Periprosthetic Knee Infection – Part 2: Treatment

Infecção periprotética do joelho – Parte 2: Tratamento

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Abstract

Several treatment modalities are proposed for periprosthetic infections, with variable success rates. However, efficacy is related to the appropriate selection of cases for each type of treatment.

Debridement with implant retention is indicated in acute infections with fixed implant, and its success depends on the type of infection, comorbidities of the host, and virulence of the etiological agent.

One- or two-stage revision is required in cases in which biofilm is forming, or of implant loosening. The choice between performing the review in one or two stages depends on factors such as etiological agent identification, pathogen virulence, local and systemic host factors.

Rescue procedures such as arthrodesis, amputation, resection arthroplasty or even antibiotic suppression are reserved for cases in which the infection has not been eradicated.

Keywords

- arthroplasty, replacement, knee
- surgical site infection
- treatment
- surgical review
- antibiotic

Resumo

Diversas modalidades de tratamento são propostas para as infecções periprotéticas, com índices de sucesso variáveis. No entanto, a eficácia está relacionada à seleção adequada dos casos para cada tipo de tratamento.

O desbridamento com retenção do implante é indicado em infecções agudas com implante fixo, e seu sucesso depende do tipo de infecção, das comorbidades do hospedeiro e da virulência do agente etiológico.

A revisão em um ou dois estágios se impõem nos casos em que haja formação de biofilme, ou nos quais se tenha afrouxamento do implante. A escolha entre realizar a revisão em um ou dois estágios depende de fatores como identificação do agente etiológico, virulência do patógeno, fatores locais e sistêmicos do hospedeiro.

Os procedimentos de salvamento como artrodese, amputação, artroplastia de ressecção ou, ainda, supressão antibiótica são reservados para os casos em que não se conseguiu erradicação da infecção.

Palavras-chave

- artroplastia do joelho
- infecção de sítio cirúrgico
- tratamento
- revisão cirúrgica
- antibiótico

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Introduction

Before we start the treatment of infection in total knee arthroplasty, ideally, we should have the etiological agent correctly identified and a patient clinically balanced in order to tolerate the surgical interventions that are to come.

It is also desirable that we have good images of the compromised knee so that we can carry out appropriate planning of the surgical treatment to be implemented.

Since, due to biofilm formation, surgical debridement is required for its removal, the main surgical alternatives are joint debridement with implant retention (JDIR), single-stage revision, and two-stage revision. In case these procedures fail, rescue procedures may be required.

Joint Debridement and Implant Retention

Joint debridement is the treatment of infection without removal of the prosthesis, replacing only polyethylene. To optimize its result, it is essential that the infectious process is in the acute phase, when the bacterial biofilm is not yet mature.[1] In addition to time, other criteria should be considered, such as the absence of fistulas, and that the prosthesis is fixed and functional.[2] Joint debridement and implant retention is supported by the II-ICM-2018 (II International Consensus on Muscleskeletal Infection – 2018), with 80% agreement.[3]

Due to the heterogeneity of the studies, JDIR success rate ranges from 16 to 100%, with an overall average of $\sim$ 50%.[4] Cases of poor results may be related to biofilm formation in a shorter time.[5]

Iza et al.[6] found in a retrospective analysis of cases submitted to JDIR a significant difference between the success rate in patients with acute postoperative infection (93%) and acute hematogenous infection (58%). They also observed a much lower success rate in cases infected with *Staphylococcus aureus* (33%) compared with other bacteria (82%).[6] The low success rate in infections caused by *S. Aureus* has also been reported by several other studies.[7,8]

Two scores were developed to predict the risk of JDIR failure.

The KLIC-Score, described for early acute infection, evaluates 5 factors, assigns points to each one, and calculates the chance of failure according to the score obtained (►**Table 1**).[8]

CRIME80, described for late acute hematogenous infection, defines 7 predictors of outcome (►**Table 2**).[7] The authors found as the main predictor of success the exchange of modular components (polyethylene), so the subtraction of a point when it is performed. According to the score obtained, they attribute the chance of JDIR failure.

The literature is also controversial regarding the impact that a failed JDIR causes in a subsequent treatment with removal of implants.

