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Research Paper

Complications after spacer implantation in the treatment of hip joint infections

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Abstract

The aim of this retrospective study was to identify and evaluate complications after hip spacer implantation other than reinfection and/or infection persistence.

Between 1999 and 2008, 88 hip spacer implantations in 82 patients have been performed. There were 43 male and 39 female patients at a mean age of 70 [43 – 89] years. The mean spacer implantation time was 90 [14-1460] days. The mean follow-up was 54 [7-96] months. The most common identified organisms were S. aureus and S. epidermidis. In most cases, the spacers were impregnated with 1 g gentamicin and 4 g vancomycin / 80 g bone cement.

The overall complication rate was 58.5 % (48/82 cases). A spacer dislocation occurred in 15 cases (17 %). Spacer fractures could be noticed in 9 cases (10.2 %). Femoral fractures occurred in 12 cases (13.6 %). After prosthesis reimplantation, 16 patients suffered from a prosthesis dislocation (23 %). 2 patients (2.4 %) showed allergic reactions against the intravenous antibiotic therapy. An acute renal failure occurred in 5 cases (6 %). No cases of hepatic failure or ototoxicity could be observed in our collective. General complications (consisting mostly of draining sinus, pneumonia, cardiopulmonary decompensation, lower urinary tract infections) occurred in 38 patients (46.3 %).

Despite the retrospective study design and the limited possibility of interpreting these findings and their causes, this rate indicates that patients suffering from late hip joint infections and being treated with a two-stage protocol are prone to having complications. Orthopaedic surgeons should be aware of these complications and their treatment options and focus on the early diagnosis for prevention of further complications. Between stages, an interdisciplinary cooperation with other facilities (internal medicine, microbiologists) should be aimed for patients with several comorbidities for optimizing their general medical condition.

Key words: hip joint infection, hip spacers, spacer dislocation, prosthesis dislocation

Introduction

Antibiotic-loaded cement spacers have become a popular procedure in the treatment of hip joint infections over the past two decades. Depending on the definition of infection eradication and reinfection, hip spacers have reportedly a success rate of > 90 % [1].

Although hip spacers are established as an adequate treatment option in the management of these infections, several complications might occur between stages and, hence, endanger the functional outcome. Besides a reinfection and/or infection persistence, mechanical complications, such as spacer fracture, spacer dislocation, and femoral fracture, or systemic side effects (renal or hepatic failure, allergic reactions) might lead to prolonged treatment courses between

stages. These complications are certainly rare and the exact incidence of the above mentioned complications, respectively, is still unknown. Moreover, it is unclear whether a higher incidence of complications between stages might be associated with a higher incidence of mechanical complications after the prosthesis reimplantation at the site of a hip spacer implantation.

Hence, the aim of the present retrospective study was to register and define complications after hip spacer implantation and prosthesis reimplantation, respectively, in the treatment of late hip joint infections. Specific attention was paid to the aforementioned mechanical complications, systemic side effects as well as general complications.

Patient – Methods

All patients' records that have been treated by hip spacer implantation in our institution between 01.01.1999 and 30.06.2008 have been retrospectively evaluated regarding following parameters: primary surgical indication, causative pathogen organism, time between infection manifestation and spacer implantation, duration of spacer implantation, spacer articulation, impregnation of bone cement, systemic antibiotics, and implant type at reimplantation. Moreover, mechanical complications (spacer dislocation, spacer fracture, femoral fracture, prosthesis dislocation after reimplantation) and systemic side effects (renal and hepatic failure, respectively, allergic reactions, ototoxicity) as well as general postoperative complications were also documented. Only patients with a sufficient documentation regarding all above mentioned parameters were included in the study.

From the initially 101 identified patients, 19 patients were excluded due to insufficient documentation. From the remaining 82 patients, there were 43 male and 39 female patients at a mean age of 70 [43 – 89] years. According to the McPherson classification [20], 15 patients were categorized as IIIA1, 4 as IIIA2, 1 as IIIA3, 25 as IIIB1, 9 as IIIB2, 17 as IIIC1, 10 as IIIC2, and 1 as IIIC3.

