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# Success Rates for Initial Eradication of Peri-prosthetic Knee Infection Treated with a Two-stage Procedure

**Andrzej Kaminski[1(A,B,C,D,E,F)], Mustafa Citak[1(B)], Thomas Armin Schildhauer[1(A,D,E)], Tobias Fehmer[2(A,D,E)]**

[1] Department of General and Trauma Surgery, BG-Universitaetsklinikum 'Bergmannsheil' Ruhr-Universitaet Bochum, Germany
[2] Nordwest-Krankenhaus Sanderbusch GmbH, Department of Orthopaedic Surgery, Sande, Germany

## SUMMARY

**Background.** In Germany, rates of primary total knee arthroplasty procedures and exchange arthroplasty procedures continue to rise. Late-onset peri-prosthetic infection constitutes a serious complication whose management may be dependent upon the spectrum of micro-organisms involved. The aim of this study was to provide a retrospective analysis of the effectiveness of initial eradication measures performed as part of a two-stage procedure.

**Material and methods.** Between 2002 and 2008, a total of 328 patients who had received a first-time diagnosis of chronic peri-prosthetic knee infection following total knee arthroplasty (TKA) subsequently underwent surgery at our clinic. The surgical approach consisted of a two-stage procedure, with the initial procedure consisting of the removal of the prosthesis and radical debridement, followed by insertion of an antibiotic-loaded static spacer. The effectiveness of the procedure was assessed after six weeks, with each patient undergoing a number of clinical and laboratory-based tests, including knee joint aspiration.

**Results.** Staphylococcus aureus strains were responsible for 68% (n=223) of the total number of cases of peri-prosthetic knee infection. 19% of cases (n=62) showed evidence of gram-negative bacteria, while MRSA accounted for 15% (n=49) of cases. Six weeks after completion of the above-named treatment regimen, eradication of infection was considered successful in 289 patients (88.1%). Eradication was unsuccessful in 22% of MRSA infections (n=11) and 7% of MSSA infections (n=23).

**Conclusion.** The treatment regimen outlined in this report is capable of achieving satisfactory results in the management of late-onset peri-prosthetic knee infection, with one exception: patients with infections caused by MRSA showed high failure rates.

**Key words:** periprosthetic infection, MRSA, eradication

## BACKGROUND

In Germany, the number of TKAs continues to rise. According to The Federal Office for Quality Assurance (Bundesgeschäftsstelle für Qualitätssicherung, BQS), an organisation tasked with monitoring how statutory quality assurance regulations are implemented in German hospitals, a total of 136,259 primary TKAs were performed in 2007. By 2008, this figure had risen to 145,996 [1]. Estimates for the year 2009 suggested a total of 175,000 primary TKAs [2]. As a direct consequence of this development, rates of revision TKAs have also increased over the same period, with 9,565 recorded in 2007 and 10,376 in 2008 [1]. The sheer number of procedures performed means that current surgery rates are higher than anywhere else in Europe [3-5]. The risk of developing peri-prosthetic knee infection following TKA increases with the degree of invasiveness of the procedure and the morbidity of the patient. Infection rates after elective TKA have been reported to be as high as 2% [6-8]. However, in the field of exchange arthroplasty rates of up to 20% have been reported, with exact values depending upon pre-existing co-morbidities and previous surgical procedures [7,9]. Not only does peri-prosthetic knee infection represent a serious complication of this type of surgery, the costs associated with treating peri-prosthetic knee infection also exceed the cost of revision procedures that are undertaken for reasons other than infection. [10].

Two-stage exchange arthroplasty is universally recognised as an effective treatment in peri-prosthetic knee infection [11]. Removal of the prosthesis and radical debridement are routinely followed by the insertion of a temporary antibiotic-loaded spacer. A repeat TKA is only attempted after a number of weeks, once the infection has been completely eradicated.

The aim of this study was to provide a retrospective analysis of the effectiveness of the infection eradication method described in this report, with particular emphasis on the spectrum of micro-organisms involved.