Rajgopal et al.[9] retrospectively analyzed the results of patients submitted to a 2-stage review and found an increased failure rate, worse functional scores, and a higher rate of wound complications in patients with a previous history of JDIR.

Similarly, Lizaur-Utrilla et al.[10] also found better results in functional scores and range of motion (ROM) in patients who were not submitted to JDIR prior to review in 2 stages.

Kim et al.,[11] however, in a retrospective study, found no difference in the results of patients submitted to review as the first treatment option when compared with those after JDIR failure.

Two-stage review

This method is best indicated in chronic infections, in patients with systemic involvement,[12–14] when bacteria

Table 1 KLIC Score

KLIC-SCORE	
Chronic renal failure *(K for kidney)*	2 points
Liver cirrhosis *(L for liver)*	1.5 point
TKA indication *(I for Index)*	If fracture or revision, 1.5 point
Cemented prosthesis *(C for cement)*	2 points
CRP value *(C for CRP)*	If > 11.5mg/dL, 2.5 points
JDIR Score x chance of failure	
$\leq$ 2 points	4.5%
2.5 to 3.5 points	19.4%
4 to 5 points	55%
5.5 to 6.5 points	71.4%
$\geq$7 points	100%

Abbreviations: CRP, c-reactive protein; JDIR, joint debridement with implant retention; TKA, total knee arthroplasty.

Table 2 CRIME 80 Score

CRIME80	
Chronic obstructive pulmonary disease (*C for COPD*)	2 points
CRP value >15mg/dL *(C for CRP)*	1 point
Rheumatoid Arthritis (R for *Rheumatoid)*	3 points
Indication of prosthesis (*I for Indication*)	if fracture, 3 points
Male *(M for Male)*	1 point
Exchange of modular components *(E for Exchange)*	(–)1 point
Age > 80 years old	2 points
JDIR Score x chance of failure	
(–) 1 point	22%
0 point	28%
1 to 2 points	40%
3 to 4 points	64%
$\geq$ 5 points	79%

Abbreviations: CRP, c-reactive protein; JDIR, joint debridement with implant retention.

identification is not available[12,13] or when it is resistant to available antibiotics (fungi, gram negatives and *S aureus).*[3,13] The technique has few formal contraindications;[3,12] it can be applied at any stage of infection (acute or chronic)[12,13] with high success rates, being considered the gold standard.[15–18] However, two-stage treatment is associated with longer hospitalization time, functional recovery and, consequently, higher costs,[19–21] as well as with higher mortality in 1 postoperative year.[19,22]

The first stage consists of the removal of the prosthesis. At the surgical access, a skin spindle including the previous scar and fistula(s) should be excised.[13,23] At this stage, the implants are removed by the same access of the primary arthroplasty, preserving, as far as possible, the bone stock, followed by broad debridement with the exeresis of all inflammatory and necrotic tissues and of compromised sections of the articular capsule, with the preservation, if possible, of collateral ligaments.[13,21,23,24] Then, the wound, the joint cavity and the medullary canal are irrigated, using pulsatile washing with at least 10 to 12 liters of saline solution, and some antiseptic solution can be used optionally.[21,24]

Fragments of debrided material should be sent for culture and histopathology.[25] The crop must consist of three to six samples from different areas of the knee, with cultivation time of at least 14 days.[13,24,26] The explanted components can be submitted to sonication to break the biofilm and the washing of these components may be sent to culture, which can be useful in cases of infections with negative culture.[26] In situations in which there is positivity for other tissue samples, the positivity of the sonicated fluid should only be taken into account if there are >5 colony forming units (CFUs).[27]

Histopathological tissue analysis may also be a diagnostic confirmation factor in cases with negative synovial fluid cultures and suspected aseptic loosening, with sensitivity of 75% in freezing cuts, with a threshold of 5 PMN/field.[28] Histopathology by perioperative freezing, histopathological analysis by staining and/or immunohistochemistry are very useful; however, they are examiner-dependent, as defined by the CIIM-2018.[28]

After surgery, the patient is accompanied with serial dosage of inflammatory markers and evaluation of local and systemic clinical improvement.[29,30] If there is no improvement, or no reduction in inflammatory markers, a new debridement should be carried out with spacer change.[31] If there is clinical and laboratory improvement, reimplantation is carried out with a prosthesis whose degree of constriction and need for correction of bone failures will be individualized for each case.[3,21] In the review surgery, a new debridement and sample collection is performed for culture and histopathological analysis by freezing in order to evaluate the presence of subclinical persistent infection.[3,24]

Some controversies regarding the 2-stage review, such as the type of spacer, the moment, and the conversion criteria, as well as the period of antibiotic therapy,[13] still need clarification.

