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ORIGINAL STUDY

Evaluation of ninety-six periprosthetic hip joint infections seen within five consecutive years

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Periprosthetic hip joint infections (PHJI) are severe complications.
In 2003 Zimmerli published a well-noted treatment algorithm for PHJI. The aim of this study is to evaluate outcome, analyze the applied treatment regimen and compare it to the proposed algorithm.
We evaluated the outcome of 96 PHJI treated at our institution between 2008 and 2012 and analysed adherence to the algorithm and outcome in coherence with the algorithm.
The operations performed were irrigation and debridement with exchange of mobile parts (45%), two-stage exchange (36%), one-stage exchange (12%) and permanent explantation (7%). 47% were acute infections, 53% were chronic. Staphylococcus aureus was the most common pathogen. The overall success rate was 88%. In 12% of the cases the chosen operation didn't follow the algorithm. Of these only 10% was successfully treated with the primary operation.
We find that the algorithm proposed by Zimmerli is a useful tool and easy to translate into clinical practice. When followed it yields a high success rate.

Keywords : Periprosthetic infection ; hip infection ; prosthetic exchange ; prosthesis treatment algorithm.

INTRODUCTION

Periprosthetic hip joint infections (PHJI) are a severe complication following total hip arthroplasty (THA). After aseptic loosening and dislocation, PHJI is the most common reason for revision surgery after THA *(5)*. These infections result in significant patient morbidity, lead to complex revision surgery and are an on-going challenge for the orthopaedic surgeon *(8,27,33)*.

The incidence of PHJI is estimated to be between 0.2-.6% in primary THA *(9,13)*. Continuous advancement, e.g. preoperative antibiotic prophylaxis and the improvement of aseptic techniques in the operating theatre, leads to a reduced risk of infection after prosthetic surgery *(10,12,16)*, but together with an aging and growing population the demand for hip replacement surgery is increasing, and with it the absolute number of PHJIs *(9,13)*.

In a suspected PHJI, it is important to get a fast and reliable diagnosis, as treatment strategies differ depending on the duration of the ongoing infection *(18,20,22,32)*. Since no single laboratory test, radiological or clinical examination has shown

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reliable sensitivity or specificity to diagnose a PHJI, a multimodal approach is indicated, including a combination of radiographs, laboratory and clinical tests. Various algorithms have been found helpful to reach a reliable diagnosis *(4,14,23,25)*.

Over the last years standardized treatment regimens have been introduced and evaluated. Patients treated according to these algorithms have been reported to show a better outcome *(3,29)*. Also, the potential advantages of different surgical interventions and the use of a spacer have been evaluated *(30,31)*. Importantly, the need for interdisciplinary collaboration by combining surgical intervention and antimicrobial therapy is of great importance *(3,12,17,32)*.

In 2003 Zimmerli and colleagues published a much noted article describing a detailed treatment algorithm for periprosthetic joint infection (PJI), which is probably the best known and most commonly used algorithm for the treatment of PJI *(32)*. Based on time of manifestation, type of infection, condition of implant, soft tissue conditions and additional problems, various operative strategies combined with antibiotic medication have been suggested.

In this study we analyse the outcome of 96 cases of PHJI treated at our institution between January 2008 and December 2012, with a minimum follow-up period of one year after the last surgical intervention. The aim of this study is to evaluate outcome, analyze the applied treatment regimen and compare it to the algorithm suggested by Zimmerli et al. *(32,33)*.

METHODS

For this study we included and retrospectively analyzed all patients with a proven PHJI treated in our institution between January 2008 and December 2012. The minimal documented follow-up was 12 months

In our study we defined a PHJI according to the criteria from the Proceedings of the International Consensus Meeting on Periprosthetic Joint Infection, established in 2013 *(19)*. The definition of PHJI was either a sinus tract communicating with the prosthetic joint or two positive cultures with phenotypically identical organisms, or fulfilling three of the minor criteria out of five, namely elevated serum CRP (acute >100 mg/L, chronic 10 mg/L), synovial fluid white blood cell count (acute >10.000, chronic > 3000 cells/ul), elevated synovial fluid polymorphonuclear neutrophil percentage (acute>90%, chronic >80%), positive histological analysis of periprosthetic tissue or a single positive culture. All patients, who met these inclusion criteria were included in this study.