## MATERIALS AND METHODS

Between 2002 and 2008, a total of 328 patients who had received a first-time diagnosis of chronic peri-prosthetic knee infection following total knee arthroplasty subsequently underwent surgery at our clinic. Cases of infection after partial knee replacement were not included in this study. Chronic infection was defined according to Tsukayama et al. [12]. In all cases, diagnosis was made at the earliest six weeks after the initial surgical procedure. Diagnostic procedures were the same for all patients. In addition to having peripheral blood samples taken to establish levels of C-reactive protein and white blood cells, all patients also underwent knee joint aspiration. Microbiologic cultures were prepared and analysed in our own laboratory. The treatment regimen was the same for all patients. The surgical approach consisted of a two-stage procedure, with the initial procedure consisting of the removal of the prosthesis and radical debridement, including complete synovectomy. Where inflammatory changes were present, the posterior cruciate ligament and collateral ligaments were also removed. Where damage to the quadriceps and patellar tendons was severe, these were also removed. This was then followed by the insertion of an industry-standard antibiotic-loaded static spacer containing gentamicin (Refobacin® Bone Cement R, Biomet). In patients whose infection was known to be due to MRSA, the spacer was also loaded with vancomycin (2000 mg vancomycin per 40 g Refobacin® Bone Cement powder). In order to ensure spacer stability, the spacer was inserted with the help of two intramedullary (femoral and tibial) carbon rods, which overlapped in the area of the old knee joint (Figures 1a and 1b). Postoperative treatment consisted of antibiotic therapy selected in

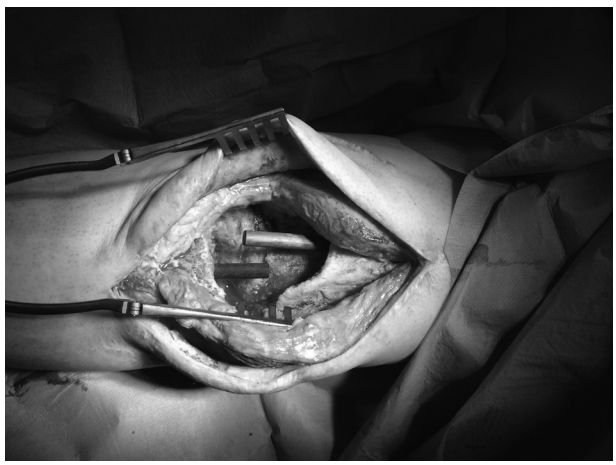

Fig. 1a. Intra-operative photograph showing surgical site after radical debridement. The collateral ligaments have been removed. Carbon rods have been inserted into the medulla of the femur and tibia in such a way as to overlap in the area where the knee joint used to be situated. This ensures good stability following insertion of the cement spacer.

Fig. 1b. Intra-operative photograph showing surgical site after cement has hardened

accordance with the individual patient's antibiogram profile. Antibiotic therapy was administered for a duration of five weeks. Six weeks after surgery, i.e. after an additional week without antibiotic treatment, knee joint aspiration and blood tests (levels of C-reactive protein and white blood cells) were performed in order to assess the effectiveness of treatment. Treatment effectiveness was measured according to a number of different parameters: no fistulas/fistula tracts or wound secretions must be visible at the time of reassessment; patients must not present with a raised temperature or fever (>37°); microbiological cultures prepared following knee joint aspiration must not show any signs of bacterial growth after two weeks of incubation, and blood samples must not show increased levels of either C-reactive protein or white blood cells. Patients who met all of these criteria were considered to be free from infection, and were subsequently able to undergo definitive surgical revision (secondary TKA vs. knee arthrodesis). Patients who did not meet all of these criteria were not considered free from infection and had to undergo additional diagnostic procedures and/or treatment aimed at managing their infection.

