Strategies in prevention and treatment of prosthetic joint infections

Veltman, E.S.

CHAPTER

5

Hip and Knee Section, Treatment, Two-Stage Exchange:

Proceedings of International Consensus on Orthopaedic Infections

(J Arthroplasty. 2019 Feb;34(2S):S439-S443.)

Arash Aalirezaie
Mansour Abolghasemian
Thiago Busato
Douglas Dennis
Mohammad Ghazavi
Michael Kelly
Yair D. Kissin
Martijn Kuijpers
Jeffrey Lange
Paul Lichstein
Dirk-Jan F. Moojen
Rudolf W. Poolman
Berend W. Schreurs
Job Diego Velazquez Moreno
Ewout S. Veltman

QUESTION 1:

What is the optimal timing for reimplantation of a 2-stage exchange arthroplasty of the hip and knee?

Recommendation:

The optimal timing for reimplantation of a 2-stage exchange arthroplasty of the hip or knee has not been established. Reimplantation may be performed when the treating medical team feels that the infection is under control.

Level of Evidence: Moderate
Delegate Vote: Agree: 93%, Disagree: 4%, Abstain: 3% (Super Majority, Strong Consensus)

Rationale:

There is no conclusive evidence for defining the optimal timing between resection arthroplasty and reimplantation in a 2-stage revision arthroplasty for periprosthetic joint infections (PJIs). Multiple studies have reported time to reimplantation ranging from a few weeks to several months or even years.[1-11] Literature has used various definitions for PJI 2-stage treatment success or failure as well as different variables influencing the timing of reimplantation. Due to this heterogeneity, they have failed to answer this question. Success of treatment with a 2-stage arthroplasty varies between <70% and 100%, with no direct correlation to the spacer time interval.[1,2,6,7,9,11]

Several studies have reported on time to reimplantation and its influence on success or failure. Haddad et al reported no increase in reinfection rates by reducing the interval to 3 weeks.[5] Sabry et al found that an increased duration between resection and reimplantation was associated with higher rates of infection recurrence in a cohort of 314 infected TKAs treated with 2-stage exchange arthroplasty.[7] Their median interval between stages was 103 days (range, 2-470 days). A study by Kubista et al also found that a longer time period between spacer insertion and reimplantation was associated with increased PJI recurrence.[8] In contrast, Babis et al obtained a 100% success rate when using a long interval - mean 9 months (range, 8-12 months) in a group of patients with a high percentage of multi-resistant bacteria.[9]

One common belief is that a delayed second stage or reimplantation will result in higher rate of treatment success. However, this is not based on strong evidence and may lead to an unnecessary long inter-stage interval with its associated morbidity.

Aali-Rezaie et al, in a recent, large retrospective cohort study evaluating patients with 2-stage exchange arthroplasty, did not detect a clear association between time to reimplantation and treatment failure.[10] Furthermore, they found that delaying the time to reimplantation did not significantly improve treatment success of 2-stage exchange arthroplasty. In addition, Vielgut et al found, in a study of 76 hip infections, that patients who had their reimplantation between 4 and 11 weeks had a significantly higher success rate when compared to less than 4 and greater than 11 weeks.[6]

When deciding on the optimal timing for reimplantation, most surgeons prefer to rely on a combination of clinical evaluations, such as a completely healed wound, no pain, and serologic tests trending downward after a period of antibiotic therapy.[11] Various studies recommend a complete work up with normalized laboratory and clinical variables to assure infection control before reimplantation.

QUESTION 2:

Is it safe to retain a stable cement mantle, for later use, in patients undergoing resection arthroplasty for periprosthetic joint infections (PJIs)?

Recommendation:

Meticulous debridement and removal of all foreign material, including cement, should be part of resection arthroplasty in the management of periprosthetic joint infections (PJIs). Limited data suggest that under strict conditions and following a meticulous surgical technique, a stable cement mantle in the femur may be left in place for later use in order to minimize damage to the femoral bone stock.