The most common primary surgery was a primary total hip arthroplasty followed by bacterial coxitis. Data about primary surgical procedures is summarized in Table 1.

There were 60 mono-, 12 bi-, and 3 polymicrobial infections. In 7 cases no causative pathogen organism could be identified, however, the histopathological findings revealed in all cases signs of osteomyelitis, respectively. The most common identified organism was Staphylococcus aureus followed by Staphylococcus epidermidis (Table 2).

Table 1: Primary surgical indications and antibiotic impregnation of the bone cement at the site of spacer implantation in the treatment of hip joint infections.

Primary surgery	n=	Antibiotic impregnation of hip spacer (/80 g bone cement)	n=
primary THA	45	1 g Gentamicin + 4 g Vancomycin	77
bacterial coxitis	15	1 g Gentamicin + 0.8 g Teicoplanin	8
aseptic cup loosening	8	1 g Gentamicin + 4 g Cefotaxim	2
osteosynthesis for femoral neck fracture	5	1 g Gentamicin + 2 g Clindamycin	1
aseptic stem loosening	3		
dual head prosthesis	3		
osteosynthesis for intertrochanteric fracture	1		
septic femoral head necrosis	1		
resection of heterotopic ossifications	1		

THA: total hip arthroplasty

Table 2: Pathogen organisms in late hip joint infections.

Organism	n=
S. aureus	25
S. epidermidis	25
E. faecalis	8
MRSA	8
E. coli	6
ß-hem. Streptococci	5
Ps. aeruginosa	3
C. albicans	3
a-hem. Streptococci	2
K. pneumoniae	2
S. capitis	1
S. haemolyticus	1
S. hominis	1
S. agalactiae	1
E. faecium	1
P. mirabilis	1
Str. auginosus	1
Bacillus sp.	1
Streptococci sp.	1
Peptostreptococci sp.	1
gram+ cocci	1
(no further specification)	

MRSA: methicillin-resistant S. aureus

Antibiotics were administered in all cases after consultation with our Microbiologic Institute. The most common combination used was vancomycin and rifampicin followed by clindamycin and flucloxacillin (data not shown in a table). If no bacterium could be isolated, a broad spectrum antibiosis (flucloxacillin and clindamycin) was prescribed. If the general medical condition allowed for it and no antibiotic-related complications occured, antibiotics were given intravenous for the first 4 weeks followed by oral antibiotics for another two weeks.

In these 82 patients, 88 spacer implantations have been performed (in 5 patients spacer exchange,

in one case bilaterally). The time between infection manifestation and spacer implantation was meanly 6 [1-108] weeks. All infections were late infections except for the cases suffering from a bacterial coxitis. The mean spacer implantation time was 90 [14-1460] days. The mean follow-up of these 82 patients was 54 [7-96] months.

All patients have been treated by the same one-size custom-made spacer. The spacer has been intraoperatively produced by means of a two-parted mould. The mould consists of polyoxymethylene (POM). In all cases Refobacin – Palacos (0.5 g gentamicin/ 40 g cement) has been used due to its superior elution characteristics compared with other bone cements [1]. For the spacer production 80 g of polymethylmethacrylate (PMMA) are required. Depending on the causative pathogen organism and its sensitivity profile the bone cement was optionally loaded with a second antibiotic. In cases of a preoperative unidentified bacterium or if the infection was revealed during the operation for presumed aseptic conditions, the combination of 1 g gentamicin/ 4 g vancomycin/ 80 g PMMA was routinely used. Each spacer has a head diameter of 50 mm, a stem length of 10 cm, and a total surface area of 13300 mm² [3].

In case of acetabular defects a special mould is also available. The acetabular component has an inside/outside diameter of 53/ 56 mm and a total surface area of 4410 mm² [3].