Joint spacers are classified as static, mobile, prefabricated or handcrafted.[18,24,32,33] The static ones are better indicated in cases of extensor apparatus insufficiency, large bone defects, wound healing problems, and ligament instability.[3,32] They are associated with complications such as postoperative stiffness and bone loss. This, in particular if there is dislocation of it, more frequent in artisanal spacers and obese patients.[3,13,32,33]

Articulated or mobile spacers can be modeled with antibiotic cement with prefabricated mold,[3,32] a new component,[34,35] or the removed reprocessed with flash sterilization.[36] The advantages of articulated spacers are preserving ROM, a better of quality of life, and lessening the need for extended approaches at the revision1.[8,32,37] Although, some studies hasn't shown statistical differences in ROM between static and articulated spacers in long term, and articulated spacers are associated more frequently with joint instability and breakage, specially in prefabricated spacers.[3,18,33,35]

Yu et al.[38] showed in their systematic review that dynamic spacers with metallic femoral component articulated with tibial polyethylene have higher reinfection rates than spacers made entirely of cement. There is controversy in this regard in the literature.[32,35]

Although most authors did not find superiority among the types of spacers regarding the cure of infection,[3] Romanò et al.,[39] in a systematic review, observed that dynamic spacers have a higher rate of eradication.

The criteria for reimplantation are also grounds for controversy,[16,29,30] because the ability to define whether the infection is cured still requires further studies.[40]

Some authors recommend the review within 6 to 8 weeks.[13] This measure decreases hospitalization costs in relation to protocols that suggest longer intervals, which can extend to up to 16 weeks, without any difference in reinfection rates.[40] Intervals >16 weeks are associated with an increased incidence of relapses.[13,40]

Several parameters for reimplantation were proposed, such as the criteria for diagnosis of periprosthetic infection of the Musculoskeletal Infection Society (MSIS). These criteria include inflammatory markers (C-reactive protein [CPR], Erythrocyte Sedimentation Rate [ESR], and D-Dimers), cytometry, biochemical markers, and aspirate culture.[41] The MSIS infection criteria have high specificity and low sensitivity for persistent infection, with a high positive predictive value (PPV) and a low negative predictive value (NPV),[30] so several persistent infections are underdiagnosed.[26,30]

The leukocyte count of the joint aspirate also has a high NPV at values $<3{,}000$ cells/uL.[16,30] The culture of joint aspirate before the review also has high specificity and low sensitivity for persistent infection, besides a great correlation with the germ of possible reinfections.[24,30,31] It should not be a routine procedure for cases with clinical and laboratory improvement.[31] The II-ICM-2018 could not define a definitive parameter for reimplantation, and even in cases of clinical and laboratory improvement, the persistence of the infection is still suspected.[30]

Perioperative histopathological analysis by freezing has high specificity and PPV, but low sensitivity and NPV.[13,16,30] Meanwhile, Fu et al.[40] found high sensitivity and specificity in their series of 81 cases.

During the review procedure, local conditions should be reevaluated and at least four culture samples must be collected.[24] In the case of positivity, intravenous antibiotic therapy guided by the results should be initiated.[3]

The period of antibiotic therapy is a matter of controversy. The CIIM-2018 suggests a minimum period of 4 to 6 weeks, but the parenteral and oral percentage should be individualized by the microorganism detected in the culture, as well as by the response to treatment.[42] The CIIM-2018 and other studies show that oral antibiotic therapy extended for at least 3 months after review decreases the rate of reinfection.[42] It is worth remembering that these strategies should be decided together with the infectologist and the general practitioner, emphasizing the multidisciplinary character that should guide the treatment of periprosthetic infections.

