Two-stage revision of implant-associated infections after total hip and knee arthroplasty

Zweizeitige Revision bei Implantat-assoziierter Infektion nach Hüft- und Knieendoprothesen

Abstract

Septic loosening of total hip and knee endoprostheses gains an increasing proportion of revision arthroplasties. Operative revisions of infected endoprostheses are mentally and physically wearing for the patient, challenging for the surgeon and a significant economic burden for healthcare systems. In cases of early infection within the first three weeks after implantation a one-stage revision with leaving the implant in place is widely accepted. The recommendations for the management of late infections vary by far. One-stage revisions as well as two-stage or multiple revision schedules have been reported to be successful in over 90% of all cases for certain patient collectives. But implant associated infection still remains a severe complication. Moreover, the management of late endoprosthetic infection requires specific logistics, sufficient and standardized treatment protocol, qualified manpower as well as an efficient quality management. With regard to the literature and experience of specialized orthopaedic surgeons from several university and regional hospitals we modified a commonly used treatment protocol for two-stage revision of infected total hip and knee endoprostheses. In addition to the achievement of maximum survival rate of the revision implants an optimisation of the functional outcome of the affected artificial joint is aimed for.

Keywords: total hip and knee arthroplasty, implant-associated infection, treatment protocol, spacer

Zusammenfassung

Bei Revisionseingriffen wächst der Anteil der Behandlung septisch be dingter Lockerungen von Hüft- und Knie-Endoprothesen. Für den Patienten stellt die Revisionsoperation infizierter Endoprothesen eine mentale und physische Belastung dar, für den Chirurgen sind sie eine Herausforderung und für das Gesundheitssystem eine beträchtliche wirtschaftliche Belastung. Bei der Frühinfektion innerhalb der ersten drei Wochen nach Implantation ist eine einzeitige Revision, bei der das Implantat im Körper verbleibt, weithin akzeptiert. Dagegen gehen die Empfehlungen für das Management von Spätinfekten deutlich auseinander. Sowohl bei einzeitigen als auch bei zwei- oder mehrzeitigen Implantatwechseln wird von Erfolgsraten von über 90% für bestimmte Patientengruppen berichtet. Dennoch zählen Implantat-assozierte Infektionen weiterhin zu den schweren Komplikationen. Zudem erfordert das Management von Spätinfekten eine besondere Logistik, angemessene und standardisierte Behandlungs vorgaben, qualifiziertes Personal sowie ein effizientes Qualitätsmanagement.

Basierend auf wissenschaftlichen Veröffentlichungen und den Erfahrungen spezialisierter orthopädischer Chirurgen verschiedener Universitätskliniken und Regionalkrankenhäuser haben wir einen häufig verwendeten Behandlungsalgorithmus für zweizeitige Revisionen infizierter Hüft- und Knie-Endoprothesen modifiziert. Neben dem Erreichen einer
maximalen Standzeit der Revisionsimplantate besteht das Ziel darin, das Funktionsniveau der betroffenen künstlichen Gelenke zu verbessern.

Schlüsselwörter: Hüft- und Knie-Totalprothesen, Implantat-assoziierte Infektion, Behandlungsalgorithmus, Spacer

Introduction

Approximately 160,000 primary hip and 146,000 primary total knee arthroplasties are performed annually in Germany [1], [2]. Periprosthetic infections are described to occur in only 1% of all primary hip arthroplasties [3]. But in patients with existing risk factors such as diabetes, rheumatoid arthritis or after aseptic revision the risk of a late infection escalates up to >5% [4], [5], [6]. Due to the demographic changes implant-associated infections will gain increasing importance for patients, orthopaedic surgeons and healthcare systems. As a result, deep infection has taken over the second place of reasons for reoperation (25.9% of all reoperations) within the first two years after implantation [7]. The mean annual economic revision burden of total hip and knee arthroplasties has reached up to 20% [8]. Complicated septic revisions caused costs of 50,000 Euro or even more [9]. Hence, the clinical and economic impact of implant-associated infections after total hip and knee arthroplasty must be expected to gain significance in the future. The period for grading an implant-related infection as “early infection” ranges from 3 weeks to 3 month postoperatively in literature [10], [11], [12]. Over the last few years there is a clear tendency to limit “early infections” to the first 3 to 4 weeks postoperatively because of a more profound knowledge of the pathophysiology of infection and the responsible microorganisms. Whether an early or late periprosthetic infection does occur this has crucial impact on the therapeutic approach. There is broad consensus to treat an early deep infection surgically (debridement, irrigation) but with retention of the femoral and acetabular component [6], [10], [12], [13]. However, an exchange of the femoral head and polyethylene insert should be performed since bacterial biofilms are found on these implants [14]. As opposed to this, the question how “late infections” should be treated is still undecided and lively discussed in the literature [3], [10], [12], [15], [16], [17], [18]. But there is a consensus that basically a treatment algorithm should be established for medical, economical and forensic reasons [16]. Besides the fact that the treatment needs to be standardized, this must hold true for the diagnostics of periprosthetic infections. Especially in cases of low-grade infections, infections with biofilm-producing bacteria or small colony variants and preceding antibiotic therapy, the classical diagnostic procedures (e.g. preoperative joint fluid aspiration, intraoperative swabs) are insufficient [10], [19], [20].