Depending on the occurrence of the first signs and symptoms the infection was defined as early (<3 months), delayed (3-24 months) or late (>24 months) after primary prosthetic implantation. Additionally, the infection was classified according to symptom duration independent of the time point of primary implantation as acute (symptoms shorter than three weeks) or chronic (symptoms longer than three weeks) *(32,33)*.

The surgical therapies performed were: irrigation and debridement with exchange of mobile parts (femoral heads and acetabular inserts), one-stage exchange of the prosthesis, two-stage exchange or permanent explantation of the prosthesis. Whether a spacer was used for a two-stage exchange or not was determined by the personal preference of the operating surgeon. Additional operative revisions were performed due to persistent signs of infection and/or not normalized or stagnant infection parameters.

The type of antibiotic therapy and treatment duration were determined in an interdisciplinary approach between orthopaedic surgeons, internists and an infectious disease specialist. Depending on the microorganism and clinical and biochemical improvements, the duration of antibiotics, and the time to re-implantation were determined. All detected pathogens were evaluated.

The data were prospectively assessed and collected and retrospectively analysed. The clinical information was retrieved from the patient records and microbiological information system, as well as from the digital radiological system.

The radiographs were retrospectively analysed to determine whether loosening of the prosthesis existed. Signs indicative of loosening were considered to be: lucent zones, localized cortical hypertrophy or component migration.

Operation reports were used to account for data such as: number of revisions as well as the interval between explantation and re-implantation.

The treatment outcome was documented. Success was classified as no clinical or radiological signs of infection at follow-up ≥ 1 year. Failure was defined as persistence or recurrence of infection at follow-up ≥ 1 year or patient death due to PHJI-related sepsis.

According to the report by Zimmerli and colleagues *(32)* there are conditions which call for a two-stage exchange operation, namely, extended abscess formation, difficult to treat bacteria, the existence of a sinus tract or prosthetic loosening.

It is not always possible to diagnose these conditions at onset and therefore there is a risk of misclassification, e.g. a preoperatively unknown type of bacteria. Thus, the initial opinion and treatment decision has to be changed intra- or postoperatively. In our study, these cases were referred to as "expected failures" (EF). The course of treatment for the EF is seen in Figure 1. The treatment performed was evaluated for its individual merit, thus testing the feasibility of the algorithm in clinical praxis.

Finally, the treatment conducted was compared with the treatment algorithm suggested by Zimmerli.

Statistics were performed using SPSS (IBM SPSS, Version 20.0. Armonk, NY: IBM Corp). A Chi-square test was used for comparison of groups; values of $p > 0.05$ were defined as significant.

Swiss Ethics Committee approval was given for this retrospective study and all patients were asked to consent to the use of their anonymized data.

MATERIAL AND METHODS

In accordance with the above mentioned criteria, we identified a total of 96 PHJIs in 93 patients. Ten patients with 11 PHJIs had to be excluded because they were lost to follow up: 7 patients died within one year of treatment for PHJI but due to an illness not related to the prosthetic infection. One patient with a personality disorder and bilateral PHJIs and one patient with an IV drug addiction refused further follow up and one patient moved away and could not be contacted. Finally, a total of 83 patients with 85 PHJIs were included (51 men, 32 women). The mean age at diagnosis of infection was 67 years (31-90 years). The mean duration of follow-up after the last surgical intervention was 24 months (12-60 months).

In 78% the primary indication for the total hip arthroplasty was osteoarthritis (66/85), fracture being the second most common indication at 14% (12/85) followed by other indications at 8% (7/85).

The most common clinical sign of infection is pain *(13)* and it was present as a cardinal symptom in 80% of the patients (68/85). Of the remaining cases of PHJI six showed chronic symptoms with a fistula or oozing wound. Eleven PHJIs with acute onset of symptoms showed an oozing wound without pain.

35% (30 PHJI) were early infections, 26% (22 PHJI) delayed and 39% (33 PHJI) late. In 47% of the patients the symptom duration was shorter than three weeks and was therefore classified as acute. 53% were classified as a chronic infection.