Studies also try to demonstrate risk factors for treatment failure. Fu et al.[40] found that perioperative biopsy by positive freezing, atypical germs, and presence of fistula had a high rate of reinfection. Surprisingly, infections with negative culture have reinfection rates similar to those of positive culture, and they are not considered a risk factor for failure.[43]

Single-stage review

Single-stage review is indicated when the etiological agent is known, sensitive to available antibiotic therapy, there is no systemic involvement of the patient, and the patient is not immunocompromised.[19,21,44]

It is contraindicated when there is soft tissue injury that does not allow primary closure of the surgical wound, in the presence of nonexcisable fistula with the scar of previous access, in the impossibility of rigorous debridement, in the presence of severe bone defect, when the etiological agent is multiresistant, or in the absence of effective antibiotic therapy against the isolated germ.[44]

Aiming to reduce morbidity and the cost of treatment, the single-stage review seeks to achieve the same results in terms of eradication of infection and durability of the two-stage review.[15,19–22,24] Some studies have shown that single-stage review in selected patients may have similar or even better results[21,45,46] than the two-stage review.[3]

The success of this type of review increases considerably with the prior identification of the etiological agent.[22] Previous joint puncture with synovial fluid cultures for an extended period of 14 days is mandatory.[22,24,47]

Some authors did not find a difference in outcome in single-stage reviews without prior identification of the etiological agent.[14,48,49] There are reports of revisions at a stage performed "inadvertently", when apparently aseptic revisions were actually septic after intraoperative cultures became positive.[19]

Fungal infections by *S. epidermidis* and *S. aureus* have a worse evolution and higher incidence of failures.[3,15,21] Citak et al.[48] show that Enterococcal infection is 14 to 21 times more likely to be reinfected. Klatte et al.,[47] although they indicate single-stage review as an alternative to fungal infection, showed in their results two failures in four cases. Ji et al.[50] show that single-stage revision may be an alternative in fungal infections. However, two of the seven cases presented reinfection, having been treated only with debridement and antifungals.[50]

The presence of fistula is a controversial contraindication for single-stage revision. While some authors have described a high rate of reinfections in patients with fistula,[21,24,46] others did not find significant difference in reinfection compared with those of the two-stage review, since the fistula can be excised along with the surgical scar in the joint capsule.[24,44,46]

The presence of bone defects is also a debatable contraindication to single-stage revision. Zahar et al.[22] define that bone defects should be filled with cement with antibiotics. In 59 patients with a mean follow-up of 10 years, the reinfection rate was of 8.47% (5/59), 7 patients presented with aseptic loosening (11.86%) and there were 25 more patients (42.37%) at high risk of release.[21]

A single-stage review should follow a strict protocol to increase its success rate.[21] The procedure consists of two phases:

First, implants and all cement should be removed, along with broad and aggressive synovectomy, with radical resection of necrotic and devitalized tissues.[15,20,22] However, how aggressive the debridement should be is a controversial issue. Some authors advocate resection of collateral ligaments, which requires the implantation of constricted prosthesis in rotational hinge,[22] while others advocate preservation of the medial collateral ligament (MCL), which allows the use of prosthesis with varus-valgus constriction.[15,51]

In this first phase, at least six fragments of different parts of the knee are sent for culture and histopathology.[15,46] The wound, the medullary canal and the joint are irrigated with 10 to 15 liters of 0.9% saline solution, preferably with pulsatile washing, and an antiseptic, iodinated or chlorhexidine-based solution associated or not with hydrogen peroxide solution of can be used.[15,20–22,46] After irrigation, the wound is temporarily sutured and protected with sterile iodated adhesive field. All surgical and instrumental fields used in explanting and debridement surgery are exchanged and, if possible, exchange or hygiene of the surgical environment itself should be performed.[15,20–22,46]

In a second phase, the patient is prepared with new fields and surgical instruments. The sutures are removed, and the wound is again irrigated with 0.9% saline solution. The prosthesis is implanted using cement with integrated antibiotic, not exceeding 10% of the weight-dose, according to the antibiogram of the infectious agent.[15,21,22,46,47] Rods are used to improve the stability of the prosthesis to the bone, and this should have appropriate constriction for the case.[22,46] Bone defects should be addressed according to their size, with small flaws being filled with cement and larger flaws with wedges, blocks, or metal cones, avoiding the use of allograft.[15,46]

