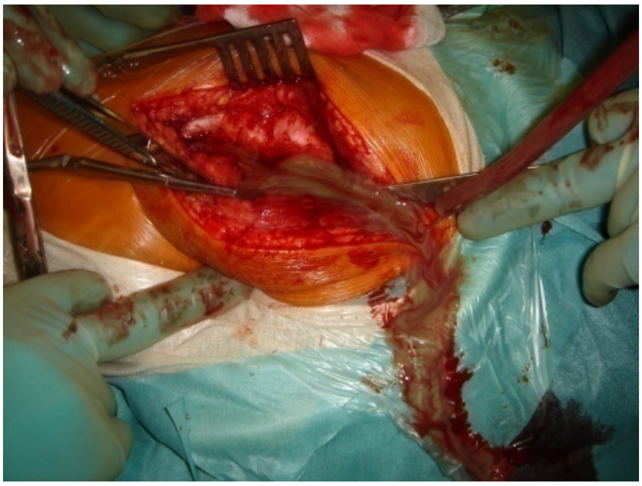
Results: During the study period, 117 patients with infected HA were identified. We excluded 2 patients due to missing data. The average age was 69 years (range, 33-102 years); 42% were female. HA was mainly performed for osteoarthritis (n=84), followed by trauma (n=22), necrosis (n=4), dysplasia (n=2), rheumatoid arthritis (n=1), osteosarcoma (n=1) and tuberculosis (n=1). 28 infections occurred early (≤3 months), 25 delayed (3-24 months) and 63 late (≥24 months after surgery). Infected HA were treated with (i) two-stage exchange in 59 patients (51%, cure rate: 93%), (ii) one-stage exchange in 5 (4.3%, cure rate: 100%), (iii) debridement with change of mobile parts in 18 (17%, cure rate: 83%), (iv) debridement without change of mobile parts in 17 (14%, cure rate : 53%), (v) Girdlestone in 13 (11%, cure rate: 100%), and (vi) two-stage exchange followed by removal in 3 (2.6%).

Patients were followed for an average of 3.9 years (range, 0.1 to 9 years), 7 patients died unrelated to the infected HA. 15 patients (13%) needed additional operations, 1 for mechanical reasons (dislocation of spacer) and 14 for persistent infection: 11 treated with debridement and retention (8 without change; and 3 with change of mobile parts) and 3 with two-stage exchange. The average number of surgery was 2.2 (range, 1 to 5).

The infection was finally eradicated in all patients, but the functional outcome remained unsatisfactory in 20% (persistent pain or impaired mobility due to spacer or Girdlestone situation).

Conclusions: Non-respect of current treatment concept leads to treatment failure with subsequent operations. Precise analysis of each treatment failure can be used for improving the treatment algorithm leading to better results.

Introduction:



There has been a marked increase in the number of total hip replacements undertaken during the last few decades. In Switzerland, hip joint arthroplasty was 1.9/1000 in 2002 to 2.4/1000 inhabitants in 2008. In 2009 17,251 patients had THA 2,975 patients had hemi-arthroplasty in Switzerland. This increase is also accompanied by a rise in the number of associated complications. (1).

Unfortunatelly results of treatment after infection of an arthroplasty vary enormously and the rate of successful control of infection by revision hip arthroplasty can lie between very low 30% but go up to 80%–100%. (2)

Joint arthroplasty is an operation, which has good results regarding pain, mobility and quality of life. This is especially true for those patients who suffered osteoarthritis. HA infection is potentially very dangerous. It can lead to serious illness and high cost for the patients and the population (5). In recent years, significant progresses have been made to decrease the rate of infection as antimicrobial prophylaxis and laminar flow operating rooms have been introduced. The rate of infection of total hip prosthesis is described to lie around 1-2% in the literature. (6,7,8)

Infected HA are classified in 3 categories; early (develops in the 3 first months after surgery) delayed (between 3 to 24 months after surgery) and late (after 24 months after surgery) (5).