Level of Evidence:	Limited
Delegate Vote:	Agree: 63%, Disagree: 29%, Abstain: 8% (Super Majority, Weak Consensus)

Rationale:

Historically, resection arthroplasty for periprosthetic joint infections (PJIs) involved removal of all the foreign material including cement, as these materials can act as a nidus for the biofilm and persistence of infection.[12-16] However, removal of the cement mantle increases operative time and causes increased morbidity through bone loss and fractures. The in-cement revision technique is a useful, well-described technique used

in aseptic conditions to avoid the tedious task of cement removal and therefore avoid complications associated with cement extraction.[17-21] Retention of an intact cement mantle in cases of resection arthroplasty for PJI would be preferable to avoid the morbidity associated with its removal and would make subsequent reimplantation technically easier.

The concern for retaining cement in the setting of PJI has been supported by in vitro studies. Kendall et al examined microbial growth of staphylococcal species on the surface of antibiotic-loaded cement discs incubated in broth. While the broth itself was sterilized by the discs after 96 hours, growth was consistently seen on the surface of the cement discs themselves. The cement, therefore, seemed to be a habitable surface for continued growth of bacteria, despite elution of antibiotics.[22] Mariconda et al demonstrated that fluid around antibiotic-loaded cement that is sonicated can yield positive cultures, even if aspiration fluid was culture-negative, indicating that biofilms can persist on antibiotic-loaded cement.[23] Tunney et al and Minelli et al showed that the biofilm could form even on antibiotic-loaded cement, depending on the inoculum and the type and dosing of the antibiotic agent.[24,25] Although Griffin et al could not demonstrate biofilm formation in explanted spacers, Ma et al demonstrated that 30.7% of spacers had bacterial contamination at the time of the second stage.[26,27] This laboratory data should give some cause for concern for the retention of cement in the setting of infection, even if loaded with antibiotics.

The clinical data on this topic are extremely limited. There are 2 case series that examine this specific issue, both involving a stable cement mantle in revision total hip arthroplasty for infection. Morley et al reviewed 15 total hips with 2-stage revisions for PJIs while retaining the original cement mantle, and reported infection-free outcomes in 14 of 15 patients.[28] The authors used very strict selection criteria for the patient cohort including a stable cement mantle, prior use of antibiotic loaded cement, and meticulous burring of the cement mantle to remove the biofilm and liberate antibiotics as vital to the success of this technique. In a similar study, however, Leijtens et al reported success in only two of 10 patients undergoing 2-stage revision total hip arthroplasty for infection at an average of 26 months.[29] It should be noted that this study did not mention whether the existing cement mantle contained antibiotics or not.

There is only one level IV study showing good results with a retained stable cement mantle for later use in resection arthroplasty in the treatment of PJIs. Although this technique presents theoretical advantages, there is a lack of robust evidence in the

literature to support its routine use. Direction for further research might include the use of chemical debridement agents, such as dilute povidone-iodine, chlorhexidine irrigation, and/or acetic acid preparations, which some evidence suggests might help eradicating microbes and biofilms in some settings.[30] The role of chemical debridement agents in eliminating sessile bacteria and biofilms on the surface of retained cement has yet to be explored. With further research, the answer to this question might become known.

QUESTION 3:

Should surgeons make an effort to remove cement that has extruded into the pelvis or at difficult anatomical positions in patients with periprosthetic joint infections (PJIs)?

Recommendation:

The orthopaedic surgeon should carefully consider whether the potential benefits of cement extraction from the pelvis or difficult anatomical positions outweigh the potential risks of persistence of infection.

Level of Evidence:	Consensus
Delegate Vote:	Agree: 85%, Disagree: 9%, Abstain: 6% (Super Majority, Strong Consensus)

Rationale:

Extrusion of cement during primary arthroplasty is reported to occur in 25% of patients.[31] Bacteria can form a biofilm on foreign bodies in patients with prosthetic joint infections.[32] Therefore, in patients with periprosthetic joint infections (PJIs), who are undergoing resection arthroplasty, it is recommended that the prosthesis and all foreign material including bone cement be removed and thorough debridement performed. Whether or not cement in the pelvis or in difficult anatomic positions contributes to the risk of persistent infection after revision arthroplasty has not been studied.

When cement is extruded into the pelvis or difficult anatomic positions during primary arthroplasty, there is a risk of neurological (obturator nerve palsy, femoral or sciatic nerve involvement), urological (such as a foreign body in the bladder wall), or vascular (with compression of the external iliac vein) complications.[33-38] During extraction of

extruded cement, the risk of these complications may be even greater due to the manipulation needed for extraction.