In the 2018 consensus, the recommended period for intravenous antibiotic therapy after single-stage review is 7 to 14 days, followed by oral antibiotic therapy for a total period of 6 to 8 weeks, with a limited level of evidence and

73% agreement,[52] which is corroborated by other authors.[22,46] However, several studies show that extended parenteral antibiotic therapy protocols for 6 weeks decrease reinfection rates.[15,21,42]

It is worth remembering, once again, that the antibiotic therapy strategy, as well as the many adverse reactions related to its use, should be managed in a multidisciplinary manner with the help of the infectologist and of the general practitioner.

Single-stage and two-stage review

Single-stage revisions, in selected cases, have a lower or similar reinfection rate to two-stage revisions. It presents as advantages lower costs, lower mortality rate, shorter hospitalization time and functional recovery. Thus, if there are no contraindications, this option should be considered.[19]

A meta-analysis of 2016 that analyzed 10 single-stage review studies against 108 two-stage review studies, found similar reinfection rates of ~6.4%.[53]

Thakrar et al.,[14] in a 2019 systematic review, showed comparable results in single- and two-stage reviews in relation to the reinfection index in patients without systemic or immunocompromised involvement. However, they pointed out that most studies are retrospective or observational and lack quality studies such as randomized clinical trials.

It is important to note that, while at the 2013 IIC the agreement rate among panelists on the indications and contraindications of the single-stage review was 78%,[54] at the 2018 IIM, with evaluation of more studies, the agreement was of 93%, with a moderate level of evidence.[44]

Rescue measures

In cases of periprosthetic knee infection refractory to previous treatments, treatment options consist of:

- arthrodesis
- transfemoral amputation
- resection arthroplasty
- antibiotic suppression

Rescue measures should be indicated early for patients who have many comorbidities.[3] In cases of treatment failure in patients without many comorbidities, it can be treated with another two-stage review attempt. McPherson type C hosts have better results with arthrodesis or amputation.[3]

The functional result of arthrodesis has been shown to be superior to that of amputation. Few amputee patients can adapt to the prosthesis and walk again.[3,55] On the other hand, most patients submitted to arthrodesis have preserved walking capacity.[3] In the study by Mozella et al.,[56] 44% of the patients submitted to amputation were able to be protetized, only 27.78% were community ambulators and 56% became wheelchair users.

Patients classified as host type C and with soft tissue involvement requiring coverage procedures have a high rate of recurrence of infection requiring arthrodesis, amputation or antibiotic suppression.[57,58]

Resection arthroplasty has the theoretical advantages of limb preservation, of no need for implants or synthesis material, possibility of knee flexion and theoretical gait capacity with immobilizer and compensation of dysmetry.[59]

Antibiotic suppression is indicated as a rescue measure in patients who are unable to undergo new surgical procedures.[55] Antibiotic toxicity, oral availability and infection suppression capacity should be considered in order to indicate this type of treatment.[55]

Conflict of Interests
The authors declare that there is a conflict of interest. Dr. Barreto reports personal fees from Stryker Latin America, outside the submitted work.

