VASSO M, CAPASSO L, CORONA K, POLA E, TORO G, SCHIAVONE PANNI A. Periprosthetic knee infection: treatment options. *Orthopedic Reviews*. 2022;14(4). doi:10.52965/001c.37537

General

Periprosthetic knee infection: treatment options

MICHELE VASSO[1], LUIGI CAPASSO[2], KATIA CORONA[3], ENRICO POLA[1], GIUSEPPE TORO[1], ALFREDO SCHIAVONE PANNI[1]

[1] Multidisciplinary Department of Medicine for Surgery and Orthodontics, University of Campania "Luigi Vanvitelli" - Naples (Italy), [2] San Giovanni Calibita "Fatebenefratelli - Isola Tiberina" Hospital - Rome (Italy), [3] Department of Medicine and Health Sciences "Vincenzo Tiberio", University of Molise, Campobasso (Italy)

Keywords: knee, periprosthetic, Total knee arthroplasty, treatment options, dair, single stage, two stage, SALVAGE PROCEDURES, Suppressive antibiotics, infection

https://doi.org/10.52965/001c.37537

Orthopedic Reviews

Vol. 14, Issue 4, 2022

Infection is one of the most catastrophic complication following total knee arthroplasty (TKA) and represents the second most common cause of TKA failure. Treatment of a patient with periprosthetic joint infection (PJI) could require often costly and prolonged hospital stays, weeks or months of antibiotic therapy, and multiple surgical procedures. The best management is still highly debating, whereas many treatment options are available. These include suppressive antibiotics, arthroscopic irrigation and debridement, open debridement with insert exchange, single-stage reimplantation and two-stage reimplantation. The choice of the treatment depends on many variables, including integrity of implant, timing of the infection, host factors (age, health, immunologic status), virulence of the infecting organism and wishes of the patient. The aim of this review is to provide a comprehensive understaning of the different options for knee PJIs.

INTRODUCTION

Total knee arthroplasty (TKA) is a well-recognized excellent surgical strategy for the treatment of severe degenerative diseases of the knee, reliable and reproducible, effective in eliminating pain and improving function.[1] However, despite continued technical improvements and advanced prophylactic strategies, complications continue to occur with this procedure. Infection is one of the most catastrophic complication following TKA and represents the second most common cause of TKA failure.[2,3] Treatment of a patient with periprosthetic joint infection (PJI) could require often costly and prolonged hospital stays, weeks or months of antibiotic therapy, and (often) multiple surgical procedures. The increasing number of TKAs that are every year performed in all over the world has resulted in a concomitant rise in bacterial infections, and despite the use of systemic antibiotic prophylaxis, strict hygienic protocols, and special sterile enclosure with laminar flow, the infection rate in primary TKA is between 1% and 3%.[4–9] The Musculoskeletal Infection Society (MSIS) and the Infectious Disease Society of America (IDSA) devised criteria to standardize the definition of PJI in 2011,[1,10,11] but most recently, a new 2018 evidence-based PJI definition has been published which demonstrates improved performance for diagnosing hip and knee PJI on formal external validation ; the International Consensus Meeting (ICM) algorithm for diagnosing PJI demonstrate a higher sensitivity of 97.7% compared to the MSIS (79.3%) and International Consensus Meeting definition (86.9%), with a similar specificity of 99.5%.[12] The prevalence of resistant bacteria infecting TKAs has increased in the last 15 years, mainly due to the over-consumption of antibiotics in community and healthcare settings, inappropriate strategies of antibiotic prophylaxis and treatment, and increased stay in intensive care units. Controversy remains about the best management of the periprosthetic infections sustained by resistant organisms. Moreover, after revision, the final survivorship of the implant (and of the limb) is still unknown when resistant organisms are involved.[13]

The optimal outcome of a PJI is represented by eradication of the infection and restoration of a painless and well-functioning joint. The best management is still highly debating, whereas many treatment options are available. These include suppressive antibiotics, arthroscopic irrigation and debridement, open debridement with insert exchange, single-stage reimplantation and two-stage reimplantation. The choice of the treatment depends on many variables, including integrity of implant, timing of the infection, host factors (age, health, immunologic status), virulence of the infecting organism and wishes of the patient. While each of these methods may be appropriate for a given patient, two-stage revision has been reported to be the most successful procedure with a success rate of more than 90%.[14–16] Anyway, in the presence of a low-grade PJI, especially when acute, open debridement with insert exchange or single-stage reimplantation have been proposed as valid surgical alternatives with less surgical impact to the patient.[13,16,17] However, these success rates have not been stratified because of type and virulence of infecting organism. Certainly, treatment of low-grade PJI has been reported to be more successful than treatment of infections caused by resistant organisms.[13,16,17] Unfortunately,

sometimes the impossibility of eradication of the germ and some local and general conditions of the patient, do not allow a joint reconstructive treatment and a complete recovery from the infection therefore conservative therapies are necessary such as chronic suppressive antibiotic therapy, or even limb salvage procedures such as arthrodesis and resection arthroplasty, fortunately increasingly rare.[8,15]

The aim of this review is to provide a comprehensive understaning of the different options for knee PJIs.