## RESULTS

The spectrum of micro-organisms found during pre-operative and/or intra-operative microbiological screening was as follows (Fig. 2): Staphylococcus aureus accounted for 68% (n=223) of micro-organisms found, while gram-negative bacteria accounted for 19% (n=62). Methicillin-sensitive (MSSA) and methicillin-resistant (MRSA) strains of Staphylococcus aureus were present at a ratio of 3.5:1 (173:49). MRSA accounted for 15% (n=49) of cases. Six weeks after the end of the treatment regimen outlined above, eradication of infection was considered successful in 289 patients (88.1%).

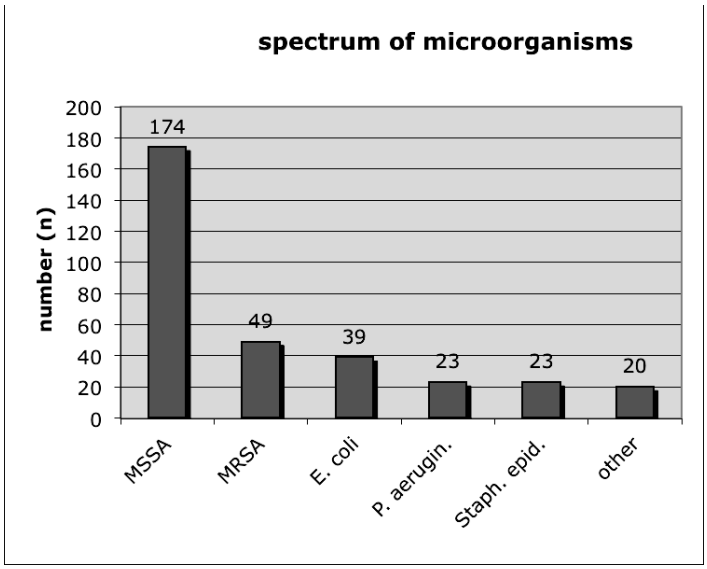


Fig. 2. Spectrum of micro-organisms prior to surgery to remove infection

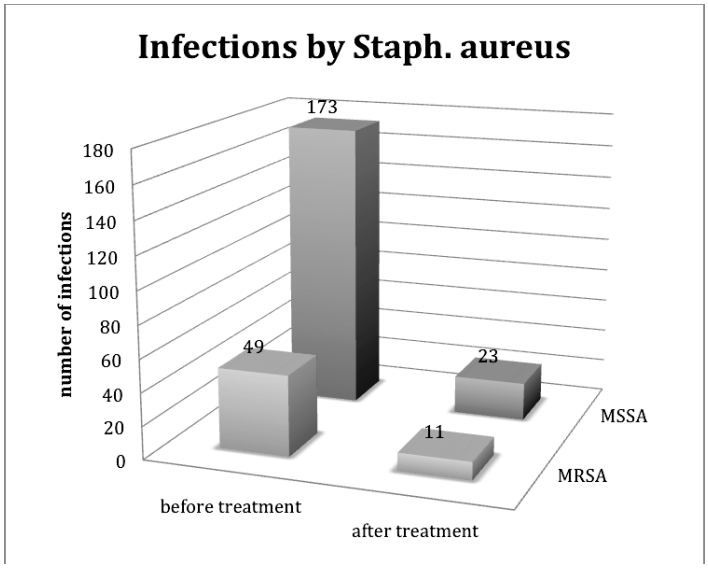


Fig. 3. Adjustment of treatment regimen depending on methicillin-resistance of Staphylococcus aureus strains involved

Persistent MRSA infections were found in 28% (n=11) of patients who did not respond to treatment. In short, 22% of primary MRSA infections remained unresolved after 6 weeks. Among patients with MSSA infections, the treatment failure rate was 7% (n=23) (Fig. 3).