Radiographically, signs of loosening were seen in 28 patients. Sixteen being late infections (57%) and twelve being delayed (43%). None of the early infections showed radiographic signs of loosening.

The pathogenic distribution is presented in table I. S. aureus and coagulase negative staphylococcus were the most common pathogens, followed by polymicrobial infections.

The patients received prophylactic antibiotics according to interdisciplinary recommendations until the microorganisms could be identified. The mean duration of antibiotic treatment was 35 days (6-199 days) intravenously and 98 days (0-180 days) orally.

After arrival at our Institution the median delay before operation was 1.2 days (range 0-12 days) for the acute infections.

The primary operations performed were an irrigation and debridement with exchange of mobile parts (I&D) in 45% (38 PHJI), a two-stage exchange in 36% (31 PHJI), a one-stage exchange in 12% (10 PHJI), and a permanent explantation in 7% (6 PHJI).

The initial operative strategy had to be changed in 11 cases based on intraoperative/postoperative findings. In four cases the strategy had to be changed postoperatively, i.e. after the first operation, due to

Table I. — Pathogenic distribution

S.aureus, n (%)	22 (25.9%)
Coagulase neg. staphylococcus, n (%)	18 (21.1%)
Streptococcus, n (%)	5 (5.9%)
Enterococcus, n (%)	3 (3.5%)
Gram-negative Bacilli, n (%)	6 (7.1%)
Propioni species, n (%)	10 (11.8%)
Multi-resistant germ, n (%)	6 (7.1%)
Polymicrobial infections, n (%)	15 (17.6%)

detection of multiresistant bacteria cultured from the intraoperative biopsies. In five cases due to an extended abscess formation into the deep tissues. In two cases the prosthesis was explanted and a two stage exchange was done to address loosening.

A cement spacer was used in 11% of the two-stage operations. The median interval between explantation and re-implantation when performing a two-stage exchange was 6.6 weeks (range 2.3-61.6 weeks). The mean number of revisions after removing the implant was 1.6 (range 0-3).

Totally, 22 patients with 22 PHJI were treated (1-5 operations) in other hospitals due to their infection prior to referral to our institution.

RESULTS

An overview of our results is presented in Figure 1. It shows whether the indication for an intervention was based on the Zimmerli criteria or not, and whether the treatment was successful or a failure. The table also shows the further treatment in cases of persistent infection (Figure 1). The overall success rate, defined as no clinical or radiographic signs of infection after at least 1 year, was 88% (75/85).