SUPPRESSIVE ANTIBIOTICS

Suppressive antibiotic therapy has been reserved for patients medically unable to undergo further multiple surgeries.[18,19] This treatment has had little reported success in eradicating infection, also in low-grade PJIs.[13,20] Suppressive antibiotics require a stable implant and a low-virulence organism. Moreover, the infecting organism must be susceptible to oral antibiotics and the patient must be tolerant of these antibiotics, perhaps for extended periods of time or even lifelong.[21,22]

DAIR

DAIR (debridement, antibiotics and implant retention) is a viable option with an acceptable success rate that can be used as a first surgical procedure for patients who have a well-fixed, functioning prosthesis without a sinus tract. It is principally indicated in acute infections (early post-operative or hematogenous) with no more than four weeks of symptoms (most favourable being less than seven days). The infecting organism has to be isolated and known as well as its sensitivity to antibiotics; in this regard, DAIR is particularly indicated in the presence of low-grade PJIs.[13,16,17] Boyer et Cazorla[23] using a decision algorithm increased the chances of DAIR being successful: the KLIC score[24] applies to early postoperative infections and the CRIME-80 score[25] applies to hematogenous infections. They, following a decision algorithm, resolves the infection in about 75% of cases. The functional outcomes and quality of life are close to those of patients who have undergone primary joint replacement. A failed DAIR contraindicates a second identical procedure. As above mentioned, in the setting of a low-grade PJI, a DAIR protocol could be indicated in healthy patients affected by acute gram-positive infection with a stable and well-functioning prosthesis and good soft tissue envelope with no sinus tract.[26,27] When attempting component retention, thorough debridement, and rapid antibiotic treatment prior to the accumulation of biofilm are paramount for a successful outcome.[28,29] Polyethylene exchange is always preferred, as it allows complete synovectomy and better debridement of the posterior synovium, and eliminates biofilm formation on the polyethylene.[28,30] One reason for the failure of arthroscopic debridement is likely due to the inability to eliminate biofilm at the polyethylene–prosthesis interface and debride the posterior aspect of the knee.[27,29] Organism-specific intravenous antibiotic therapy is continued for 4–6 weeks post-operatively, eventually followed by oral antibiotic administration.

SINGLE STAGE REIMPLANTATION

Single-stage exchange arthroplasty for PJI has recently increased in popularity among selected patients. The procedure has multiple advantages, such as less morbidity and better functional outcomes, reduced length of stay and less overall costs.[31,32] Single-stage reimplantation could avoid some of the problems of two-stage procedure, such as stiffness and arthrofibrosis resulting from a period with a spacer in situ. Furthermore, debridement and a single-stage strategy allows to retain the prosthetic components, clearly improving the comfort for the patient.[33] The reported success rates of single stage reimplantation in highly selected patients has been reported between 75% and 95%.[34,35] Preoperative identification of the causative micro-organisms is mandatory in single-stage exchange since polymicrobial infections and atypical and gram-negative organisms have been associated with a higher failure rate. Low-grade PJI has been potentially susceptible to a single-stage reimplantation due to the low virulence and antibiotic-resistance of the infecting bacteria.[29,30] Factors associated with a successful single-stage reimplantation include pathogen identification before revision, infections caused by gram-positive bacteria, absence of sinus tract, and use of antibiotic-loaded bone cement for new components fixation. Adequate bone stock and soft tissue coverage are necessary, and the patient must be fit enough to undergo multiple procedures if needed.[34] Single-stage reimplantation involves explant of all components and cement, thorough aggressive debridement, copious irrigation, and reimplantation of new and appropriate prosthetic components with antibiotic-impregnated cement, followed by 6-12 weeks of systemic antibiotic therapy. Then, oral antibiotic therapy should be considered for 3-6 additional months based on recommendations infectious disease specialist.[36]

Singer et al[37] reported that single-stage revision achieved a 95% of success rate, and higher knee scores compared to two-stage revisions in low-grade TKA infections. Higher rates of recurrent infection appeared to be associated with chronic infections of hinged protheses. A recent article by Dagneaux et al[38] suggested the single-stage reimplantation as a more convenient treatment for PJIs when compared to high morbidity of the two-stage revision. Single-stage procedure avoids the painful interval with the cement spacer and the inevitable muscular atrophy. Rehabilitation can start immediately, therefore reducing the risk of knee stiffness, and the patients are quicker to return to independent activities. The clinical and functional results following a single-stage reimplantation appear better, with improved patient-reported outcomes.[39] Finally, another benefit of a single-stage protocol is that reimplantation is much simpler, whereas technical challenges of the two-stage revision such as a difficult surgical exposure and the possible severe bone loss are avoided.[39–42]