## DISCUSSION

A broad range of surgical options is available for the treatment of periprosthetic knee infections, some of which are in direct competition with each another. Treatment including synovectomy and lavage alone, i.e. not including prosthesis removal, has been shown to result in failure rates of between 63-70 % [13,14]. Although one-stage exchange arthroplasty procedures are currently under discussion, these have so far been used only in a very limited number of cases [7]. Two-stage procedures, on the other hand, are considered the gold standard in revision procedures, and are known to achieve infection eradication rates of between 85-100% [15,16]. It is also generally accepted as fact that the duration of treatment is significantly longer in patients with peri-prosthetic knee infections due to MRSA [10]. This applies to both the number of days spent in hospital and the number of emergency procedures and outpatient visits required [10].

Successful eradication of infection was measured according to a number of different parameters. Although joint aspiration formed an integral part of the diagnostic procedure used in this study, it is difficult to evaluate its validity based on the study data available. Evaluations of the procedure have been inconclusive, particularly with regard to its sensitivity, which Johnson et al. [17] reported as reaching only 12%, while Fink et al. [18] reported a sensitivity of 72.5%. Data on the procedure' specificity have been far more consistent, with most studies reporting values in excess of 95%, and others reporting values as high as 100% [18,19,20,21]. Gollwitzer et al. [22] suggested that in addition to a range of different incubation and sampling techniques, such conflicting reports might also be attributable to differences in the gold standards used in the diagnosis of prosthetic joint infections [22]. Joint aspiration remains a widely used and important procedure, and has become a routine requirement prior to exchange arthroplasty [23]. In our study, aspiration cultures were prepared one week after the end of antibiotic treatment. The AAOS guideline recommends that "patients be off antibiotics for 2 weeks before obtaining intra- articular culture (Strength of Recommendation: Consensus)" [24]. In 2010, our own procedures were adapted to reflect these recommendations. In order to increase the predictive value of our assessment procedures, additional parameters were included to help us assess the effectiveness of infection eradication measures. The use of peripheral blood samples to asses the level of C-reactive protein is of particular significance in this respect. This test has been reported to have a sensitivity of between 67% and 100% [18,20,21] but considerably lower specificity [20,21]. Where joint aspiration and CRP results obtained during the course of the first surgical procedure suggest that the infection has been eradicated, this should therefore be confirmed during the second surgical procedure, via cultures and histological examination of intra-operatively sampled tissues.

The procedures outlined above achieved a good success rates in patients with late-onset peri-prosthetic infection. The only exceptions were patients with infections due to MRSA. Several studies have reported unsatisfactory eradication rates in patients with peri-prosthetic infections involving multi-resistant bacteria [25,26,27,

28,29]. Depending on the type of study involved, reinfection rates have been reported as between 24% and 33% [27,28,29]. However, Azzam et al. [30] argue that the majority of these patients present with multiple co-morbidities, resulting in doubts being raised with regard to the effectiveness of a two-stage approach to the treatment of patients with infections due to multi-resistant organisms [30]. Although the impact of co-morbidities such as diabetes, tobacco use, exogenous steroid dependency, rheumatoid arthritis, and renal insufficiency has been studied [27], results have so far failed to provide a definitive answer. Mittal et al. [27] cited malnutrition as an additional risk factor in patients with infections due to multi-resistant organisms. An albumin level of <3.5 g/dL, a total lymphocyte count of <1500, and a serum transferrin level of <262 mg/dL have all been found to increase the risk of infection [27].

Although no general recommendations have been made, the suitability of exchange arthroplasty has been called into question in relation to these patients. While amputation is not recommended as an equally valid alternative [30], this treatment option should be considered in cases where reimplantation has failed. Knee arthrodesis may also represent an alternative in some cases. However, the feasibility of this option will depend on the extent of bone loss encountered. A three-stage procedure that is currently under development, and that involves early spacer exchange prior to definitive surgical treatment, may provide an alternative. However, as far as we are aware, published data on the effectiveness of this procedure remain inconclusive.

There are currently no established guidelines on treatment protocols, including the duration of antibiotic treatment and the appropriate route of administration. Instead, it would appear that every hospital follows its own treatment regimen [27]. The retrospective nature of our study may have introduced recall bias: details of dosage and route of administration (intravenous vs. oral) of antibiotics received after hospital discharge were not always accurately recorded in medical records.