Early infection occurs within the first 3 months after surgery and is typically associated with clear, unmistakable signs and symptoms such as pain, warmth and redness in and around the implant. Highly virulent microorganisms such as Staphylococcus aureus or Gram negative Bacillus cause this type of infection. Delayed infection occurs between 3 and 24 months after surgery. It is associated with subtle signs and symptoms such as persistent joint pain and is caused by less virulent bacteria; notably Coagulase-negative Staphylococcus and Propionibacterium acnes. Late infection is generally hematogenous: the bacteria frequently come from the skin and the urinary tract and are highly virulent. However the hematogenous route can occur at all time (5,8,9).

The most common microorganisms causing infected prosthesis are Coagulase-negative Staphylococcus and Staphylococcus aureus, depending on the study. Less frequently, Streptococcus spp, Enterococcus, Propionibacterium acnes and Gram-negative bacteria are also to be found (6, 9).

One of the main characteristics of these microorganisms is their ability to produce a biofilm that conceals the infection from the immune system. Bacteria living in this biofilm enter slow growing states that make them difficult to be eradicated with antibiotic therapy. Furthermore there is no microcirculation on the implant that can allow the antibiotic and host immune system to reach the surface of the elements of the artificial joint.

The goal of the treatment of infected arthroplasties is to eradicate the infection by conserving a long-term pain-free functional extremity, which depends upon eradication of the infection.

Long-term suppressive antimicrobial therapy is used if surgery is contra-indicated, but this only temporarily controls the symptoms without eradicating the infection. (5) To successfully treat an infected arthroplasty both surgical and antibiotic treatment are mandatory (5,9).

The algorithm published by Zimmerli and al in 2004 (5) gives an excellent and clear treatment plan concerning the management of an infected prosthetic joint.

According to Zimmerli's algorithm, the treatment options are the following (5):

> -Debridement with retention for infection with clinical symptoms for less than 3 weeks, a stable implant, good condition of the surrounding soft tissue, no sinus tract and available antimicrobial agent with action against organisms living in biofilm.

- One-stage exchange if the patient doesn't fulfill the above criteria but if the soft tissue is intact or only slightly compromised, if there is no difficult-to –treat pathogen and no severe co-morbidity.

- Two-stage exchange for infections with compromised surrounding soft tissue. A short interval (2-4 weeks) and an anti-microbial impregnated bone cement spacer is used except if there is a difficult-to-treat pathogen like rifampicin resistant staphylococcus, quinolone resistant Gram negative, fungi and Enterococcus. In the latter case a longer interval (6-8 weeks) and no spacer are used.

- Implant removal without replacement or joint arthrodesis are reserved for the patients with severe immuno-suppression, active i.v. drug abuse or if there is no functional improvement to be expected after the operation, or with high co-morbidity.

There is considerate debate concerning the optimal treatment of infected hip arthroplasties, due to the absence of well-designed prospective randomized, controlled trials. Therefore, in this present retrospective and prospective study we evaluate the characteristics of infected THA and both the functional and microbiological outcome according to the surgical and antimicrobial treatment, the type of infection, and the type of microorganism.

In our study, we focus more precisely on the failure of surgical and antimicrobial treatments, and the reasons for their failure. In this study we also look at whether the surgical treatment respects Zimmerli's algorithm.

Patients and methods:

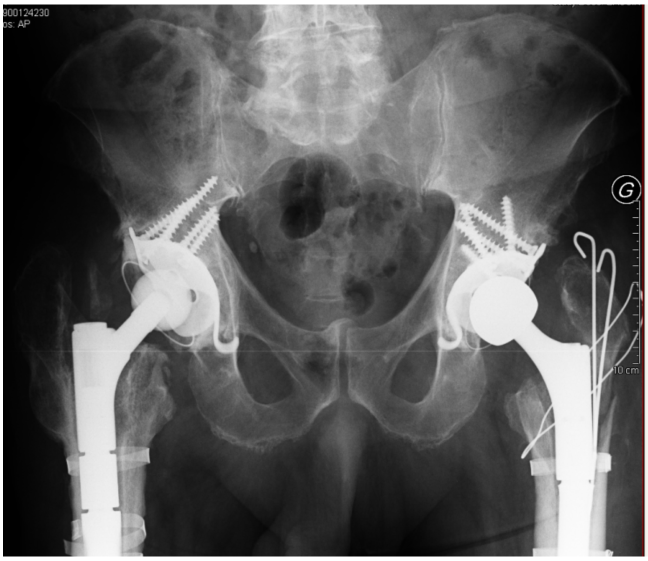
This is a retrospective study from 1997 to 2007 and prospectively between 2008 and 2010. This study was conducted on all patients who were hospitalized in the CHUV during this period for an infected HA, i.e. 117 patients.