With regard to the literature and the experience of specialized orthopaedic surgeons from several university and regional hospitals we modified a commonly used treatment protocol [12]. A common concept allows to merge outcome data and to share expensive resources (e.g. laboratories, staff training, materials). Moreover, the presented algorithm is the basis for a prospective follow-up study which is especially focussed on infections with multi-resistant bacteria and treatment with improved temporary spacers.

Diagnostic and Treatment Protocol

A periprosthetic infection is assured if clinical signs such as a fistula or purulent wound secretion occur. Otherwise we combine the information from the clinical examination, laboratory (white blood cell count (WBC), C-reactive protein (CRP) and erythrocyte sedimentation rate (ESR)), radiographs (osteolyses) and a mini-incision biopsy (aspirate tissue for microbiological/histological examination) to identify periprosthetic infections according to Maurer et al. [17] and Laffer et al. [21]. After diagnosing a periprosthetic infection the further treatment is carried out with respect to following therapy algorithm (Figure 1).

Early infection

In case of an early infection without risk factors at least the polyethylene component (hip, knee) and femoral head (hip) should be changed to enable cleaning of the metalback surfaces by antiseptics (e.g. Octenisept®, Schülke und Mayr GmbH, Norderstedt, Germany) and pulsatile lavage. A complete one-stage exchange is indicated when risk factors are present (Table 1, Table 2). From our point of view implant loosening, significant soft-tissue damage, and complicated-to-treat bacterial colonization as “absolute” are certain risk factors meaning that each of them requires at least a complete one-stage exchange. In individual cases even a two-stage exchange may be indicated. The risk factors we refer to are consistent with the Cierny-Mader criteria which are originally part of an osteomyelitis staging system [11], [22], [23]. Since these factors are known to impair wound healing and to encourage periprosthetic infections we rate them as “relative” factors. In absence of any “absolute” risk factors the orthopaedic surgeon should assess the individual “relative” risk profile of the patient in order to decide whether a partial or complete exchange is preferable. With multiple and/or very severe “relative” risk factors (local and systemic) even a two-stage exchange may be considered. If a cemented component fixation is necessary, antibiotics should be added to the cement adapted to the microbiological results. Even in case of negative or missing previous microbiological status the use of revision cement containing certain antibiotics (e.g. gentamycin, vancomycin and clindamycin) is recommended.
Figure 1: Algorithm “periprosthetic infection”

Table 1: Risk factors for endoprosthesis-related infections

| “absolute” risk factors                                      | “relative” risk factors                  |
|-------------------------------------------------------------|------------------------------------------|
| signs of implant loosening                                  | systemic risk factors (Cierny-Mader)    |
| significant soft-tissue damage                             | local risk factors (Cierny-Mader)       |
| microbiology: complicated to treat                          |                                          |
| (multiple) previous revision operations                    |                                          |

Table 2: Relative risk factors for endoprosthesis-related infections according to Cierny-Mader [22, 23].

| Type of compromise | Factors (“relative risk factors”) |
|--------------------|----------------------------------|
| Systemic          | Malnutrition                     |
|                   | Renal, hepatic failure           |
|                   | Diabetes mellitus                |
|                   | Chronic hypoxia                  |
|                   | Immune disease                   |
|                   | Malignancy                       |
|                   | Extremes of age                  |
|                   | Immunosuppression/immune deficiency |
| Local             | Chronic lymphedema               |
|                   | Venous stasis                    |
|                   | Major-vessel compromise          |
|                   | Arteritis                        |
|                   | Extensive scarring               |
|                   | Radiation fibrosis               |
|                   | Small-vessel disease             |
|                   | Neuropathy                       |
|                   | Tobacco abuse (≥2 packs/d)       |
Moreover, any one-stage revision should include an exchange of gloves, instruments and sterile covering after pulsatile lavage. Tissue samples for microbiological and histological analyses are obtained intraoperatively in a standardized manner (Table 3) in order to adapt the postoperative double antibiotic treatment. Without clinical, histological and microbiological sign of an infection after revision surgery i.v. antibiotics are administered for 2 weeks, otherwise for 4 weeks.