References

1 Argenson JN, Arndt M, Babis G, et al. Hip and Knee Section, Treatment, Debridement and Retention of Implant: Proceedings of International Consensus on Orthopedic Infections. J Arthroplasty 2019;34(2S):S399–S419
2 Osmon DR, Berbari EF, Berendt AR, et al. Infectious Diseases Society of America. Diagnosis and management of prosthetic joint infection: clinical practice guidelines by the Infectious Diseases Society of America. Clin Infect Dis 2013;56(01):e1–e25
3 Parvizi J, Gehrke T. Anais do 2o. Encontro do Consenso Internacional (ICM) em Infecção Musculoesqueletica [Internet]. ICM Philly 2019 [citado 22 de março de 2020]. Disponível em: https://icmphilly.com/document/icm-document-translations/icm-document-portugues-brasil-translation/
4 Choo KJ, Austin M, Parvizi J. Irrigation and Debridement, Modular Exchange, and Implant Retention for Acute Periprosthetic Infection After Total Knee Arthroplasty. JBJS Essential Surg Tech 2019;9(04):e38
5 Son WS, Shon OJ, Lee DC, Park SJ, Yang HS. Efficacy of Open Debridement and Polyethylene Exchange in Strictly Selected Patients with Infection after Total Knee Arthroplasty. Knee Surg Relat Res 2017;29(03):172–179
6 Iza K, Foruria X, Moreta J, et al. DAIR (Debridement, Antibiotics and Implant Retention) less effective in hematogenous total knee arthroplasty infections. J Orthop Surg Res 2019;14(01):278
7 Wouthuyzen-Bakker M, Sebillotte M, Lomas J, et al. ESCMID Study Group for Implant-Associated Infections (ESGIAI) Clinical outcome and risk factors for failure in late acute prosthetic joint infections treated with debridement and implant retention. J Infect 2019;78(01):40–47
8 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(08):786.e9–786.e17
9 Rajgopal A, Panda I, Rao A, Dahiya V, Gupta H. Does Prior Failed Debridement Compromise the Outcome of Subsequent Two-Stage Revision Done for Periprosthetic Joint Infection Following Total Knee Arthroplasty? J Arthroplasty 2018;33(08):2588–2594
10 Lizaur-Utrilla A, Asensio-Pascual A, Gonzalez-Parreño S, Miralles-Muñoz FA, Lopez-Prats FA. Negative impact of prior debridement on functional outcome of subsequent two-stage revision for early knee periprosthetic infection. Knee Surg Sports Traumatol Arthrosc 2019;27(07):2309–2315
11 Kim K, Zhu M, Cavadino A, Munro JT, Young SW. Failed Debridement and Implant Retention Does Not Compromise the Success of Subsequent Staged Revision in Infected Total Knee Arthroplasty. J Arthroplasty 2019;34(06):1214–1220.e1
12 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(08): 495–502
13 Kini SG, Gabr A, Das R, Sukeik M, Haddad FS. Two-stage Revision for Periprosthetic Hip and Knee Joint Infections. Open Orthop J 2016;10(Suppl-2, M2):579–588
14 Thakrar RR, Horriat S, Kayani B, Haddad FS. Indications for a single-stage exchange arthroplasty for chronic prosthetic joint infection: a systematic review. Bone Joint J 2019;101-B(1_Supple_A, Suppl A)19–24
15 George DA, Konan S, Haddad FS. Single-Stage Hip and Knee Exchange for Periprosthetic Joint Infection. J Arthroplasty 2015; 30(12):2264–2270
16 Lee YS, Chen AF. Two-Stage Reimplantation in Infected Total Knee Arthroplasty. Knee Surg Relat Res 2018;30(02):107–114
17 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(08):e1629
18 Lichstein P, Su S, Hedlund H, et al. Treatment of Periprosthetic Knee Infection With a Two-stage Protocol Using Static Spacers. Clin Orthop Relat Res 2016;474(01):120–125
19 Negus JJ, Gifford PB, Haddad FS. Single-Stage Revision Arthroplasty for Infection-An Underutilized Treatment Strategy. J Arthroplasty 2017;32(07):2051–2055
20 Rowan FE, Donaldson MJ, Pietrzak JR, Haddad FS. The Role of One-Stage Exchange for Prosthetic Joint Infection. Curr Rev Musculoskelet Med 2018;11(03):370–379
21 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(01):8–14
22 Zahar A, Kendoff DO, Klatte TO, Gehrke TA. Can Good Infection Control Be Obtained in One-stage Exchange of the Infected TKA to a Rotating Hinge Design? 10-year Results. Clin Orthop Relat Res 2016;474(01):81–87
23 Bonanzinga T, Tanzi G, Iacono F, Ferrari MC, Marcacci M. Periprosthetic knee infection: two stage revision surgery. Acta Biomed 2017;88(4S):114–119
24 Gehrke T, Alijanipour P, Parvizi J. The management of an infected total knee arthroplasty. Bone Joint J 2015;97-B(10, Suppl A)20–29
25 Barton CB, Wang DL, An Q, Brown TS, Callaghan JJ, Otero JE. Two-Stage Exchange Arthroplasty for Periprosthetic Joint Infection Following Total Hip or Knee Arthroplasty Is Associated With High Attrition Rate and Mortality. J Arthroplasty 2019;•••: S0883540319311374