We analyzed the electronic data and the medical charts of all the patients to find: the first implantation, the time of hospitalization, the surgical and infectious therapies, signs and symptoms of the infection, radiological and infectious parameters. We also checked to see if there were complications during hospitalization. And finally, we looked at the follow –up and the microbial and functional outcomes. Outcome analysis was performed at outpatient visits, followed by contacting patients, their relatives and/or treating physicians afterwards.

Criteria of inclusion/exclusion:

All the patients who were hospitalized in the CHUV with a documented infected HA during the period between January 1997 and December 2010 were included. Two patients were excluded due to lack of data.

<u>Definitions:</u>



THA Infection:

A case is defined as a HA infection when one or more of the following criteria is present (5):

- Sinus tract communicating with the joint space
- Growth in tissue or synovial fluid cultures (low-virulent micro-organisms required two specimens with growth of the same micro-organism)
- Visible purulence at implant site (as determined by the surgeon)
- Acute inflammation on tissue histopathology (as determined by the pathologist).
- New: Positive sonication (>50 CFU/ml) or calorimetry (9)

Surgical therapy:

Debridement and retention: Debridement involves removal of the hematoma, fibrous membranes, and devitalized bone and soft tissue. The mobile parts can be changed (DC) or not (DN).

One -stage exchange: Includes removal of all foreign material, debridement, and re-implantation of a new prosthesis during the same procedure.

Two-stage exchange (short 2 weeks vs. long 6 weeks interval): Implantation of the new prosthesis is delayed for a variable period of time. An anti-microbial impregnated bone cement spacer is usually inserted.

Girdlestone: involves removing the prosthesis, hematoma, fibrous membranes, and devitalized bone and soft tissue.

Outcome evaluation

Good surgical outcome is defined as the success of the first surgical approach without additional surgery to eradicate the infection.

Good microbiological outcome is defined as the eradication of the infection at final follow-up.

Good final outcome is defined as a painless, functional hip joint

Results:

Demographic data:

A total of 117 patients were identified, of whom 2 were excluded due to lack of data. Table 1 summarizes the demographic data. The average age is 69 years; 42% of the patients were female. The average time follow-up after the first surgery for THA was 46.52 months.

Table 1: demographic data

Number of patients	115
Average (range), years	69y (33y-102y)
Female	48 (41.7%)
Average follow-up (months)	46.52 (1.4-275,3)

Characteristic of infected prosthesis

Table 2 summarizes the characteristic of infected prosthesis. 100 patients had a THA and 15 had a hemi-prosthesis. The main reason for the first implantation was osteoarthritis (84 cases, 73.04%), traumatic (22 cases, 19.13%), rheumatic arthritis (1 case, 0.86%), necrosis of femoral head (3 cases, 2.58%), osteosarcoma

(1 case, 0.86%), tuberculosis (1 case, 0.86%), hip dysplasia (2 cases, 1.72%). In 28 cases (24.34%)we found early infection, delayed infection was proven in 25 cases (21.34%) and late infection was present in 63 cases (54.13%).