**Late infection**

Within the early period of the late periprosthetic infection (3 weeks to 3 month after arthroplasty) in absence of any risk factors a complete one-stage exchange is justified (Figure 1). Otherwise we conduct a two-stage revision with a 6 weeks temporary spacer interval (Figure 2). Handmade or ready-made antibiotic loaded cement spacers are widely accepted. Hip stems with an antimicrobial TiCuN-coating can also be used for selected patients. Regardless of the chosen type of spacer it must maintain the length of the soft-tissue and stabilize the affected joint. Application of an external orthosis may provide additional joint stability. Tissue samples for microbiological and histological analyses are obtained intraoperatively (Table 3). The explanted endoprosthetic implants are additionally analyzed by a sonification culture in case of low-grade infection or negative previous microbiology despite clear infection signs according to Maurer et al. [17]. The double antibiotic treatment is adapted to the antibiogram and administered for 4 weeks (2 weeks i.v., 2 weeks p.o.).

Joint fluid (cytology) and tissue samples (microbiology, histology) are obtained 6 weeks postoperatively. After 2 weeks incubation the results are evaluated along with the clinical and laboratory findings. Especially the ESR and CrP should not be significantly elevated. If there are no signs of infection, 8 weeks after implant removal the revision endoprosthesis can be implanted accompanied by antibiotic treatment for 2 weeks (intraoperative microbiology negative or 4 weeks (intraoperative microbiology positive). Thereby multiple samples (two for microbiology and one for pathology) are taken from the periarticular tissue and intramedullary space. Otherwise in case of any signs of infection the antibiotic treatment is prolonged from two to four weeks.

In case of persisting signs of infection 8 weeks after implantation of the spacer, a revision operation including debridement and spacer exchange is indicated (Figure 2). Tissue samples are taken in a standardized manner (Table 3) to acquire a full-field analysis of the present microbiological colonization. After 2 weeks it must be decided whether re-implantation is possible or an individual concept is needed for the patient.

**Discussion**

In case of a necessary revision surgery of total joint arthroplasty it is crucial to distinguish between aseptic or septic revision because treatment is completely different. The diagnosis “periprosthetic infection” may be clear when purulent secretion and signs of septicemia are apparent. But in cases of suspected septic loosening the preoperative laboratory and puncture fail to identify bacterial colonization in up to 20% of all cases [15], [20], [24], [25]. A mini-incision biopsy (e.g. automatic needle) obtaining tissue for a permanent histology is recommended to increase diagnostic sensitivity [26]. Particularly the microorganisms causing low-grade infections could be failed to identify by culture [27]. Aiming to acquire the complete spectrum of microorganism causing septic loosening especially for biofilm-producing bacteria or in case of previous antibiotic treatment sonification and 16S PCR of explanted devices have to be conducted. PCR and culturing the sonification fluid is likely to raise sensitivity of cultures significantly, but possibly wrong-positive results have to be critically evaluated [28], [29], [30]. The treatment of periprosthetic infections is undisputed in case of peracute respectively high-grade infection [31]. An urgent revision surgery with evacuation of pus is indicated. After gaining the tissue samples a calculated antibiotic therapy is initiated and should be adapted after receiving the microbiological results. Septic or multimorbid patients may need a two-stage explantation. Loose and easy removable implant parts as well as necrotic tissue are removed within the first operation, remaining cement or well-integrated implant parts are explanted after non-surgical stabilization of the patient.

In patients with early infection a one-stage procedure is widely accepted [6], [10], [12], [13]. Since most patients with an early infection lack significant risk factors due to the directly preceding arthroplasty, a one-stage partial

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**Table 3: Standardized extraction of tissue samples for microbiological and histological analysis [51] in the course of the revision operation including the explantation of the total hip/knee endoprosthesis**

| diagnostic     | joint  | site of tissue sample                      |
|----------------|--------|-------------------------------------------|
| histology      | hip    | interface membrane: femur, acetabulum (center) |
|                | knee   | interface membrane: femur, tibia           |
| microbiology   | hip    | approach (subcutaneous), capsule, femur (medullary space proximal and distal), acetabulum (center, periphery) |
|                | knee   | approach (subcutaneous), capsule, femur (intramedullary space proximal and distal), tibia (intramedullary space proximal and distal) |