TWO-STAGE REIMPLANTATION

The strategy that involves the use of cement spacer, intravenous antibiotic therapy and successive revision TKA is still considered the gold standard for the management of the PJIs. This treatment is considered the first choice not only for chronic but also for acute infections, especially in the presence of resistant bacteria.[16,17,43] During the first stage, all prosthetic components and cement are removed, and an antibiotic-loaded cement spacer is positioned into the joint. After 6-12 weeks of concomitant specific antibiotic therapy, the spacer is removed and a revision TKA is implanted. The strategy of using antibiotic-loaded cement spacers and intravenous (with or without oral) antibiotics with delayed exchange arthroplasty is considered the state-of-the-art with a reported success rate of 88-96% in infection eradication and function preservation.[43–46] There are many advantages using cement spacers: space preservation; reduction of the scar tissue that could compromise soft-tissue elasticity and thus balancing during reimplantation; improvement of patient's comfort between the stages; delivery of high-dose local antibiotics to the knee greater than intravenous administration.[14] Three types of cement spacers have been proposed for the treatment of PJIs: block spacers and two types of articulated spacers. These latter are distinguished in two types. The first one is made completely of antibiotic-impregnated cement, with or without preformed moulds. The second one is made of metal and plastic components, coated with antibiotic-impregnated cement (composite spacer).[13,16,17]

In the setting of a two-stage revision, reimplantation is performed when sufficient clinical, radiographic, and laboratory (ESR and CRP) evidence support the absence of an infection.[47] Anyway, some factors could affect the reliability of these hematic biomarkers: low-virulence bacteria, antibiotics in the cement spacer and recent systemic antibiotic administration. Therefore, some authors have proposed obtaining repeated cultures by knee aspirations at least two-week antibiotic cessation and before reimplantation to determine whether infection is still present.[47] Recently, it has been introduced a combined measurement of synovial fluid CRP and alpha-defensin protein levels. In fact, while synovial fluid α-defensin test alone demonstrated a sensitivity of 97% and a specificity of 96% for the diagnosis of periprosthetic joint infection, the combination of this test with CRP demonstrated a sensitivity of 97% and a specificity of 100%.[48] Anyway, nor repeated aspiration of the knee joint and nuclear medicine investigations are not routinely performed before the second stage. In patients with rheumatoid arthritis and chronic inflammatory diseases, laboratory markers might not normalize; therefore, their substantial improvement over time helps to guide the timing of reimplantation. Other factors that can be used to guide the decision to reimplantation, in these patients, is the wound appearance and the results of the aspirate before reimplantation.[49]

In case of suspected persistence of the infection, cement spacer should be revised (multiple stage reimplantation).[22] Similarly, if at the time of reimplantation the intraoperative frozen sections indicate a state of persistent acute inflammation, an antibiotic-loaded cement spacer should be re-applied.[47,50] Generally, the revision prosthesis is fixed with antibiotic-loaded cement. After reimplantation, intravenous antibiotics are administered for at least 4-5 days and stopped if the intraoperative cultures result negative. If intraoperative cultures are positive, instead, antibiotics must be continued for at least 6 weeks, based on recommendations of the infectious disease specialist.[35,49,51]

SALVAGE PROCEDURES

RESECTION ARTHROPLASTY

Resection arthroplasty is a salvage procedure that involves the removal of all components, debridement of the infected soft tissues and the bone without re-implantation of new components. The procedure has a very limited indication, primarily reserved for low-demanded patients with polyarticular rheumatoid or other chronic arthritis with limited ambulatory demands, while it is less tolerated with single joint involvement. Resection arthroplasty involves limited functional ambulation (all cane or walker), but it preserves modest motion for ADLs. Relative contraindications are represented by single joint disease or high ambulatory demand. Anyway, intravenous antibiotics should be administered for at least 4-6 weeks postoperatively, choosing antimicrobial drugs specific for the infecting organism detected during surgery.[22] The prognosis for resection arthroplasty is fair to poor, with a recurrent infection in 11% of the patients, instability in 83% of the patients, pain common, and with an only 56% satisfaction rate reported.[52]

ARTHRODESIS

Knee arthrodesis for recurrent PJI is a limb salvage procedure that simultaneously provides a stable limb for weight-bearing and effective eradication of the chronic infection. Knee arthrodesis is a final resort for limb salvage that is appropriate for patients with multiple recurrent revisions for infection, a history of failed 2-stage exchanges, medical comorbidities, and an inability to tolerate multiple additional procedures. Another important consideration is whether the patient has a poor soft-tissue envelope that leaves knee arthrodesis as the only viable option. The procedure is a definitive surgery to eliminate return trips to the operating room. This technique involves knee arthrodesis using a long intra-medullary rod inserted proximally through the piriformis fossa that spans the entire medullary canal of the femur and the tibia. Before insertion, the surgeon may elect to create a long antibiotic cement-coated intramedullary rod. The rod is locked proximally and distally. An alternative method for large bone defects (.6 cm) at the level of the knee is to create intercalary antibiotic-impregnated cement spacers.[53]