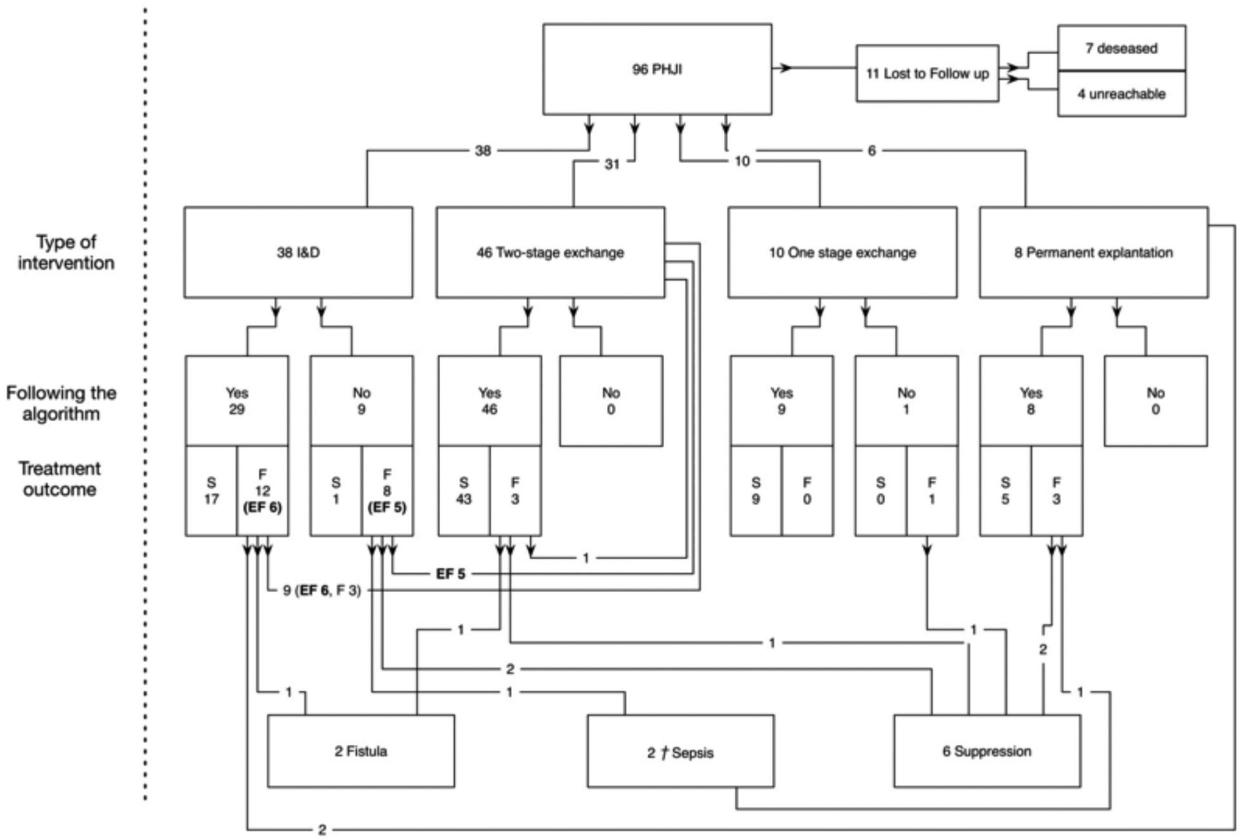
In 12% (10/85) of the cases the chosen operative strategy did not follow the Zimmerli algorithm. Of these only one was successfully treated with the primary intended operation. This was statistically significant ($p < 0.05$)

In 38 cases we performed an I&D. Eleven out of 38 were intraoperatively or retrospectively defined as EF according to the algorithm, leaving a total of 27 cases to evaluate in this group. The EF were further treated and evaluated in the two-stage exchange group.

In the cases where the algorithm was followed, infections were successfully treated in 74% (17/23) of cases. The ones not in line with the criteria showed poorer results with a success rate of only 25% (1/4) ($p=0.055$). The success rate for the group I&D is therefore 67% (18/27).

Table II. — Overview of outcome according to different parameters

	Success rate	
Infection type		
Early	27/30 (90%)	
Delayed	19/22 (86%)	
Late	30/33 (91%)	
	Success rate following criteria	**Success rate not following criteria**
Type of therapy		
I&D	17/23 (74%)	1/4 (25%)
One-stage exchange	9/9 (100%)	0/1 (0%)
Two-stage exchange	43/46 (94%)	0/0
Permanent explantation	5/8 (63%)	0/0



PHJI: Periprosthetic hip joint infection

I&D: Irrigation, debridement and exchange of mobile parts

S: Success

F: Failure

EF: expected failures (difficult to treat bacteria, sinus tract, extended abscess formation, loosening),

Fig. 1. — An overview of treatment and outcome. The diagram shows whether the indication for an intervention adhered to the algorithm or not and whether the treatment was successful or a failure. If the treatment failed, the further treatment strategy is shown. The table also shows the treatment/outcome in cases of persistent infection.

31 Patients were primarily included in the two-stage exchange group. 15 PHJI were additionally included due to expected failures or failures from the I&D group. All patients in this group were treated according to the Zimmerli algorithm. The overall success rate was 94% (43/46). Due to persistent infection one patient had to undergo a second two-stage exchange operation that was then successful. Two patients refused further treatment. One patient was given antibiotic suppression therapy and the other developed a fistula.

A one-stage exchange was performed in 10 cases. One patient in this group was not treated according to the Zimmerli criteria, because he refused to undergo a two-stage exchange. In this patient a one-stage exchange was done to lower the bacterial load and afterwards antibiotic suppression therapy was started.