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exchange is sufficient. Some authors recommend a negative pressure therapy (NPT) (V.A.C.®, KCI Wiesbaden, Germany) combined with a suction/irrigation system [32], [33]. But due to the limited success rates of 50% to 60% [15], [32] the vacuum assisted closure therapy remains an option for isolated cases [13], [34]. But how patients with non-fulminant periprosthetic late infection should be treated is still discussed in literature controversially. One-stage as well as two-stage revisions have been reported to be successful in 80% to 100% [3], [15], [18], [35], [36]. One-stage concepts are described to be advantageous concerning duration of hospitalization, functional outcome, and economic aspects [15], [18], [24], [37]. But most of the proponents retract from their one-stage concept, whenever the bacterial colonization is unclear or not easy to treat, the patient’s general condition is reduced, soft-tissue is compromised or if the patient had multiple previous operations [3], [15], [18], [37]. Though this leads to a selection of patients, De Man et al. compared 22 patients after one-stage exchange to 50 patients after two-stage exchange. Although the one-stage patients had better prerequisites, the clinical (Harris hip score) and radiological outcome did not differ after 2 years between the two groups [18]. Since the vast
majority of the patients meet the risk factors given above, we agree that in case of late infections the two-stage revision is still the “gold standard” [3], [4], [10], [12], [13], [38]. A complete removal of the colonized implants and a thorough debridement of infected tissue is the common basis for both concepts. The recommended spacer interval varies markedly in the literature from 3 weeks to >1 year, most common are 6–12 weeks [3], [10], [17]. Our two-stage protocol is based on an 8 week interval providing a 2 week antibiotic-free period before obtaining tissue samples. Due to possible residual effects of systemic and local antibiotics tissue samples are proven to increase the diagnostic sensitivity for persisting infection [20], [39], [40], [41]. As standard spacers we are using antibiotic loaded cement spacers for the knee and hip as well as TiCuN coated spacers (hip) for selected cases. However, cement spacers, especially articulating spacers, are suspected to produce wear debris leading to higher wear rates of the revision implant [3]. As an alternative, cement without zirconium dioxide particles (Copal® spacer, Heraeus Medical, Wehrheim, Germany) or hip hemi-arthroplasties with antimicrobial coating may be used in the future [42], [43], [44]. The reimplantation is performed 8 weeks after septic explantation if the preoperatively obtained tissue shows no microbiological or histological signs of infection. Furthermore, no clinical/laboratory infection signs are apparent (Figure 2). Hence the validity of laboratory parameters for diagnosing a periprosthetic infection is not entirely clarified so far [20], [45], [46], [47], [48], [49]. In particular, the ESR and CRP should be within normal range or is only slightly elevated (e.g. CRP ≤12 mg/L) [48]. The type of revision endoprosthesis (length, modularity, constrained knee, cemented/cementless fixation) depends on the quality of the bone, the type of bone defect and the condition of soft tissue structures. For cemented implants the antibiotics added to the bone cement can be adapted to the sensitivity of the bacteria [15], [17], [18]. In case of persisting infection another kind of revision surgery is indicated (Figure 2) [9], [13], [17]. Patients with not controllable infection that are multimmorbid, limited operable or have a short life expectancy may need an individual concept. Alternative treatment options comprise Girdlestone hip, knee arthrodesis, permanent fistula or amputation as a last resort [9], [15], [50].

Conclusions

Treatment of implant-associated infections after total hip and knee arthroplasty requires an experienced hospital staff and appropriate facilities (e.g. operation rooms, isolation sick chambers, intensive care unit). Moreover a wide spectrum of diagnostic (e.g. microbiology, pathology, radiology, nuclear medicine) and therapeutic possibilities (multidisciplinary physician team, individual implants, psychological support) should be provided. A treatment algorithm makes the necessary steps and decision pathways more comprehensible for the patient and new staff. The presented algorithm has been thoroughly refined with regard to the literature and the experience of specialized orthopaedic surgeons from several university and regional hospitals in Mecklenburg-Pomerania, Germany. Standardized documents (e.g. patient information sheet, study agreement) should avoid to loose important information (e.g. “mismatch” of implants, individual concepts, recurrence of infection) from the therapeutic and forensic aspect. A quality management system can help to define important aspects of the outpatient treatment such as screening for MRSA, wound care and radiological/clinical follow-up.

Notes

Competing interests

The authors declare that they have no competing interests.

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