This study has limitations. In particular, our study failed to take into account if, and to what extent, cultures and histological evaluations of intra-operatively sampled tissues confirmed whether cases previously identified as having undergone successful eradication had in fact been correctly classified as free from infection. Intra-operative tissue sampling for culture and histological examination has since become an integral part of the standard procedures used in our clinic. Although our study did not produce any long term results on the eradication rates achieved, our data confirm that the infection eradication measures described in this report appear to be effective in patients whose late-onset peri-prosthetic infection following TKA is caused by non-multi-resistant organisms. of infection [27].

The effectiveness of infection eradication measures performed as part of a two-stage procedure in patients with late-onset peri-prosthetic infection of the knee joint appears to be dependent upon the spectrum of micro-organisms involved. Compared to patients with infections caused by methicillin-sensitive strains, treatment failure rates were higher in patients with MRSA infections. While it is clear that additional treatment strategies need to be developed, a lack of published data means that any treatment recommendations given at this stage would not withstand scientific scrutiny.

## CONCLUSIONS

The treatment regimen outlined in this report is capable of achieving satisfactory results in the management of late-onset peri-prosthetic knee infection, with one exception: patients with infections caused by MRSA showed high failure rates.

## REFERENCES


1. URL: http://www.bqs-outcome.de/2008/ergebnisse/leistungsbereiche/knie_tep_erst/buaw/index_html/0003_QInhalt.html
2. Schnabel P, Borelli S. Endoprothesenregister. Höchsten Anforderungen genügen. Dtsch. Ärzteblatt 2011; 108: 2598-602.
3. Ascherl R. Infektionsmanagement bei Megaimplantaten. Orthopäde 2010; 39: 980-93.
4. Robertsson O, Bizjajeva S, Fenstad AM, et al. Knee arthroplasty in Denmark, Norway and Sweden. Acta Orthop 2010; 81:82-9.
5. Scottish arthroplasty project. Annual report 2009. URL: http://www.arthro.scot.nhs.uk/Reports/Scottish_Arthroplasty_Project_Report_2009.pdf
6. Bengston S. Prosthetic osteomyelitis with special reference to the knee: risks, treatment and costs. Ann Med 1993; 25: 523-29.
7. Hanssen AD, Rand JA. Evaluation and treatment of infection at the site of a total hip or knee arthroplasty. Instr Course Lect 1999; 48: 111-22.
8. Peersman G, Laskin R, Davis J, Peterson M. Infection in total knee replacement: a retrospective review of 6489 total knee replacements. Clin Orthop Relat Res 2001; 392: 15-23.
9. Militz M, Bühren V. Wechsel infizierter Knie- und Hüftendoprothesen. Chirurg 2010; 81: 310-20.
10. Parvizi J, Pawasarat IM, Azzam KA, Joshi A, Hansen EN, Bozic KJ. Periprosthetic joint infection. The economic impact of methicillin-resistant infections. J Arthroplasty 2010; 25: 103-7.
11. Jämsen E, Stogiannidis I, Malmivaara A, Pajamäki J, Puolakka T, Konttinen YT. Outcome of prosthesis exchange for infected knee arthroplasty: the effect of treatment approach. Acta Orthop 2009; 80: 67-77.
12. Tsukayama DT, Estrada R, Gustilo RB. Infection after total hip arthroplasty. A study of the treatment of one hundred and six infections. JBJS (Am) 1996; 78: 512-23.