From the 88 spacers implanted, 82 acted as a hemiarthroplasty, whereas only in 6 cases a spacer cup has been implanted. In 70 cases a "normal" spacer has been implanted, whereas in the remaining 18 cases a spacer head has been placed onto the in situ remained femoral stem. In the latter cases, there was either an isolated septic cup loosening at no stem infection as primary indication, or due to the type of implant primarily used or due to the femoral bone quality (associated with a higher risk of femoral fracture) we decided not to remove the femoral stem.

For loading of the bone cement, the combination of gentamicin and vancomycin was most frequently used followed by the combination of gentamicin and teicoplanin. Data about the antibiotic impregnation of hip spacers is summarized in Table 1.

After six weeks of antibiotic treatment, the antibiotics were paused and the serum C-reactive protein (CRP) checked. If its level had returned to normal, two weeks later another CRP-control was performed. If also normal, the second stage was planned if the wound had healed and the general medical condition of the patient allowed for it.

A total prosthesis reimplantation was performed in 63 cases. In 24 cases cementless components have been reimplanted, in 20 cases hybrid, in 10 cemented, and in 9 patients reverse hybrid. In one case, the prosthesis reimplantation was performed elsewhere. In 12 cases, only a cup reimplantation was performed ("spacer head" group). 5 patients passed away between stages, whereas in 7 cases the spacer remained in situ because either the patient was not willing to undergo further surgery or because the comorbidities of the patient did not allow the prosthesis reimplantation.

Results

Mechanical complications

A spacer dislocation occurred in 15 cases (17 %). From these 15 cases, 12 patients have been treated conservatively by reduction and immobilization in a hip orthesis (Newport orthesis, Fa. Ormed, Freiburg, Germany) during the remaining time between stages. The other three cases underwent further surgical procedures; in one case (combined spacer dislocation and -fracture), the spacer had been exchanged, whereas the other two cases had been treated by resection arthroplasty after recurrent spacer dislocations and unsuccessful conservative treatment.

Spacer fractures could be noticed in 9 cases (10.2 %). 7 of them were localized in the distal part of the spacer stem and were asymptomatic. The other two cases were spacer-neck fractures and had been treated by subsequent spacer exchange.

In one case a spacer protrusion was evident over time and the patient was advised to put no weight bearing on the leg.

Femoral fractures occurred in 12 cases (13.6 %). 5 out of these 12 cases occurred at the first stage and were treated by implantation of an antibiotic-coated femoral nail and spacer implantation on top. Four cases with a femoral scissure, respectively, were managed by minimal weight-bearing of the particular extremity. One case suffering from an avulsion of the minor trochanter was treated by cerclage refixation. After prosthesis reimplantation, one patient suffered from a periprosthetic fracture which was treated with a plate osteosynthesis. One patient had a fracture beneath the spacer stem and was treated by implantation of an antibiotic-coated prosthesis stem and placement of a spacer head onto the stem.

After prosthesis reimplantation, 16 patients suffered from a prosthesis dislocation (23 %). 12 cases could be successfully managed by reduction and immobilization in a hip orthesis for the following 12 weeks. The other 4 cases had recurrent dislocations and were managed by acetabular socket explantation and implantation of a constrained cup (Fa. Waldemar

Link, Hamburg, Germany), respectively.

Systemic side effects

2 patients (2.4 %) showed allergic reactions (rash and pruritus) against the intravenous antibiotics administered (in both cases combination of clindamycin and flucloxacillin). The symptoms were resolved after adjustment of the antibiotic therapy.

An acute renal failure occurred in 5 cases (6 %). 2 patients could be successfully treated conservatively, whereas 2 patients had to be treated by renal dialysis. One patient suffering from multiple myeloma passed away after renal failure and cardiopulmonary decompensation. Unfortunately, the retrospective evaluation of the patients' records did not allow any differentiation of the particular cause of the renal failure, respectively (antibiotic-impregnation of the spacer, systemic antibiotics, other medication).