26 Abdel MP, Akgün D, Akin G, et al. Hip and Knee Section, Diagnosis, Pathogen Isolation, Culture: Proceedings of International Consensus on Orthopedic Infections. J Arthroplasty 2019;34(2S): S361–S367
27 Ascione T, Barrack R, Benito N, et al. General Assembly, Diagnosis, Pathogen Isolation - Culture Matters: Proceedings of International Consensus on Orthopedic Infections. J Arthroplasty 2019;34 (2S):S197–S206
28 Bauer TW, Bedair H, Creech JD, et al. Hip and Knee Section, Diagnosis, Laboratory Tests: Proceedings of International Consensus on Orthopedic Infections. J Arthroplasty 2019;34(2S): S351–S359
29 Aalirezaie A, Abolghasemian M, Busato T, et al. Hip and Knee Section, Treatment, Two-Stage Exchange: Proceedings of International Consensus on Orthopedic Infections. J Arthroplasty 2019; 34(2S):S439–S443
30 Aalirezaie A, Bauer TW, Fayaz H, et al. Hip and Knee Section, Diagnosis, Reimplantation: Proceedings of International Consensus on Orthopedic Infections. J Arthroplasty 2019;34(2S): S369–S379
31 Preininger B, Janz V, von Roth P, Trampuz A, Perka CF, Pfitzner T. Inadequacy of Joint Aspiration for Detection of Persistent Periprosthetic Infection During Two-Stage Septic Revision Knee Surgery. Orthopedics 2017;40(04):231–234
32 Mazzucchelli L, Rosso F, Marmotti A, Bonasia DE, Bruzzone M, Rossi R. The use of spacers (static and mobile) in infection knee arthroplasty. Curr Rev Musculoskelet Med 2015;8(04):373–382
33 Faschingbauer M, Bieger R, Reichel H, Weiner C, Kappe T. Complications associated with 133 static, antibiotic-laden spacers after TKA. Knee Surg Sports Traumatol Arthrosc 2016;24(10): 3096–3099
34 Drexler M, Dwyer T, Kuzyk PRT, et al. The results of two-stage revision TKA using Ceftazidime-Vancomycin-impregnated cement articulating spacers in Tsukayama Type II periprosthetic joint infections. Knee Surg Sports Traumatol Arthrosc 2016;24 (10):3122–3130
35 Siddiqi A, Nace J, George NE, et al. Primary Total Knee Arthroplasty Implants as Functional Prosthetic Spacers for Definitive Management of Periprosthetic Joint Infection: A Multicenter Study. J Arthroplasty 2019;34(12):3040–3047
36 Chen YP, Wu CC, Ho WP. Autoclaved metal-on-cement spacer versus static spacer in two-stage revision in periprosthetic knee infection. Indian J Orthop 2016;50(02):146–153
37 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(04):256–261
38 Yu Q, Luo M, Wu S, et al. Comparison of infection eradication rate of using articulating spacers containing bio-inert materials versus all-cement articulating spacers in revision of infected TKA: a systematic review and meta-analysis. Arch Orthop Trauma Surg 2019;139(05):695–707
39 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
40 Fu J, Ni M, Li H, et al. The proper timing of second-stage revision in treating periprosthetic knee infection: reliable indicators and risk factors. J Orthop Surg Res 2018;13(01):214
41 Amanatullah D, Dennis D, Oltra EG, et al. Hip and Knee Section, Diagnosis, Definitions: Proceedings of International Consensus on Orthopedic Infections. J Arthroplasty 2019;34(2S):S329–S337
42 de Beaubien B, Belden K, Bell K, et al. Hip and Knee Section, Treatment, Antimicrobials: Proceedings of International Consensus on Orthopedic Infections. J Arthroplasty 2019;34(2S):S477–S482
43 Li H, Ni M, Li X, Zhang Q, Li X, Chen J. Two-stage revisions for culture-negative infected total knee arthroplasties: A five-year outcome in comparison with one-stage and two-stage revisions for culture-positive cases. J Orthop Sci 2017;22(02):306–312
44 Bialecki J, Bucsi L, Fernando N, et al. Hip and Knee Section, Treatment, One Stage Exchange: Proceedings of International Consensus on Orthopedic Infections. J Arthroplasty 2019;34 (2S):S421–S426
45 Capuano N, Logoluso N, Gallazzi E, Drago L, Romanò CL. One-stage exchange with antibacterial hydrogel coated implants provides similar results to two-stage revision, without the coating, for the treatment of peri-prosthetic infection. Knee Surg Sports Traumatol Arthrosc 2018;26(11):3362–3367
46 Kendoff D, Gehrke T. Surgical management of periprosthetic joint infection: one-stage exchange. J Knee Surg 2014;27(04):273–278
47 Klatte TO, Kendoff D, Kamath AF, et al. Single-stage revision for fungal peri-prosthetic joint infection: a single-centre experience. Bone Joint J 2014;96-B(04):492–496
48 Citak M, Friedenstab J, Abdelaziz H, et al. Risk Factors for Failure After 1-Stage Exchange Total Knee Arthroplasty in the Management of Periprosthetic Joint Infection. J Bone Joint Surg Am 2019; 101(12):1061–1069
49 Wang HY, Zhang Md R, Luo ZY, et al. One-Stage Arthroplasty or Revision for Seronegative Infections in Hip and Knee. Orthop Surg 2020;12(01):38–49