13. Odum SM, Fehring TK, Lombardi AV, et al. Periprosthetic Infection Consortium. Irrigation and debridement for peripros thetic infections: does the organism matter? J Arthroplasty 2011; 26: 114-8.
14. Parvizi J, Azzam K, Ghanem E, Austin MS, Rothman RH. Periprosthetic infection due to resistant staphylococci: serious problems on the horizon. Clin Orthop Relat Res 2009; 467: 1732-9.
15. Leone JM, Hanssen AD. Management of infection at the site of a total knee arthroplasty. JBJS (Am) 2005; 87: 2335-48.
16. Zimmerli W, Trampuz A, Ochsner PE. Prosthetic joint infections. N Engl J Med 2004; 351: 1645-54.
17. Johnson JA, Christie MJ, Sandler MP, Parks PF Jr, Homra L, Kaye JJ. Detection of occult infection following total joint arthroplasty using sequential technetium-99m HDP bone scintigraphy and indium-111 WBC imaging. J Nucl Med 1988; 29: 1347-53.
18. Fink B, Makowiak C, Fuerst M, Berger I, Schäfer P, Frommelt L. The value of synovial biopsy, joint aspiration and C-reactive protein in the diagnosis of late peri-prosthetic infection of total knee replacements. JBJS (Br) 2008; 90: 874-8.
19. Barrack RL, Jennings RW, Wolfe MW, Bertot AJ. The coventry award. The value of preoperative aspiration before total knee revision. Clin Orthop Rel Res 1997; 345: 8-16.
20. Kordelle J, Klett R, Stahl U, Hossain H, Schleicher I, Haas H. Infektdiagnostik nach Knie-TEP-Implantation. Z Orthop Ihre Grenzgeb 2004; 142: 337-43.
21. Panousis K, Grigoris P, Butcher I, Rana B, Reilly JH, Hamblen DL. Poor predictive value of broad-range PCR for the detection of arthroplasty infection in 92 cases. Acta Orthop 2005; 76: 341-6.
22. Gollwitzer H, Diehl P, Gerdesmeyer L, Mittelmeier W. Diagnostische Strategien bei Verdacht auf periprothetische Infektion einer Kniegelenktotalendoprothese. Orthopäde 2006; 35: 904-16.
23. Lohmann CH, Fürst M, Niggemeyer O, Rüther W. Die Behandlung von periprothetischen Infektionen. Z Rheumatol 2007; 66: 28-33.
24. Parvizi J, Della Valle CJ. AAOS Clinical Practice Guideline: diagnosis and treatment of periprosthetic joint infections of the hip and knee. J Am Acad Orthop Surg 2010; 18: 771-2.
25. Barberán J, Aguilar L, Carroquino G, et al. Conservative treatment of staphylococcal prosthetic joint infections in elderly patients. Am J Med 2006; 119: 993.
26. Salgado CD, Dash S, Cantey JR, Marculescu CE. Higher risk of failure of methicillin-resistant Staphylococcus aureus prosthetic joint infections. Clin Orthop Relat Res 2007; 461: 48-53.
27. Mittal Y, Fehring TK, Hanssen A, Marculescu C, Odum SM, Osmon D. Two-stage reimplantation for periprosthetic knee infection involving resistant organisms. JBJS (Am) 2007; 89: 1227-31.
28. Hirakawa K, Stulberg BN, Wilde AH, Bauer TW, Secic M. Results of 2-stage reimplantation for infected total knee arthroplasty. J Arthroplasty 1998; 13: 22-8.
29. Salgado CD, Dash S, Cantey JR, Marculescu CE. Higher risk of failure of methicillin-resistant Staphylococcus aureus pros thetic joint infections. Clin Orthop Relat Res 2007; 461: 48-53.
30. Azzam K, McHale K, Austin M, Purtill JJ, Parvizi J. Outcome of a second two-stage reimplantation for periprosthetic knee infection. Clin Orthop Relat Res 2009; 467: 1706-14.

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*Adres do korespondencji / Address for correspondence*
*Dr. med. Tobias Fehmer, Department of General and Trauma Surgery, BG-Universitaetsklinikum 'Bergmannsheil' Ruhr-Universitaet Bochum, Germany*
*tel.: 0049 234 3023423, fax: 0049 234 3026530, e-mail: kaminski@t-online.de*

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