When reimplantation is not possible or multiply unsuccessful, an alternative salvage procedure can be recommended to prevent the need for amputation. Although rare, PJI is the most common indication for arthrodesis.[54–56] Conway et al[54] stated that "overall outcome of a successful

arthrodesis is certainly better than the outcome of an amputation or a poor revision". Arthrodesis is used as a serious end-stage procedure when the extensor mechanism has been highly compromised, and severe bone and soft tissue loss precludes reimplantation of a prosthesis or makes it highly problematic. Arthrodesis is also indicated in patients with chronic recurrent infections in whom previous surgical attempts at infectious eradication and pain relief have failed. Moreover, arthrodesis may be performed in presence of infections by high-resistant bacteria, and in immunocompromised patients because of the high risk of infection recurrence after reimplantation of a revision TKA. Sometimes, arthrodesis is forced by desire of the patient for a more predictable solution or by its poor general medical status.[51,57] A successful arthrodesis permits ambulation and the performance of daily activities at an acceptable level of efficiency that otherwise would not be possible with a failed TKA. Arthrodesis involves removal of all components and cement, debridement of all infected and necrotic tissue, and positioning of an intramedullary nail or an external fixator. Bone grafts may be necessary. Compression plates have been also used, but very few cases of plate fixation for arthrodesis following a failed TKA are reported. Although good fusion rates have been reported, arthrodesis with plate requires large exposure and longer immobilization, and it is often compromised by recurring infection. Relative contraindications to the knee arthrodesis following PJI could be represented by highly severe bone stock, significant ipsilateral hip or ankle dysfunction or significant contralateral knee disease. Additionally, arthrodesis could represent a difficult and demanding surgical procedure, especially in patients with significant soft tissue and bone loss, and could be complicated by delayed fusion, nonunion, malunion, or persistent infection.[58] Nonunion could be caused by bone loss, persistent infection, insufficient bone grafts, malalignment and inadequate immobilization.

INTRAMEDULLARY NAIL

Knee arthrodesis using a long intramedullary rod is a very effective and efficient method of fusion. With recurrent periprosthetic knee infections, metaphyseal bone loss is common and short knee-fusion rods may not provide adequate stability. Long rods for knee arthrodesis use the diaphysis for stability and have the additional advantage of being easily accessible for removal in the event of a recurrent infection with a well-healed fusion. Long intramedullary rods also provide the additional advantages of immediate weight-bearing. Immediate weight-bearing on the affected limb is critical because often these patients have been unable to bear weight preoperatively secondary to pain and infection.[53] The intramedullary nail allows higher rate of fusion (90%) than external fixator (70-80%), but it is associated with a major complications rate (56%) including the intramedullary spread of infection with potential contamination of otherwise healthy bone.[59] Other complications may be the breakage or migration of the nail, or bone fractures. Furthermore, a potential problem associated to the use of intramedullary nail may be the need for removal that could require performing cortical windows in the femur and/or in the tibia. Intramedullary devices allow immediate postoperative full weightbearing, therefore providing a more rigid fixation and generally a shorter time to achieve a solid fusion. Additionally, internal fixation with intramedullary nail has been proven to represent the most effective technique to obtain knee fusion in the presence of severe bone loss.[60] Intramedullary nails can be anterograde that require insertion through the piriformis fossa, or modular with a retrograde femoral nail and an anterograde tibial nail that are introduced from the knee joint. Moreover, modular hardware allows for a mismatch in size between the intramedullary canals of femur and tibia. The modular systems have the obvious advantages to allow for an accurate debridement of the knee before the insertion of the nail and obtain a more correct alignment than non-modular systems. On the other hand, solid bony contact with compression has been emphasized to favor fusion at the site of arthrodesis. This, however, reduces the limb length when a large bone defect is present.[55,61,62] Finally, a relative contraindication to the use of the intramedullary nail for knee arthrodesis could be represented the presence of ipsilateral hip and/or ankle arthroplasty.

EXTERNAL FIXATION

External fixation used for arthrodesis following PJI presents some theoretical advantages when compared to intramedullary nail. The external fixator can be used with ipsilateral total hip arthroplasty, and it allows delayed skin coverage (when that is necessary). Compression and alignment can be obtained easily and adjusted after the initial procedure. Furthermore, the external fixator can be successively removed without insult to the patient. External fixation techniques are effective but come with pin-site problems. Pin-site problems are amplified in patients with obesity who have large soft-tissue envelopes, and the long intramedullary rod avoids pin problems in such patients. Antibiotic cement coating of the long intramedullary rod also provides local antibiotic delivery.[53] Complications associated to the external fixation devices could be pin tract infection, pin loosening, bone fracture at a pin site, and non-union.[55]

AMPUTATION

Above-the-knee amputation (AKA) is used for life-threatening sepsis or recurrent sepsis associated with massive bone loss or complex soft tissue defects and intractable pain after multiple revisions. Amputation is certainly considered the last resort for the treatment of a failed TKA. Amputation is highly successful in infection eradication and pain relief, but it is clearly associated with poor functional result.[63,64] Sierra et al[65] reported on the prevalence, etiology and functional outcome of the AKA following a failed knee replacement. On 18443 primary TKAs performed from 1970 to 2000 at the Mayo Clinic, nineteen (0,1%) knees were eventually followed by amputation for uncontrollable infection; other causes of amputation were periprosthetic fractures, intractable pain, severe bone loss,

vascular occlusion, and other causes unrelated to the knee replacement such as peripheral vascular diseases, tumors and diabetic neuropathy. After amputation, only six of nineteen infected knees were fitted with an external prosthesis; 14 patients were unable to walk, three ambulated with prosthesis two of whom using two crutches and one without aids, one ambulated without prosthesis using two crutches, and one used prosthesis for cosmetic reasons. These poor functional results often depend on debilitated infected patients, medical comorbidities (typical in rheumatoid arthritis) or multiple joint diseases, that make difficult walking with a prosthesis.