No cases of hepatic failure or ototoxicity could be observed in our collective.

General complications

General complications (other than the aforementioned ones) occurred in 38 patients (46.3 %).

4 patients had a draining sinus after the first stage and 6 after the second stage, respectively. Of these 10 cases, 2 resolved after local treatment, whereas the other 8 have been treated by revision, haematoma removal and pulsatile lavage. None of these patients had a reinfection or infection persistence during follow-up.

6 patients suffered from a pneumonia which could be treated successfully with antibiotics in all cases.

In 5 cases after spacer implantation and in 2 cases after prosthesis reimplantation a cardiopulmonary decompensation emerged which could be successfully managed by adjustment of the cardiac medication and fluid restriction, respectively.

One patient denied a prosthesis reimplantation. In this case, the patient started to increase weight-bearing on the leg 3 months after spacer implantation. 13 months later, X-rays revealed an asymptomatic acetabular fracture without any spacer dislocation. At a follow-up of 52 months the patient is still free of any infection signs and has no complaints at an almost free range of motion.

4 patients developed postoperatively a transitory psychotic syndrome which regressed over the first 2 weeks, respectively.

3 patients had an antibiotic-associated colitis by Clostridum difficile and have been orally treated with vancomycin. Also 3 patients had a central venous catheter – associated sepsis. A thrombosis, epileptic seizures, and lower urinary tract infections could be noticed in 2 cases, respectively. A pleura empyema, a heparin-induced thrombocytopenia (HIT), a case of pelviperitonitis with bladder necrosis and subsequent surgical intervention, a cholecystitis with subsequent cholecystectomy, a myocardial infarction, and an infarction of the A. cerebri media could be observed in one case, respectively.

2 patients passed away after the first stage and 2 after the second stage due to cardiopulmonary decompensation, respectively. As already mentioned, one patient suffering from multiple myeloma passed away after renal failure and cardiopulmonary decompensation.

The overall complication rate was 58.5 % (48/82 cases).

Discussion

A reinfection and/or infection persistence are the most feared complications after hip spacer implantation because they can be both associated with subsequent surgical revisions and higher morbidity and mortality rates, respectively. However, several other complications might also occur during a two-stage treatment protocol for late hip joint infections which can also lead to prolonged treatment courses and endanger the functional outcome. Although these complications are frequently not mentioned or insufficiently documented in the literature, they are surely of no minor value compared with an infection persistence or reinfections.

Mechanical complications

Mechanical complications belong certainly to the most important complications after hip spacer implantation because they are often associated with subsequent surgical interventions and may impair the functional outcome.

The exact incidence of mechanical complications is unknown. Hereby, several parameters might play a role: the spacer's production (hand-made vs. standardized), the spacer's geometry, the head/neck ratio, acetabular and/or femoral defects, mismatch of spacer's head size to the acetabulum size, the art of femoral fixation, muscular insufficiency, prior surgical revisions, poor bone quality, and incompliance of the patient with regard to partial weight bearing.

A review of the literature about hip spacers showed a tendency that hand-made spacers might dislocate more often than standardized-made ones [1]. However, a significant difference could not be assessed due to inhomogenities of the patients' collectives and insufficient documentation regarding the spacer production and fixation, respectively.

Leunig et al. [18] were one of the first who tried

to interpret and explain these findings. The authors have recognized that the geometrical form of the spacer plays an important role. In spacers which were free of complications, the neck to head-ratio was significantly lower (0.76±0.05) than in those with dislocations (0.96±0.19). A second factor associated with failure was an insufficient deep anchorage in the intramedullary canal, being 22±33 mm in the failure group, while complication-free spacers were on average attached to a depth of 57±41 mm.