Table 2: Characteristics of infected prosthesis:

TYPE OF PROSTHESIS	
- THA	100
- HEMI- HA	15
Reason of arthroplasty	
- Osteoarthritis	84 (73.04%)
- Traumatic	22 (19.13%)
- Rheumatid arthritis	1 (0.86%)
- Osteosarcoma	1 (0.86%)
- Necrosis of the hip head	2 (1.72%)
- Hip dysplasia	2 (1.72%)
- Tuberculosis	1 (0.86%)
Type of infection	
- early (3months)	28 (24.34%)
- delayed (3-24 months)	25 (21.73%)
- late (24 months)	63 (54.78%)

Surgical Procedure:

In 59 cases (51.3%) there was a two-stage exchange (2S), in this type of surgery there were 4 re-operations (6.77%). 5 patients (4.34%) had a one- stage exchange (1S). In the debridement group, there were 18 debridements with change of the mobile parts (DC) (15.65%) and 4 re-operations (16.6%), 17 debridements with no change (DN) (14.78%) and with 8 re-operations (47.1%). The Girdlestone procedure (R) was carried out in 13 cases (11.30%). Finally there were 3 patients (2.60%) with a spacer followed by a Girdlestone procedure(S+R).

Table 3: Surgical Procedure

2S (4 re-operations, 6.77%)	59	51.3%
1S	5	4.34%
DC (3 re-operations, 16.6%)	18	15.65%
DN (8 re-operations, 47.1%)	17	14.78%
R	13	11.3%
S+R	3	2.6%

Microbiology:

The pre-operative microbiology was positive in 44 cases (38.20%), was negative in 32 patients (27.8%) and not done in 39 cases (33.9%). 78 patients (67.82%) had positive per-operative microbiology. In 37 cases (32.17%), no pathogen was found. Sonication was done on only 21 patients, 7 were sterile and 14 were positive. Both microbiology (per-operative and pre-operative) were positive in 25 patients (21.73%), the per-operative microbiology was positive alone in 55 cases (47.82%), positive only in pre-operative in 19 people (16.52%). And both negative in 16 cases (13.91%). Tables 4 and 5 explain the details of the microbiology.

Table 4: Microbiology:

Pre-operative microbiology		
• positive	44	38.2%
• sterile	32	27.8%
• not done	39	22.9%
Per-operative microbiology		
• positive	78	67.8%
• sterile	37	32.2%
Sonication		
• not done	94	81.7%
• positive	14	12.2%
• sterile	7	6.1%

Table 5: Microbiology

Both positive	22	21.7%
Only pre-operative	19	16.5%
Only per-operative	55	47.8%
Both negative	16	13.9%

In 65 cases (83.2%) a single pathogen was discovered from the per-operative microbiology (bone, soft tissue, prosthesis and/or synovial fluid), and 13 (16.8%) poly-microbial infections were identified. Table 6 summarizes which pathogens were discovered in the per-operative microbiology.

Table 6: Per-operative microbiology:

Staphylococcus aureus	16	21%
MRSA	6	7.8%
Coagulase-negative Staphylococcus	17	22%
MRSE	7	9.09%
Enterococcus spp(1)	3	3.89%
Streptococcus spp(2)	5	6.49%
Propionibacterium spp(3)	4	5.20%
Gram negative(4)	4	5.20%
Polymicrobial(5)	13	16.80%
Others gram positive(6)	2	2.60%
Candida	1	1.29%

(1) 2 were described as enterococcus spp and 1 enterococcus faecalis, (2) streptococcus sanguinis, streptococcus oralis, streptococcus agalactiae, streptococcus mitis, ß-hemolytic streptococcus (C group), (4) 2 were Echerichia Coli, one Pseudomonas aeruginosa, one Citrobacter koseri (5): klebesiella pneumoniae+peptostreptococcus, Eschericha Coli+enterococcus spp, enterococcus spp+ coagulase negative staphylococcus, Coagulase negative staphylococcus: epidermidis+hominis+ E. Coli+ propionibacterium acne, Propionibacterium acnes+staphylococcus aureus, Staphylococcus aureus+Enterococcus spp, Staphylococcus capitis+Staphylococcus auricularis,+staphyloccus simulans, Staphylococcus capitis+staphylococcus hominis, coagulase negative staphylococcus+ propionibacterium acnes, Staphylococcus epidermidis+MRSE, staphylococcus haemolyticus+staphylococcus caprae, peptostreptococcus magnus+staphylococcus epidermidis, Streptococcus Dysgalaticae+Pseudomonas aeruginosa+staphylococcus aureus (6) Bacillus Cereus, Peptostrepococcus magnus

Treatment

For 59 patients (51.3%) an initial 2-stage exchange surgical strategy was pursued with a fairly high success rate. Only 4 patients (6.77%) had to be re-operated: 1 for mechanical problems (dislocation of the spacer) and 3 (5.08%) for infectious disorder (MRSA, S. aureus, poly-microbial infection). For 2 of these 3 cases of infection, the surgical option chosen was replacement of the spacer while the 3rd patient underwent a 2-stage exchange operation for the second time.