Recently, Carr et al[66] reported about outcomes in the treatment of failed septic TKA comparing arthrodesis and above-knee amputation. They found a greater percentage of patients older than 80 years in the AKA group compared with patients of the arthrodesis group.[66] Moreover, comorbidities such as diabetes mellitus, congestive heart failure, coronary heart disease, chronic kidney disease, and chronic obstructive pulmonary disease were observed much more often in the AKA group compared with the arthrodesis group. Currently, patients with more comorbidities are preferred for AKA instead of arthrodesis in septic failure of TKA. However, it should be noted that a decrease in functional status after AKA is inevitable. Only half of the patients achieved independent ambulation.[66]

CONCLUSION

In patients with acute low-grade knee PJIs, DAIR procedure could a reasonable and acceptable choice to save the implant, although characterized by a relatively high failure rate. When a failed DAIR or a chronic PKI occur, resection of all components appears mandatory. Single stage reimplantation has the potential to decrease the number of surgeries and costs and improve the comfort for the patient. Single-stage exchange is particularly indicated when the patients present minimal soft tissue defect allowing primary wound closure, and in the setting of low-grade infections with high possibility to eradicate the infecting organism, absence of systemic sepsis and absence of extensive comorbidities. Two-stage reimplantation is still considered the gold standard for the management of PJIs and present the highest success-rates in eradicating infection. Two-stage reimplantation, generally chosen only for chronic PJIs, is considered the first choice also in case of acute infections when the infecting organism is not known, and in the presence of multidrug-resistant bacteria. Salvage procedures are nowadays indicated as limb- or life-threatening PJIs.

REFERENCES

1. Insall JN. Total knee replacement. In: Insall JN, ed. *Surgery of the Knee*. Churchill Livingstone; 1984:587.

2. Kasahara Y, Majima T, Kimura S, Nishiike O, Uchida J. What are the causes of revision total knee arthroplasty in Japan? *Clin Orthop Relat Res*. 2013;471(5):1533-1538. doi:10.1007/s11999-013-2820-2

3. Hackett DJ, Rothenberg AC, Chen AF, et al. The economic significance of orthopaedic infections. *J Am Acad Orthop Surg*. 2015;23:S1-S7. doi:10.5435/jaaos-d-14-00394

4. Buechel FF. The infected total knee arthroplasty: just when you thought it was over. *J Arthroplasty*. 2004;19(4 Suppl 1):51-55. doi:10.1016/j.arth.2004.03.001

5. Durbhakula SM, Czajka J, Fuchs MD, Uhl RL. Antibiotic-loaded articulating cement spacer in the 2-stage exchange of infected total knee arthroplasty. *J Arthroplasty*. 2004;19(6):768-774. doi:10.1016/j.arth.2004.02.036

6. Fulkerson E, Valle CJD, Wise B, Walsh M, Preston C, Di Cesare PE. Antibiotic susceptibility of bacteria infecting total joint arthroplasty sites. *J Bone Joint Surg Am*. 2006;88(6):1231-1237. doi:10.2106/jbjs.e.00004

7. Johnson AJ, Sayeed SA, Naziri Q, Khanuja HS, Mont MA. Minimizing dynamic knee spacer complications in infected revision arthroplasty. *Clin Orthop Relat Res*. 2012;470(1):220-227. doi:10.1007/s11999-011-2095-4

8. Siddiqui MMA, Lo NN, Ab Rahman S, Chin PL, Chia SL, Yeo SJ. Two-year outcome of early deep MRSA infections after primary total knee arthroplasty: a joint registry review. *J Arthroplasty*. 2013;28(1):44-48. doi:10.1016/j.arth.2012.04.007

9. Volin SJ, Hinrichs SH, Garvin KL. Two-stage reimplantation of total joint infections: a comparison of resistant and non-resistant organisms. *Clin Orthop Relat Res*. 2004;(427):94-100. doi:10.1097/01.blo.0000143559.34143.3d

10. 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. doi:10.1097/00003086-200111000-00003

11. McPherson EJ, Patzakis MJ, Gross JE, Holtom PD, Song M, Dorr LD. Infected total knee arthroplasty. Two-stage reimplantation with a gastrocnemius rotational flap. *Clin Orthop Relat Res*. 1997;(341):73-81. doi:10.1097/00003086-199708000-00013