Regarding the femoral fixation of hip spacers, there exist to our knowledge 3 methods: i) press-fit, ii) partially or totally cementation, and iii) the "glove" – technique [3]. The latter technique has been recently described and provides a stable fixation onto the proximal femur at facilitating the spacer's explantation since the spacer can be removed at one piece and there is no need for removal of any cement debris compared with other normal cementation techniques. However, it is unclear, which of the above mentioned techniques is the most superior one in the prevention of spacers' dislocations regarding the femoral part.

In the literature, the dislocation rates after hip spacer implantation may strongly vary depending on the art of the spacer's production as well as the fixation method. Leunig et al. [18] reported dislocations of the hip in 5 of 12 patients after use of hand-formed spacers, whereas Magnan et al. [19] and Duncan et al. [9] could notice a rate of 1/10 and 3/13 dislocations after implantation of a standardized hip spacer, respectively. On the other hand, Ries and Jergesen [26], Koo et al. [16], Shin et al. [30] and Takahira et al. [33] could not observe any dislocation during implantation of standardized spacers, respectively.

In our collective we could notice a spacer dislocation rate of 17 %. This rate might appear high, however, this is the rate of a 10-year collective. Over the years we have gained experience with this treatment option, and advances in the surgical technique, instruments and fixation method have led to a reduced rate over the last years. We have also made the experience that careful education of the patients by our physiotherapists with regard to walking attitude, partial weight bearing and joint motion is very important in the prevention of dislocations. Certainly, a disadvantage of our treatment protocol is the one-size spacer which has been implanted in all cases. Perhaps, if we have had several moulds for spacer production and each case would have been treated by a more "anatomical" spacer, the dislocation rate might have been lower.

The rate of spacer fractures in our series was approximately 10 %. Interestingly, the majority of the cases had no symptoms at all and only in 2 cases the spacer had to be exchanged in an additional surgery. For prevention of a spacer fracture, the surgeon may consider inserting a metallic endoskeleton into the spacer; however, literature data are scarce about this topic. Schöllner et al. investigated in vitro the mechanical properties of gentamicin-loaded hip spacers after insertion of Kirschner wires [31]. Stress experiments showed an average failure load of 1.6 kN. The insertion of the K-wires prevented any dislocation of the spacer fragments, but did not significantly improve the mechanical properties. Kummer et al. compared in vitro the mechanical properties of commercially available hip spacers containing a substantial stainless steel central core with experimental spacers containing Steinmann pins, intramedullary nails with two lag screws and Charnley prostheses, respectively [17]. The authors reported that all constructs based upon the Charnley prostheses and the commercial spacers did not fail at 3000 N; the other two constructs failed at significant lower loads (pins at 832 N and nails at 1275 N, respectively). Thielen et al. investigated in vitro the mechanical stability of reinforced hip spacers (either a rod pin with a 5 mm diameter or a "full-stem" endoskeleton; both consisting of titanium grade two) compared with non-reinforced spacers [34]. At cycling testing, non-reinforced spacers failed at 400-600 N, whereas rod-reinforced spacers failed at 1000-1300 N. "Full-stem" reinforced spacers failed at 2380-4311 N, depending on the thickness of endoskeleton used (6/8/10 mm). To our knowledge, there are no clinical data available that have demonstrated that the insertion of a metallic endoskeleton significantly improves the mechanical properties of hip spacers or reduces the rate of mechanical complications.

Moreover, it is still unclear whether the insertion of a metallic endoskeleton has a negative influence on the pharmacokinetic properties of the spacer. Experimental data have shown that the release of commercially-impregnated antibiotics from hip spacers is significantly increased in the presence of an endoskeleton, whereas the elution of additional, incorporated antibiotics is decreased [2]. Until this question is answered, we recommend that metallic endoskeletons should not be routinely inserted into hip spacers in clinical practise, but only in exceptional cases for patients with a higher fracture risk (poor patient compliance, high Body-Mass-Index, poor bone quality or osteoporosis).