1-stage exchange was the surgical strategy chosen for 5 patients (4.34%).

For 18 patients (15.65%) the surgical strategy pursued was debridement with change of the mobile part. In this group, 3 patients (16.66%) had persistant infection (MRSA, P. aeruginosa, polymicrobial infection). All 3 had to undergo repeated surgery. The surgical strategy differed in each of these 3 cases: for 1 patient a Girdlestone procedure was employed; for 1 a 2-stage exchange was performed; the third patient first had an operation for a spacer, which was followed by a Girdlestone procedure.

For 17 patients (14.78%) the surgical strategy pursued was debridement with no change of mobile parts. There was a high failure rate due to persistent infection: 8 patients (47.1%) had to be re-operated. 2-stage exchange was the surgical strategy pursued for the majority of these cases (5 patients, 62.5%) Girdlestone procedure was the surgical procedure opted for in 2 patients (25%). Two further surgical procedures were decided on for the final patient of this group: first two spacers, then Girdlestone (MRSA's infection)

20 patients had a Girdlestone procedure but only 13 as first surgical procedure, 3 had spacers and then a Girdlestone and 4 had another surgical procedure as first procedure such as debridement without change of mobile parts.

Outcome

The mean time of follow-up after the first surgery for the THA infection was 46.52 months (range 1.4-275.3). During this time, it averred that the mean surgery rate required was 2.19 (range 1-5 surgeries). It may be noted that two patients died during their hospitalization but not from THA infection.

The overall final outcome can be considered fair to good with a success rate of 82.6%. Successful eradication of the microbiological infection by means of the various elected surgical procedures was virtually excellent: 98% –given that two patients died of other, non-related causes during the follow-up period.

100 episodes of HA infections (85.47%) were eradicated after the first surgical procedure option. 14 episodes of recurrent infection necessitated a second operation. One case encountered mechanical difficulties, which required further surgery. However after all the secondary surgical procedures, the microbial outcome was completely satisfactory; all infection was eradicated.

The functional outcome referring to the successful surgical procedure more precisely the prosthesis itself can be considered fairly good with a 69.56% success rate. The Girdlestone procedure had the best for the successful eradication of THA infection in 20 episodes; while this was fully satisfactory re microbiology, it cannot be considered successful regarding the functional outcome due to the resulting reduced mobility.

Discussion:

An infected HA can be treated by different surgical procedures. These procedures lead to different results for the same type of infection and the same microbiology.

This study shows that debridement without change of mobile parts is the least appropriate surgical procedure to eradicate an infected THA. 47.1% of the patients for whom this surgical procedure was chosen required further surgery. A comparison of this study with other studies (11,12,16) confirms similar high, or indeed higher, failure rates: Betch et al in *Treatment of Joint Prosthesis in accordance with Current Recommendations Improves Outcomes,* 68 cases of infected prosthesis, 50% failure after debridement without change of mobile parts; Trebse et al in *Treatment of Infected Retained Implants* reported a 70% failure rate after debridement and retention in 24 cohort patients. Likewise Veuthey et al presented at EBJIS 2010 *Characteristic and Outcome of Knee Prosthetic Joint Infections* and reported a 93% failure rate after debridement without change of mobile parts. (11,12,16)

This surgical procedure (debridement without change of mobile parts) has not been applied in the CHUV for 5 years now. (last case in 2006).