It is common wisdom and belief among surgeons that foreign material in an infected joint may harbor the biofilm formed by the infecting organism. Leaving behind foreign material during resection arthroplasty and debridement, thus, runs the theoretical risk of allowing for the biofilm and infection to persist and could therefore potentially jeopardize the success of surgical debridement. The latter dogma has actually never been proven in a conclusive study. It is also known that removal of foreign material, such as cement, from anatomically sensitive and/or inaccessible areas may require a wider surgical approach (such as laparotomy for extruded cement into the pelvis) or manipulation of structures such as organs (e.g., bladder, bowel), vessels (e.g., vena cava or major veins), or nerves (e.g., sciatic or plexus). The manipulation of these structures may threaten the life of the patient and/or lead to catastrophic complications. Thus, we believe surgeons should exercise their wisdom when dealing with patients with PJIs and extruded cement or other foreign materials in anatomically sensitive and/or inaccessible areas.

QUESTION 4:

Does the use of non-antibiotic impregnated allograft for bone defects during reimplantation increase the risk of recurrence of SSIs/PJIs?

Recommendation:

There is no evidence to demonstrate that using non-antibiotic impregnated allograft for management of bone defects during reimplantation (following PJIs) increases the risk of recurrence of SSIs/PJIs.

Level of Evidence:	Limited
Delegate Vote:	Agree: 88%, Disagree: 9%, Abstain: 3% (Super Majority, Strong Consensus)

Rationale:

Systematic reviews were undertaken using PubMed, Cochrane Library, SCOPUS, and Google Scholars databases and relevant papers were reviewed. During review, it became evident that there is a dearth of information directly assessing treatment of periprosthetic joint infections (PJIs) when a non-antibiotic impregnated allograft was

used. Overall, 51 articles were reviewed in full. The evidence is summarized in the following paragraphs.

Following the increased popularity of the use of allograft bone in tumor surgery in 1970s, infection has become a major concern.[39] The early reports of infection rates range from 13.2% by Mankin et al to 11.7% by Lord et al and were followed by 7.9% in a comprehensive report by Mankin et al in 2005.[40-42] All authors believed that higher rates of infection could be attributed to the disease nature, extent, duration, and complexity of the procedures and not related to the allograft itself.[40-42]

Tomford et al in a retrospective study reviewed 324 patients who received allografts and showed a negligible clinical incidence of infection.[43] The incidence related to the use of large allografts was approximately 5% in bone tumor and 4% in revision of a hip arthroplasty. These rates of infection were not substantially different from those that have been reported in similar series in which sterilized prosthetic devices were used.[44] One of the early reports of allografts in revision total hip arthroplasty (THA) was published by Berry et al.[44] They used bone allografts in 18 patients during 2-stage revision of septic THA failures. At a mean of 4.2 years after reimplantation, only 2 patients had a recurrence of the infection (11%).

Several retrospective cohort studies have evaluated the use of allograft bone during total hip reimplantation surgery, the second stage of planned 2-stage exchange arthroplasty for infection. The majority of these studies have demonstrated recurrent infection rates of 0 to 9% in cohorts consisting of 11-27 patients with midterm to long-term follow-up.[5,44-49] Two studies reported less favourable reinfection rates of 11% (18 patients, mean 4.2 year follow-up) and 14% (57 patients, mean 9 year follow-up) .[50,51]

Traore et al reported a higher rate of 20% for reinfection at mean 3 years.[50] Loty et al reported a cohort of 90 cases with 8 (9%) reinfections over an unknown follow-up period in 1-stage hip revision for infection.[51] Lange et al performed a systematic review on using bulk allograft for second-stage reimplantation of hip arthroplasty and revealed a reinfection rate of four of 43 (9.3%) at an average follow-up of 6 years.[52] This was comparable to the reinfection rate reported for 2-stage revision without using allograft. Alexeeff et al also had no recurrence of infection in 11 septic failures of THA that underwent 2-stage revision THA using massive structural allografts and were followed for an average of 47.8 months.[48]

Tsahakis et al reported on 15 cases that used allograft for revision knee surgery, and of the three infected knees in their case series, there was no recurrence of infection.[53] Wilde et al performed a retrospective review of 16 revisions TKAs with allograft.[54] There were two infected cases and neither of these experienced reinfection. Stockley et al reviewed 32 deep-frozen irradiated allografts used for the reconstruction of bone defects in 20 knees with an average follow-up of 4.2 years.[55] Three knees developed infection (9.3%), and one of these was a revision for infection. However, they did not believe that the allograft was the source of sepsis.