Femoral fractures occurred in 12 cases (13.6 %) in our series. Hereby, a differentiation should be made between those at the first stage, between stages, and after prosthesis reimplantation, respectively. Moreover, not every fracture has to be surgically treated, as

seen in our collective. Some predisposing factors which might lead to a femoral fracture include osteoporosis, poor bone quality due to prior surgeries or bone defects resulting after the prosthesis explantation. In these cases the orthopaedic surgeon should plan the first and second stage taking into consideration the possibility of a bone fracture and reconstructive strategies regarding both infection eradication and fracture treatment.

The etiology of dislocations after total hip arthroplasty is often multifactorial. In their review work, Pulido et al. identified female gender, older patients, neurological dysfunction or cognitive impairment, and a preoperative diagnosis of osteonecrosis of the femoral head, femoral neck fracture and/or inflammatory arthritis as patient risk factors for early dislocation after primary THA [24]. The presumed etiological factors for late instability include long standing malpositioning of the components, trauma, deterioration in muscle, mass, neurological status impairment and polyethylene wear [24].

The postoperative dislocation rate following reimplantation after two-stage treatment protocols has been reported to range from 6 to 18 % [6, 12]. In their study, Hsieh et al. reported a dislocation rate of 14.3 % in patients treated by resection arthroplasty compared to 1.8 % in patients treated by insertion of an antibiotic-loaded hip spacer at a mean follow-up of 4.9 years [6]. Hartmann and Garvin reported a 14.7 % dislocation rate in patients having prosthesis reimplantation after infection compared with 1.7 % in patients having revision for aseptic failure [11]. Fehring et al observed a 25% dislocation rate in 56 hips despite adequate soft tissue tension and appropriately placed prosthetic components [10]. The authors tried to interpret these findings, but found no statistical differences between dislocators and nondislocators regarding head size, acetabular component size, neck length, liner design, time between stages, abduction angle of the acetabular component and leg length discrepancy, respectively. Fehring and colleagues supposed that this high rate might have been related to the use of nonarticulating spacers and the use of articulating spacers might have had an effect on these results.

Despite the assumption of Fehring and colleagues, we could observe in our collective a prosthesis dislocation in 23 % of the cases. We believe that this high dislocation rate after prosthesis reimplantation can be explained by following thesis: every surgical procedure causes trauma to the local tissues, leading to muscle and bone loss. Proper debridement of the infected hip requires often debridement of bone. Bone loss makes proper component position difficult, leading to potential malposition and increasing the risk of instability. Multiple surgical revisions also increase the risk of developing abductor dysfunction. As the abductors become less functional, their important role in hip stability is lost. We believe this is a very important topic, and patients undergoing a two-stage protocol in the treatment of hip joint infection should be preoperatively informed about it, especially those having already undergone surgical revisions for infection management. Perhaps, it would be advisable to use constrained acetabular components in these cases.

Hip joint instability after two-stage treatment is still a major problem. Fehring et al. estimated that approximately 400 patients would be needed for the standard power value of 80% for the aforementioned statistical differences [10]. Such a number is difficult to achieve in a single-center study, however, in a multicenter study other factors, such as surgeon-related parameters (experience, surgical technique, instruments) may influence the outcome.

Systemic side effects

Antibiotic-loaded beads and spacers can locally release high antibiotic concentrations which vastly exceed those after systemic administration with no or low systemic toxicity. Salvati et al. have investigated urine and serum samples after implantation of gentamicin-loaded cement and beads in 38 and 18 patients, respectively, and could observe no toxic effects in these patients at very low gentamicin levels [28]. Springer et al. could also not observe any toxic effects even after a very high impregnation of knee spacers with antibiotics (average 3 g vancomycin + 3.6 g gentamicin / 40 g PMMA) in 34 patients and concluded that drug delivery device with a high antibiotic/cement-ratio should be regarded safe for clinical use [32].