12. Goswami K, Parvizi J, Maxwell Courtney P. Current Recommendations for the Diagnosis of Acute and Chronic PJI for Hip and Knee—Cell Counts, Alpha-Defensin, Leukocyte Esterase, Next-generation Sequencing. *Curr Rev Musculoskelet Med*. 2018;11(3):428-438. doi:10.1007/s12178-018-9513-0

13. Vasso M, Schiavone Panni A, De Martino I, Gasparini G. Prosthetic knee infection by resistant bacteria: the worst-case scenario. *Knee Surg Sports Traumatol Arthrosc*. 2016;24(10):3140-3146. doi:10.1007/s00167-016-4010-8

14. Romanò CL, Gala L, Logoluso N, Romanò D, Drago L. Two-stage revision of septic knee prosthesis with articulating knee spacers yields better infection eradication rate than one-stage or two-stage revision with static spacers. *Knee Surg Sports Traumatol Arthrosc*. 2012;20(12):2445-2453. doi:10.1007/s00167-012-1885-x

15. Kurd MF, Ghanem E, Steinbrecher J, Parvizi J. Two-stage exchange knee arthroplasty: does resistance of the infecting organism influence the outcome? *Clin Orthop Relat Res*. 2010;468(8):2060-2066. doi:10.1007/s11999-010-1296-6

16. Vasso M, Del Regno C, Corona K, D'Apolito R, Schiavone Panni A. Articulated spacer provides long-term knee improvement after two-stage reimplantation. *Knee Surg Sports Traumatol Arthrosc*. 2016;24(10):3100-3105. doi:10.1007/s00167-016-4238-3

17. Vasso M, Braile A, Ascione F, et al. Two-stage reimplantation in periprosthetic knee infection. *Eur Rev Med Pharmacol Sci*. 2019;23(2 Suppl):51-58. doi:10.26355/eurrev_201904_17474

18. Masters JP, Smith NA, Foguet P, Reed M, Parsons H, Sprowson AP. A systematic review of the evidence for single stage and two stage revision of infected knee replacement. *BMC Musculoskelet Disord*. 2013;14(1). doi:10.1186/1471-2474-14-222

19. Kalore NV, Gioe TJ, Singh JA. Diagnosis and management of infected total knee arthroplasty. *Open Orthop J*. 2011;5(1):86-91. doi:10.2174/1874325001105010086

20. Hofmann AA, Goldberg T, Tanner AM, Kurtin SM. Treatment of infected total knee arthroplasty using an articulating spacer: 2- to 12-year experience. *Clin Orthop Relat Res*. 2005;(430):125-131. doi:10.1097/01.blo.0000149241.77924.01

21. Buechel FF. The infected total knee arthroplasty: just when you thought it was over. *J Arthroplasty*. 2004;19(4):51-55. doi:10.1016/j.arth.2004.03.001

22. Frommelt L. Principles of systemic antimicrobial therapy in foreign material associated infection in bone tissue, with special focus on periprosthetic infection. *Injury*. 2006;37(2):S87-S94. doi:10.1016/j.injury.2006.04.014

23. Boyer B, Cazorla C. Methods and probability of success after early revision of prosthetic joint infections with debridement, antibiotics and implant retention. *Orthop Traumatol Surg Res*. 2021;107(1S):102774. doi:10.1016/j.otsr.2020.102774

24. Tornero E, Morata L, Martínez-Pastor JC, et al. KLIC-score for predicting early failure in prosthetic joint infections treated with debridement, implant retention and antibiotics. *Clin Microbiol Infect*. 2015;21(8):786.e9-786.e17. doi:10.1016/j.cmi.2015.04.012

25. Wouthuyzen-Bakker M, Sebillotte M, Lomas J, et al. Timing of implant-removal in late acute periprosthetic joint infection: A multicenter observational study. *J Infect*. 2019;79(3):199-205. doi:10.1016/j.jinf.2019.07.003

26. Fehring TK, Odum SM, Berend KR, et al. Failure of irrigation and débridement for early postoperative periprosthetic infection. *Clin Orthop Relat Res*. 2013;471(1):250-257. doi:10.1007/s11999-012-2373-9

27. Choi HR, von Knoch F, Zurakowski D, Nelson SB, Malchau H. Can implant retention be recommended for treatment of infected TKA? *Clin Orthop Relat Res*. 2011;469(4):961-969. doi:10.1007/s11999-010-1679-8

28. Gardner J, Gioe TJ, Tatman P. Can this prosthesis be saved?: implant salvage attempts in infected primary TKA. *Clin Orthop Relat Res*. 2011;469(4):970-976. doi:10.1007/s11999-010-1417-2

29. Kuiper JWP, Vos SJ, Saouti R, et al. Prosthetic joint-associated infections treated with DAIR (debridement, antibiotics, irrigation, and retention): analysis of risk factors and local antibiotic carriers in 91 patients. *Acta Orthop*. 2013;84(4):380-386. doi:10.3109/17453674.2013.823589

30. Buller LT, Sabry FY, Easton RW, Klika AK, Barsoum WK. The preoperative prediction of success following irrigation and debridement with polyethylene exchange for hip and knee prosthetic joint infections. *J Arthroplasty*. 2012;27(6):857-864.e644. doi:10.1016/j.arth.2012.01.003