Permanent removal of the device was done primarily in 6 cases and in two cases after a failed I&D. This was due to poor general condition, a complicated infection situation with multiresistant bacteria and no functional improvement with a prosthesis.

The overall success rate in the permanent explantation group was 63% (5/8). However, this group obviously represents a negative selection. (Table II)

Initially ten PHJI (12%) were not treated according to the algorithm as proposed by Zimmerli. Of these ten cases nine showed initial treatment failure.

Nine were incorrectly treated with I&D.

Of these only one was successfully treated. 5/8 were later successfully treated by a two stage revision. Of these five three should have been explanted initially due to abscess formation. One delayed acute infection was incorrectly treated at the onset with an I&D. The inappropriate treatments were performed by a surgeon who lacked the experience and skills to perform the proper treatment. One patient was just debrided initially because the right mobile parts were not available.

3/8 ended up as failures. One of these patients was considered inoperable in terms of a two-stage revision due to advanced tumour disease and poor general health. Two patients refused to undergo the recommended treatment and were therefore treated with an I&D as a minimal operative therapy. Finally, these two received a suppression therapy and one died due to infection-related sepsis.

One patient that was included in the one-stage exchange group did not follow the recommendations but refused additional surgery in the sense of a two-stage exchange. Therefore, the only option for this patient was antibiotic suppression therapy. (Figure 1)

DISCUSSION

PHJI remains a major challenge to the orthopaedic community. In this study we evaluated the treatment of a large number of PHJI treated at our hospital within a 5 year period. We analysed our treatments and outcomes with reference to the treatment algorithm presented by Zimmerli et al. *(32)*.

This study confirms that an interdisciplinary treatment algorithm yields predictable success in the treatment of PHJI. We found that by using the evaluated Zimmerli algorithm, better results could be achieved within one year of follow up compared to other treatment strategies.

The overall success rate differs between the surgical treatments performed. However, our results show that good results can be achieved for all surgical interventions. The two-stage revision, being the most cumbersome and time-consuming intervention, is a reliable strategy with an overall success rate of 94%. This result can be compared with reports in the literature, for example, Giulieri et al. *(12)* and Trampuz et al. who report a success rate of 90% *(27)* and Wimmer et al. of 78.3 % *(29)* for the two-stage revision. However, we think that less invasive techniques like one stage exchange or I&D can also produce a predictably good outcome if the indication for the procedure is carefully selected.

In our study the one-stage exchange operations showed a success rate of 100%, which is in line with the 94% described by Giulieri et al. *(12)*. We attribute this high success rate to appropriately selected patients with a microorganism sensitive to antibiotics that have good bioavailability.

As suggested by Berbari et al. *(2)* the most important variable that affects the outcome seems to be the type of surgical modality. In our study we showed the importance of following the Zimmerli algorithm when choosing the most appropriate surgical technique.

The least invasive operative technique is I&D and retention of the implant. This method is the most controversial, because of reported variable outcome. The success rate was 74% when treated with I&D in accordance with the Zimmerli algorithm compared with 25% for cases that did not follow the criteria. These results correspond with the increase of success rates from 40% to 60% as described by Betsch et al. *(3)* and of 62% to 88% in the study by Giulieri et al. *(12)*. Therefore, patient selection is critical for this procedure. Furthermore, intra- and postoperative findings may require a change in treatment strategy, e.g. difficult to treat bacteria or extensive abscess formation. The International Consensus Meeting on Periprosthetic Joint Infection 2013 concluded that I&D is an option for early periprosthetic PHJI, but that the available algorithm and classifications are inadequate in guiding a surgeon in selecting the appropriate surgical intervention for management of early PHJI *(19)*.

Our findings support the use of a standardized algorithm as proposed by Zimmerli et al. *(32)*. We found that patients that were treated according to the algorithm showed better outcomes after PHJI treatment. According to our results the algorithm can be used in an unselected population in everyday clinical practice with a predictably high success rate (Figure 1).