Despite these reports, an increasing number of cases have been published regarding systemic side effects after use of bone cement drug delivery systems in the past years. Van Raaij et al. reported the case of an 83 year old woman with no history of kidney disease who developed acute renal failure (ARF) after resection of an infected total knee arthroplasty and placement of a gentamicin-impregnated cement spacer (2 g gentamicin / 40 g PMMA) and 7 chains of 30 gentamicin beads (0.945 g gentamicin) [35]. Serum gentamicin levels indicated high concentrations that prompted removal of the spacer and subsequent return of normal renal function. Patrick et al. reported two similar cases of ARF in an 82 year old female and a 79 year old male patient, 5 months and 6 weeks after implantation of a vancomycin-tobramycin-loaded hip

spacer, respectively [23]. In both cases the serum tobramycin concentration was elevated, but after spacer explantation serum creatinine and antibiotic concentrations returned to within normal limits, respectively. Similar cases have also been described by Curtis et al. [7] and Dovas et al. [8] after use of tobramycin- and gentamicin-vancomycin-impregnated spacers at the site of infected total knee arthroplasties, respectively.

Koo et al. reported 2 cases of hepatic failure and 2 cases of bone marrow depression, respectively, after hip spacer implantation (1 g gentamicin + 1 g vancomycin + 1 g cefotaxime / 40 g PMMA) out of 22 cases [16]. The authors stated that the side effects were resolved after temporary withdrawal of the systemic antibiotics, however, it is unknown which systemic antibiotics have been used in each case. Isiklar et al. found one case of ARF out of 10 patients after implantation of a vancomycin-loaded hip spacer (2-3 g vancomycin / 40 g PMMA) and intravenous administration of the same antibiotic [14]. Cabrita et al. observed 1 case of renal failure and 3 cases of allergic reactions out of 33 cases of hip spacer implantation (1 g tobramycin + 1 g vancomycin / 40 g PMMA) [5]. Unfortunately, no further details are available about the systemic antibiotics used in the particular cases nor the causes of the renal failure or of the allergic reactions, respectively.

In the latest evaluation of the PROSTALAC experience, Wentworth et al. reported one case of an allergic (dermatologic) reaction to vancomycin out of 135 cases of hip spacer implantation, whereas no patients had suffered from any renal or hepatic failure [36]. Also using the PROSTALAC system, Scharfenberger et al. reported one case of neutropenia after intravenous administration of vancomycin after hip spacer implantation in 28 patients, while no cases of renal of hepatic insufficiency could be observed [29].

Despite the abovementioned reports, several points remain unclear regarding to these phenomena. Sometimes, these observations are only mentioned in the particular articles, however, no further details about the exact cause are given so that only speculations can be made. In some cases, renal failure might be attributed to the local and systemic combination of the same or different antibiotic groups with nephrotoxic potential. Interestingly, it seems that the local combination of two potentially nephrotoxic antibiotic groups (aminoglycosides and glycopeptides) alone does not always induce any systemic side effects, but when combined with an intravenous antibiotic which also has a nephrotoxic potential, this acts as a trigger and that effect might occur. Whether these patients have a genetic predisposition towards such an antibiotic treatment and the occurrence of such complications is unknown. Moreover, it is unclear if the age of the patient plays a role in the emergence of ARF. In most cases elderly patients have suffered from such systemic side effects. Furthermore, no certain explanation exists why in some cases the aminoglycoside and in others the glycopeptide generates the nephrotoxic effect. The time of ARF manifestation might also vary strongly among the reported cases without having any precise explanation for this discrepancy.

Until the exact etiology of renal or hepatic failure is cleared, perhaps it would be advisable to avoid such combinations (highly antibiotic-loaded cement and systemic antibiotics of the same group) in risk (elderly) patients as long as this is in accordance with the antibiogram of the causative bacterium and does not endanger the infection sanitation. Careful and frequent monitoring of the laboratory parameters are indicated in the detection of antibiotic-induced bone marrow depression and assist to an early adjustment of the antibiotic therapy.

Our data confirm the rare emergence of these systemic side effects. An acute renal failure occurred in 6 % of the cases, whereas allergic reactions were seen in only 2 % of the cases. Our rates are in accordance with those of the literature, however, physicians should be also aware of these infrequent complications, since they might even result to death.