31. Haddad FS, Sukeik M, Alazzawi S. Is single-stage revision according to a strict protocol effective in treatment of chronic knee arthroplasty infections? *Clin Orthop Relat Res*. 2015;473(1):8-14. doi:10.1007/s11999-014-3721-8

32. Castellani L, Daneman N, Mubareka S, Jenkinson R. Factors Associated with Choice and Success of One- Versus Two-Stage Revision Arthroplasty for Infected Hip and Knee Prostheses. *HSS J*. 2017;13(3):224-231. doi:10.1007/s11420-017-9550-z

33. Baker P, Petheram TG, Kurtz S, Konttinen YT, Gregg P, Deehan D. Patient reported outcome measures after revision of the infected TKR: comparison of single versus two-stage revision. *Knee Surg Sports Traumatol Arthrosc*. 2013;21(12):2713-2720. doi:10.1007/s00167-012-2090-7

34. Silva M, Tharani R, Schmalzried TP. Results of direct exchange or debridement of the infected total knee arthroplasty. *Clin Orthop Relat Res*. 2002;(404):125-131. doi:10.1097/00003086-200211000-00022

35. Haleem AA, Berry DJ, Hanssen AD. Mid-term to long-term followup of two-stage reimplantation for infected total knee arthroplasty. *Clin Orthop Relat Res*. 2004;(428):35-39. doi:10.1097/01.blo.0000147713.64235.73

36. Gulhane S, Vanhegan IS, Haddad FS. Single stage revision: regaining momentum. *J Bone Joint Surg Br*. 2012;94-B(11 Suppl A):120-122. doi:10.1302/0301-620x.94b11.30746

37. Singer J, Merz A, Frommelt L, Fink B. High rate of infection control with one-stage revision of septic knee prostheses excluding MRSA and MRSE. *Clin Orthop Relat Res*. 2012;470(5):1461-1471. doi:10.1007/s11999-011-2174-6

38. Dagneaux L, Limberg AK, Osmon DR, Leung N, Berry DJ, Abdel MP. Acute Kidney Injury When Treating Periprosthetic Joint Infections After Total Knee Arthroplasties with Antibiotic-Loaded Spacers: Incidence, Risks, and Outcomes. *J Bone Joint Surg Am*. 2021;103(9):754-760. doi:10.2106/jbjs.20.01825

39. Klemt C, Tirumala V, Oganesyan R, Xiong L, van den Kieboom J, Kwon YM. Single-Stage Revision of the Infected Total Knee Arthroplasty Is Associated With Improved Functional Outcomes: A Propensity Score–Matched Cohort Study. *J Arthroplasty*. 2021;36(1):298-304. doi:10.1016/j.arth.2020.07.012

40. Pangaud C, Ollivier M, Argenson JN. Outcome of single-stage versus two-stage exchange for revision knee arthroplasty for chronic periprosthetic infection. *EFORT Open Rev*. 2019;4(8):495-502. doi:10.1302/2058-5241.4.190003

41. Vaishya R, Agarwal AK, Rawat SK, Singh H, Vijay V. Is Single-stage Revision Safe Following Infected Total Knee Arthroplasty? A Critical Review. *Cureus*. 2017;9(8):e1629. doi:10.7759/cureus.1629

42. Yaghmour KM, Chisari E, Khan WS. Single-Stage Revision Surgery in Infected Total Knee Arthroplasty: A PRISMA Systematic Review. *J Clin Med*. 2019;8(2):174. doi:10.3390/jcm8020174

43. Lu J, Han J, Zhang C, Yang Y, Yao Z. Infection after total knee arthroplasty and its gold standard surgical treatment: Spacers used in two-stage revision arthroplasty. *Intractable Rare Dis Res*. 2017;6(4):256-261. doi:10.5582/irdr.2017.01049

44. Parvizi J, Tan TL, Goswami K, et al. The 2018 Definition of Periprosthetic Hip and Knee Infection: An Evidence-Based and Validated Criteria. *J Arthroplasty*. 2018;33(5):1309-1314.e2. doi:10.1016/j.arth.2018.02.078

45. Ma CY, Lu YD, Bell KL, et al. Predictors of Treatment Failure After 2-Stage Reimplantation for Infected Total Knee Arthroplasty: A 2- to 10-Year Follow-Up. *J Arthroplasty*. 2018;33(7):2234-2239. doi:10.1016/j.arth.2018.02.007

46. Ding H, Yao J, Chang W, Liu F. Comparison of the efficacy of static versus articular spacers in two-stage revision surgery for the treatment of infection following total knee arthroplasty: a meta-analysis. *J Orthop Surg Res*. 2017;12(1):151. doi:10.1186/s13018-017-0644-6

47. Kusuma SK, Ward J, Jacofsky M, Sporer SM, Della Valle CJ. What is the role of serological testing between stages of two-stage reconstruction of the infected prosthetic knee? *Clin Orthop Relat Res*. 2011;469(4):1002-1008. doi:10.1007/s11999-010-1619-7