There was a good eradication rate of THA infection after debridement with change of mobile parts, in both one-stage exchange and two-stage exchange procedures. The failure rate for debridement of the mobile parts was 16.6% and can be explained by non-adherence to Zimmerli's algorithm for the choice of surgical management and antimicrobial treatment (6). One case of failure was due to a late infection; two others were early infections but difficult-to-treat bacteria (Pseudomonas aeruginosa, polymicrobial (enterococcus) infection). This surgical procedure could have as high a success rate as one or two stage-exchanges if the cases were well selected, i.e no presence of difficult-to-treat bacteria, intact soft tissues, no sinus tract, no loosening/stable implant, early infection or occurrence of symptoms lasting for less than 3 weeks (9). In the cases we studied that resulted in failure the above criteria were not respected.

The success rate of one- and two-stage exchanges was high–above 90%. In our study only 5 patients had one-stage exchange and no second surgery was necessary. These patients were well selected (no difficult-to-treat bacteria, intact soft tissue). The success rate of this surgical procedure in comparative studies is between 86% and 100% (9,13,14). A similar success rate was also the case for 2-stage exchange procedures. The failure rate was low (6.8%) and concerned only 4 patients: one suffered mechanical failure (dislocation of the spacer) and 3 suffered from persistant infections. The two-stage exchange is the surgical procedure that presents the lowest failure risk factor, particularly for late infection and difficult-to-treat bacteria.

In our study, the intervening weeks between introduction of the spacer and reimplantation of a new prosthesis in the two-stage exchange procedure can be divided into two groups: the short interval group (2-4 weeks) and the long interval group (4 weeks and more). The short interval group concerned a minority of patients: 8 patients (13.5%); the majority, 51 patients (86%), belonged to the long interval group. The advantages of a short interval are fewer complications due to bed rest and hospitalization, reduction of costs and shorter-term recovery than the long interval group. However, regarding short interval procedures, successful treatment depends on both knowledge of the bacteria, and its belonging to a *not*-difficult-to-treat microorganism. Furthermore, the bacteria must also be sensitive to rifampicin. If all these criteria are present, the success rate is similar to the long interval group, indeed it may even be considered better given the advantages of the short interval procedure. The 8 patients in the short interval case studies experienced the same outcome as the long interval group and none of them had to be re-operated.

The success rate for two-stage exchange was 93.2%. Unfortunately, this procedure involves multiple surgeries and can lead to bad functional mobility by reducing the mobility of the joint (6,9,15).

The Girdlestone procedure is the best surgical procedure for eradication of infection, but comes with a poor functional outcome since the patient no longer has a joint prosthesis. This surgical procedure is used only in patients who have high co-morbidities such as severe immuno-suppression, extensive damage of the soft tissue, active iv-drug abuse or when a re-implantation will not improve the functional outcome (6,9). In our study, this surgical procedure was elected as the best option for 20 patients. For 13 it was selected as the first treatment; 3 patients had a spacer followed by a Girdlestone; 4 had a Girdlestone as final treatment, i.e. the Girdlestone procedure was preceded by another surgical procedure, for example one patient had a debridement without change of mobile parts but as the infection was not eradicated, had to be re-operated. The infection was eradicated in all of the patients treated with a Girdlestone. However, removal of the prosthesis impairs mobility and motion. Hence the poor functional outcome results for this surgical procedure (69%) in our study.

Conclusion:

Overall our study demonstrates the fact that when selecting the optimum surgical procedure, the type of infection, the type of bacteria found, the condition of the soft tissue and the presence of sinus tract has to be taken into consideration, and the implant stability needs to be evaluated.

Debridement with no change of mobile parts is the least appropriate surgical procedure and should not be used any more.

Overall treatment success rate of debridement with change of mobile parts and the one-stage exchange depends on patients being well-selected. This means in acute situations (symptoms ≤3weeks) with no difficult-to-treat bacteria, no soft tissue damage, no fistula and no loosening.

The two-stage exchange is the safest surgical procedure for complicated situations. The discussion regarding short and long interval re-implantation is ongoing. Given the results of our study, we would tend to recommend short interval when the required conditions are fulfilled. Further studies focusing on the re-implantation interval time should provide additional data and help us make a better decisional algorithm.

Finally, poor selection of patients and non-adherence to Zimmerli's algorithm lead to failure of the treatment.

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