General complications

Patients suffering from late hip joint infections have usually several comorbidities. General complications, especially other infections (pneumonia, lower urinary tract infections) or cardiopulmonary decompensation, might lead to a further deterioration of the immunosuppressive status of the patient and either have a negative influence on the joint infection eradication process or extend the time between stages or both.

Patel et al. investigated factors associated with prolonged wound drainage after primary total hip arthroplasty [22]. The authors found that increased drain output, prophylaxis with low-molecular-weight heparin, and morbid obesity (body mass index > 40) were independent risk factors for prolonged wound drainage, and this in return was a significant predictor of wound infection. Each day of prolonged drainage was associated with a 42% increase in the risk of wound infection. Similar findings have been also reported by Saleh et al. and Knobben et al. [15, 27]. In our collective, we have had 10 cases with a draining sinus, of which 8 had surgical treatment. None of these patients had a reinfection or infection persistence. Hereby, we believe that the early surgical revi-

sion of the haematoma is an indispensable premise in the prevention of a wound infection.

Besides draining sinus, other infections during the two-stage protocol might endanger the treatment course. Irvine et al. found in a study of 274 patients who underwent total hip replacement that of the 5 patients with deep joint sepsis who had preoperative urinary tract infections, 3 had evidence of the same organism of both the urinary tract and the hip prosthesis [13]. Pulido et al. tried recently to identify predisposing factors for periprosthetic joint infections at the site of primary hip or knee arthroplasty [25]. Urinary tract infection was one of nine factors identified after multivariable logistic regression analysis. The authors proposed that if urinary infection is preoperatively confirmed, the patients should receive appropriate antibiotic therapy for infection eradication before proceeding with joint arthroplasty. Moreover, among the predisposing factors identified in this study was the development of postoperative atrial fibrillation and myocardial infarction. The authors suggested that a possible explanation might be that all patients with serious cardiac complications receive aggressive anticoagulation with heparin or similar agents, and use of aggressive anticoagulation has been reported as an independent risk factor for periprosthetic joint infections [21]. Another explanation might be that these complications occur in patients who generally are sicker and older with pre-existent medical conditions that would retard wound healing resulting in later infection.

The emergence of a pneumonia in patients suffering from late hip joint infections might also prolong the hospitalization stay and, hence, complicate the postoperative treatment course. Although organisms causing pneumonia are infrequently identified in joint infections, there exist reports about such cases at the site of hip surgery [4, 37].

Apparently, patients with late hip joint infections are a multimorbid collective. Since general complications occur at a high rate, as our study demonstrates, an interdisciplinary cooperation with other facilities, especially with the departments of internal medicine, microbiology and haemostasiology, is advisable for adequate treatment of these complications and reduction of morbidity and mortality rates, respectively.

Conclusion

Antibiotic-loaded cement spacers are an efficient method in the treatment of hip joint infections. However, during treatment several complications might occur that might endanger the infection eradication as well as the functional outcome after prosthesis reimplantation. Our data demonstrate that > 50 % of patients suffering from hip joint infections and treated with a two-stage protocol will have some kind of complications besides reinfection or infection persistence, mostly consisting of mechanical ones (spacer fracture, -dislocation, femoral fracture, prosthesis dislocations), systemic side effects (acute renal failure, allergic reactions), and general complications (draining sinus, pneumonia, etc.). Despite the retrospective design of our study and the limited possibility of interpreting these findings and their causes, this rate indicates that these patients are prone to have some kind of complication. Orthopedic surgeons should be aware of these complications and their treatment options and concentrate on the early diagnosis for prevention of further complications. Between stages, an interdisciplinary cooperation with other facilities (internal medicine, microbiologists) should be aimed for patients with several comorbidities for optimizing their general medical condition.

Conflict of Interest

The authors have declared that no conflict of interest exists.

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