48. Deirmengian C, Kardos K, Kilmartin P, Cameron A, Schiller K, Parvizi J. Combined measurement of synovial fluid α-Defensin and C-reactive protein levels: highly accurate for diagnosing periprosthetic joint infection. *J Bone Joint Surg Am*. 2014;96(17):1439-1445. doi:10.2106/jbjs.m.01316

49. Mittal Y, Fehring TK, Hanssen A, Marculescu C, Odum SM, Osmon D. Two-stage reimplantation for periprosthetic knee infection involving resistant organisms. *J Bone Joint Surg Am*. 2007;89(6):1227-1231. doi:10.2106/jbjs.e.01192

50. Bori G, Soriano A, García S, Mallofré C, Riba J, Mensa J. Usefulness of histological analysis for predicting the presence of microorganisms at the time of reimplantation after hip resection arthroplasty for the treatment of infection. *J Bone Joint Surg Am*. 2007;89(6):1232-1237. doi:10.2106/jbjs.f.00741

51. Nazarian DG, de Jesus D, McGuigan F, Booth RE Jr. A two-stage approach to primary knee arthroplasty in the infected arthritic knee. *J Arthroplasty*. 2003;18(7 Suppl 1):16-21. doi:10.1016/s0883-5403(03)00343-7

52. Falahee MH, Matthews LS, Kaufer H. Resection arthroplasty as a salvage procedure for a knee with infection after a total arthroplasty. *J Bone Joint Surg Am*. 1987;69(7):1013-1021. doi:10.2106/00004623-198769070-00009

53. Conway JD. Knee Arthrodesis for Recurrent Periprosthetic Knee Infection. *JBJS Essent Surg Tech*. 2020;10(3):e19.00027. doi:10.2106/jbjs.st.19.00027

54. Conway JD, Mont MA, Bezwada HP. Arthrodesis of the knee. *J Bone Joint Surg Am*. 2004;86(4):835-848. doi:10.2106/00004623-200404000-00027

55. Lee S, Jang J, Seong SC, Lee MC. Distraction arthrodesis with intramedullary nail and mixed bone grafting after failed infected total knee arthroplasty. *Knee Surg Sports Traumatol Arthrosc*. 2012;20(2):346-355. doi:10.1007/s00167-011-1724-5

56. Lim HC, Bae JH, Hur CR, Oh JK, Han SH. Arthrodesis of the knee using cannulated screws. *J Bone Joint Surg Br*. 2009;91(2):180-184. doi:10.1302/0301-620x.91b2.21043

57. McQueen DA, Cooke FW, Hahn DL. Intramedullary compression arthrodesis of the knee: early experience with a new device and technique. *J Arthroplasty*. 2005;20(1):72-78. doi:10.1016/j.arth.2004.09.022

58. Waldman BJ, Mont MA, Payman KR, et al. Infected total knee arthroplasty treated with arthrodesis using a modular nail. *Clin Orthop Relat Res*. 1999;(367):230-237. doi:10.1097/00003086-199910000-00029

59. Pellegrini VD Jr. *Management of the Patient with an Infected Knee Replacement*. AAOS instructional course 221, Infected total joint arthroplasty; 2005.

60. Wiedel JD. Salvage of infected total knee fusion: the last option. *Clin Orthop Relat Res*. 2002;(404):139-142. doi:10.1097/00003086-200211000-00024

61. Bargiotas K, Wohlrab D, Sewecke JJ, Lavinge G, Demero PJ, Sotereanos NG. Arthrodesis of the knee with a long intramedullary nail following the failure of a total knee arthroplasty as the result of infection. *J Bone Joint Surg Am*. 2006;88(3):553-558. doi:10.2106/jbjs.e.00575

62. Benson ER, Resine ST, Lewis CG. Functional outcome of arthrodesis for failed total knee arthroplasty. *Orthopedics*. 1998;21(8):875-879. doi:10.3928/0147-7447-19980801-10

63. Bose WJ, Gearen PF, Randall JC, Petty W. Long-term outcome of 42 knees with chronic infection after total knee arthroplasty. *Clin Orthop Relat Res*. 1995;(319):285-296. doi:10.1097/00003086-199510000-00031

64. Pring DJ, Marks L, Angel JC. Mobility after amputation for failed knee replacement. *J Bone Joint Surg Br*. 1988;70(5):770-771. doi:10.1302/0301-620x.70b5.3192577

65. Sierra RJ, Trousdale RT, Pagnano MW. Above-the-knee amputation after a total knee replacement: prevalence, etiology, and functional outcome. *J Bone Joint Surg Am*. 2003;85(6):1000-1004. doi:10.2106/00004623-200306000-00003

66. Carr JB II, Werner BC, Browne JA. Trends and Outcomes in the Treatment of Failed Septic Total Knee Arthroplasty: Comparing Arthrodesis and Above-Knee Amputation. *J Arthroplasty*. 2016;31(7):1574-1577. doi:10.1016/j.arth.2016.01.010