Further reports by Harris et al (14 patients including 2 infected cases), Mow et al (15 structural allografts), and Engh et al (35 allografts), examined revision TKA cases and found no cases of reinfection.[56-58] Ghazavi et al reported 3 infections (7%) using bulk allograft in 38 patients including 3 infections that underwent revision. Two of the 3 cases who had previous infections experienced reinfection.[59] In a report by Clatworthy et al on 52 cases, there were 6 infections, all of which underwent revision TKA with a bulk allograft. One of the 6 patients who had a previous infection developed recurrence of infection.[60]

English et al reported their results of using impaction allografting in the second-stage reimplantation of 53 infected hip arthroplasties.[61] After a mean follow-up of 53 months, 4 patients had recurrence of infection (7.5%). In reports by Dennis et al (32 allografts) and Garino et al (8 cases of impaction allografts), there were no infections at final follow-up.[62,63]

Hockman et al reviewed 65 consecutive revision TKAs including 12 infections at a minimum 5-year follow-up.[64] Three of the 12 (25%) previously infected cases developed infections. They concluded that knees originally revised for infection were more likely to fail. Bush et al reviewed options for reconstructing massive bone loss and recommended against using allograft in some situations including chronic infections.[65] Backstein et al reported 68 cases of massive allografts for revision TKA, and 11 of these were septic revisions.[66] They found 4 infections (6.5%). The authors did not include how many of them had surgery for septic revisions. They believed that because of the large size of the used allograft bone and the number of previous surgeries the patients had, the infection rate was modest.

Lotke et al reported on 48 cases including one infection that received impaction allografting in revision TKA.[67] At an average follow-up of 3.8 years, they had 2 infections

(5%). Bezwada et al reviewed 11 knees in 10 patients who underwent revision with distal femoral allografts and stemmed components.[68] After a mean follow-up of 42 months, they had no infections. They recommended against the use of plate fixation to decrease extensive soft tissue dissection and the risk of infection.

Engh et al reported no cases of reinfection in 49 revision knees with severe tibial bone defects, 5 of which were revisions for infection.[69] Rudelli et al reported on 32 loose and infected total hip arthroplasties that underwent revision with a bone graft in a 1-stage procedure.[70] After a mean follow-up of 103 months, infection recurred in 2 (6.2%) cases.

Burnett et al reported on 28 knees that underwent revision TKA with an allograft at a follow-up of 48 months.[71] Only 1 patient (3.5%), who received cancellous graft for a contained defect, developed an infection. They did not mention if this was an infected revision. Lyall et al investigated 15 revision TKA patients, including 3 revisions for infections with severe tibial bone loss.[72] These patients were followed for a mean of 5.4 years, and they found 1 (6%) recurrence of infection at 3.5 years.

Bauman et al retrospectively reviewed 74 patients (79 knees) who had revision TKAs with structural allografts.[73] Of this cohort, 65 patients (70 knees) were followed for a minimum of 5 years or until revision or death. Five of 16 failures were secondary to infection (7.1%). Two of these patients had a history of infection and 2 had local wound problems at the time of revision surgery requiring muscle flap or skin grafting. The authors concluded that the large bulk allografts were more likely to fail secondary to infection or non-union.

In an overview on management of bone loss in revision TKR, Lombardi et al did not mention infection as a disadvantage (i.e., late resorption, fracture, non-union, or risk of disease transmission) of using an allograft.[74] Lee et al retrospectively reviewed 27 patients who underwent 2-stage revision arthroplasty using structural allografts to treat massive bone defects in infected hip arthroplasty.[49] After a mean follow-up of 8.2 years, only 1 patient (3.7%) experienced a reinfection.