50 Ji B, Zhang X, Xu B, Guo W, Mu W, Cao L. Single-Stage Revision for Chronic Fungal Periprosthetic Joint Infection: An Average of 5 Years of Follow-Up. J Arthroplasty 2017;32(08):2523–2530
51 Holland G, Brown G, Goudie S, Brenkel I, Walmsley PJ. Results of Using a "2-in-1" Single-Stage Revision Total Knee Arthroplasty for Infection with Associated Bone Loss: Prospective 2-Year Follow-Up. J Knee Surg 2021;34(05):526–532
52 Anemüller R, Belden K, Brause B, et al. Hip and Knee Section, Treatment, Antimicrobials: Proceedings of International Consensus on Orthopedic Infections. J Arthroplasty 2019;34(2S):S463–S475
53 Kunutsor SK, Whitehouse MR, Lenguerrand E, Blom AW, Beswick ADINFORM Team. Re-Infection Outcomes Following One- And Two-Stage Surgical Revision of Infected Knee Prosthesis: A Systematic Review and Meta-Analysis. PLoS One 2016;11(03):e0151537
54 Lichstein P, Gehrke T, Lombardi A, et al. One-stage vs two-stage exchange. J Arthroplasty 2014;29(2, Suppl)108–111
55 Troendlin F, Frieler S, Hanusrichter Y, Yilmaz E, Schildhauer TA, Baecker H. Persistent Fistula for Treatment of a Failed Periprosthetic Joint Infection: Relic From the Past or a Viable Salvage Procedure? J Arthroplasty 2020;35(02):544–549
56 Mozella AP, Palma IM, Souza AF, Gouget GO, Cobra HA. Amputação após falha ou complicação de artroplastia total de joelho: incidência, etiologia e resultados funcionais. Rev Bras Ortop 2013;48 (05):406–411
57 Warren SI, Murtaugh TS, Lakra A, et al. Treatment of Periprosthetic Knee Infection With Concurrent Rotational Muscle Flap Coverage Is Associated With High Failure Rates. J Arthroplasty 2018;33(10):3263–3267
58 Matar HE, Stritch P, Emms N. Higher failure rate of two-stage revision for infected knee arthroplasties in significantly compromised (host-C) patients. Knee Surg Sports Traumatol Arthrosc 2019;27(07):2206–2210
59 Goldman AH, Clark NJ, Taunton MJ, Lewallen DG, Berry DJ, Abdel MP. Definitive Resection Arthroplasty of the Knee: A Surprisingly Viable Treatment to Manage Intractable Infection in Selected Patients. J Arthroplasty 2020;35(03):855–858