We think that all procedures have their indications but the timing of intervention and proper patient selection is of paramount importance. In particular, outcomes after irrigation and debridement, exchange of mobile parts and retention of the prosthesis have been reported to vary widely. Success rates varying from 0% to 80% have been reported *(1,7)*. However, the criteria for performing debridement and retention also vary widely and low success rates can be attributed partly to inadequate patient selection (e.g. patients with chronic infections or patients that refuse to undergo a more invasive procedure). Unfortunately, many reports lack detailed information on whether an exchange of mobile parts (femoral heads and acetabular inserts) was performed or not. Furthermore, Zimmerli et al. did not include this in their algorithm. However, Choi et. al identified non-exchange of the polyethylene as an independent risk factor for failure of retention treatment of an infected knee prosthesis, therefore, we think all mobile parts should be exchanged routinely *(6)*. The International Consensus Meeting on Periprosthetic Joint Infection 2013 concluded that removable modular components should be exchanged whenever possible *(19)*.

Extending the indication for I&D beyond the one proposed in the algorithm may lead to higher treatment failure rates.

One strength of this study is that we chose to focus solely on prosthetic hip joint infections. Many studies on this subject compared prosthetic joint infections as a uniform group but not only in one anatomical region *(3,15,29)*.

The follow up time of this study was on average 24.6 months (12-60 months), which is comparable to other studies, and our results and definition of success are likewise comparable to other studies *(3,12,29)*. Again, it is worth emphasizing the complexity of this problem and heterogeneity of the patient sample.

The definition of a prosthetic infection is not consistent in current literature; therefore, a direct comparison between different studies is difficult. We chose to use the definition published in the proceedings of the international consensus meeting on periprosthetic joint infections *(19)* since 85% of all the participants (400 delegates from 52 countries) considered this definition as the most reliable. We found this definition easy to transfer into clinical practice.

The microbiological spectrum was very similar to that presented by others *(3,12,15,27–29)*. Selecting the correct antibiotic therapy is paramount in the treatment of prosthetic revision surgery *(8,17,32)*. The mean duration of antibiotic treatment in our study (35 days intravenously and 98 days orally) is in accordance with the treatment times proposed in the literature *(17)*. The type of antibiotic therapy and treatment duration for our patients were decided through interdisciplinary discussions between the orthopaedic surgeon, infectious disease specialists and internists, following current guidelines *(11,17,21,24,26,33)*.

There are limitations to the proposed algorithm, as it is not always easy to follow at the time of initial decision making: Zimmerli and colleagues describe *(32)* conditions which call for a two-stage exchange operation, e.g. extended abscess formation, difficult to treat bacteria, an existing sinus tract or prosthetic loosening. These conditions are not always possible to diagnose before the operation and are therefore possibly misclassified. Thus, the initial plan and treatment decision may have to be changed intra- or postoperatively to achieve a good outcome. Therefore, it is imperative to be able to adjust the diagnosis at any time during the course of treatment, even intraoperatively. In this study we introduced the term "expected failure" (EF) for these conditions. The evolution of these cases is presented in figure 1. The operating surgeon should be aware of this problem and be prepared to change treatment strategy.

We recognise that our study has limitations. For ethical and moral reasons the study had to be performed retrospectively, and we could not compare the outcome of the various treatment regimens in a randomized fashion. This limits and lowers the evidence level.

The minimum follow up might be regarded as a limitation of the study. We defined success as no clinical or radiological signs of infection at follow-up >1year. This might be too short in terms of detecting a low virulence microorganism, such as propioni bacteria that may manifest symptoms at a later time point, however, even two or three years might be too short to detect these.

Our study includes a high number of PHJIs treated in one hospital. To increase the evidence level an even higher number of patients would be required. This might perhaps be possible in a multicentre study. Such a study will encounter the same problems of patient inhomogeneity and the difficulty of comparing this complex problem. In addition, there would probably be greater surgeon dependent bias, for example, when it comes to selecting the surgical intervention.

In conclusion, we find that the treatment algorithm as proposed by Zimmerli and colleagues is a useful tool that is easy to translate into clinical practice. When followed it yields a high success rate. The PHJIs not treated according to the algorithm showed a significantly higher failure rate followed by additional operations.

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