Richards et al reported on a cohort of 24 patients reconstructed with femoral head allografts at the time of revision TKA and they compared them to 48 cases without allograft. All reported quality of life scores were higher in the allograft group.[75] They did not observe any failures. Wang et al reported 28 patients with femoral head allografts for revision TKA at a mean follow-up of 76 months.[76] They had no complications and no

infections. Vasso et al reviewed multiple papers on options for management of bone loss in revision TKA.[77] They concluded that modular metal and tantalum augmentation may considerably shorten operative times with a potential decrease in the incidence of complications including infection associated with the use of allografts. In a review of 27 patients who had undergone revision TKA using a fresh frozen femoral head allograft and followed for 107 months, there was 1 (3.7%) recurrence of infection.[78]

Recently, Beckmann et al performed a systematic review on the treatment of revision TKA with bony structural allografts (overall including 476 cases) and porous metal cones (overall including 223 cases).[79] They compared the failure rates using a regression model with adjustment for discrepancies in follow-up time and number of grafts used (femoral, tibial, or both). They did not separate septic revisions from aseptic revisions, but there was little difference in the infection rates between allograft and porous metal groups.

Mancuso et al also reviewed the available English literature since 2007 on options for reconstruction of bone defects in revision TKA.[80] Infection was reported in eight of 271 (3%) allografts, 43 of 662 (6%) metal cones, and 27 of 901 (3%) sleeves, indicating that the use of allografts did not lead to a higher rate of infection than metal cones or sleeves.

Sandiford et al compared femoral head structural allografts and trabecular metal cones for the management of severe bone defects during revision TKA.[81] They evaluated 30 allografts and 15 metal cones at a mean follow-up of 9 years and found no differences in pain, function, or repeat revision. The reason for revision was infection in 2 patients. They observed no reinfection in either group, although 1 patient in the allograft group developed a periprosthetic fracture and developed an infection after treatment of this fracture.

Infection is the major cause of failure in revision TKA (44.1%) [69] and the risk is even higher in patients with septic revisions.[69,82] However, given the absence of any prospective controlled studies, the paucity of comparative studies with control groups, and the conflicting data in case series, we could not reach any conclusion regarding the effect of using an allograft on the rate of infection in revision arthroplasty for septic failures.

REFERENCES

[1] Lange J, Troelsen A, Søballe K. Chronic periprosthetic hip joint infection. A retrospective, observational study on the treatment strategy and prognosis in 130 non-selected patients. PLoS One 2016;11:e0163457. https://doi.org/10.1371/journal.pone.0163457.

[2] Sakellariou VI, Poultsides LA, Vasilakakos T, Sculco P, Ma Y, Sculco TP. Risk factors for recurrence of periprosthetic knee infection. J Arthroplasty 2015;30:1618e22. https://doi.org/10.1016/j.arth.2015.04.005.

[3] Mortazavi SM, Vegari D, Ho A, Zmistowski B, Parvizi J. Two-stage exchange arthroplasty for infected total knee arthroplasty: predictors of failure. Clin Orthop Relat Res 2011;469:3049e54. https://doi.org/10.1007/s11999-011-2030-8.

[4] Wimmer MD, Randau TM, Petersdorf S, Pagenstert GI, Weißkopf M, Wirtz DC, et al. Evaluation of an interdisciplinary therapy algorithm in patients with prosthetic joint infections. Int Orthop 2013;37:2271e8. https://doi.org/10.1007/s00264-013-1995-1.

[5] Haddad FS, Muirhead-Allwood SK, Manktelow AR, Bacarese-Hamilton I. Two-stage uncemented revision hip arthroplasty for infection. Bone Joint J 2000;82-B:689e94.

[6] Vielgut I, Sadoghi P, Wolf M, Holzer L, Leithner A, Schwantzer G, et al. Two-stage revision of prosthetic hip joint infections using antibiotic-loaded cement spacers: when is the best time to perform the second stage? Int Orthop 2015;39:1731e6. https://doi.org/10.1007/s00264-015-2751-5.

[7] Sabry FY, Buller L, Ahmed S, Klika AK, Barsoum WK. Preoperative prediction of failure following two-stage revision for knee prosthetic joint infections. J Arthroplasty 2014;29:115e21. https://doi.org/10.1016/j.arth.2013.04.016.

[8] Kubista B, Hartzler RU, Wood CM, Osmon DR, Hanssen AD, Lewallen DG. Reinfection after two-stage revision for periprosthetic infection of total knee arthroplasty. Int Orthop 2012;36:65e71. https://doi.org/10.1007/s00264-011-1267-x.

[9] Babis GC, Sakellariou VI, Pantos PG, Sasalos GG, Stavropoulos NA. Two-stage revision protocol in multidrug resistant periprosthetic infection following total hip arthroplasty using a long interval between stages. J Arthroplasty 2015;30:1602e6. https://doi.org/10.1016/j.arth.2015.04.004.

[10] Aalirezaie A, Goswami K, Shohat N, Tokarski A, White A, Parvizi J. Time to reimplantation: waiting longer confers no added benefit. J Arthroplasty 2018;33:1850e4. https://doi.org/10.1016/j.arth.2018.01.073.

[11] Triantafyllopoulos GK, Memtsoudis SG, Zhang W, Ma Y, Sculco TP, Poultsides LA. Periprosthetic infection recurrence after 2-stage exchange arthroplasty: failure or fate? J Arthroplasty 2017;32:526e31. https://doi.org/10.1016/j.arth.2016.08.002.

[12] Cooper HJ, Della Valle CJ. The two-stage standard in revision total hip replacement. Bone Joint J 2013;95-B:84e7. https://doi.org/10.1302/0301-620X.95B11.32906.

[13] Fitzgerald RH. Infected total hip arthroplasty: diagnosis and treatment. J Am Acad Orthop Surg 1995;3:249e62.

[14] Gehrke T, Zahar A, Kendoff D. One-stage exchange: it all began here. Bone Joint J 2013;95-B:77e83. https://doi.org/10.1302/0301-620X.95B11.32646.

[15] Kini SG, Gabr A, Das R, Sukeik M, Haddad FS. Two-stage revision for periprosthetic hip and knee joint infections. Open Orthop J 2016;10:579e88. https://doi.org/10.2174/1874325001610010579.

[16] Tsukayama DT, Estrada R, Gustilo RB. Infection after total hip arthroplasty. A study of the treatment of one hundred and six infections. J Bone Joint Surg Am 1996;78:512e23.

[17] Duncan WW, Hubble MJW, Howell JR, Whitehouse SL, Timperley AJ, Gie GA. Revision of the cemented femoral stem using a cement-in-cement technique: a five- to 15-year review. J Bone Joint Surg Br 2009;91:577e82. https://doi.org/10.1302/0301-620X.91B5.21621.

[18] Holt G, Hook S, Hubble M. Revision total hip arthroplasty: the femoral side using cemented implants. Int Orthop 2011;35:267e73. https://doi.org/10.1007/s00264-010-1167-5.

[19] Lieberman JR, Moeckel BH, Evans BG, Salvati EA, Ranawat CS. Cement-within cement revision hip arthroplasty. J Bone Joint Surg Br 1993;75:869e71.

[20] Meek RM, Garbuz DS, Masri BA, Greidanus NV, Duncan CP. Intraoperative fracture of the femur in revision total hip arthroplasty with a diaphyseal fitting stem. J Bone Joint Surg Am 2004;86-A:480e5.

[21] Quinlan JF, O'Shea K, Doyle F, Brady OH. In-cement technique for revision hip arthroplasty. J Bone Joint Surg Br 2006;88:730e3. https://doi.org/10.1302/0301-620X.88B6.17037.

[22] Kendall RW, Duncan CP, Smith JA, Ngui-Yen JH. Persistence of bacteria on antibiotic loaded acrylic depots. A reason for caution. Clin Orthop Relat Res 1996:273e80.

[23] Mariconda M, Ascione T, Balato G, Rotondo R, Smeraglia F, Costa GG, et al. Sonication of antibiotic-loaded cement spacers in a two-stage revision protocol for infected joint arthroplasty. BMC Musculoskelet Disord 2013;14:193. https://doi.org/10.1186/1471-2474-14-193.

[24] Bertazzoni Minelli E, Della Bora T, Benini A. Different microbial biofilm formation on polymethylmethacrylate (PMMA) bone cement loaded with gentamicin and vancomycin. Anaerobe 2011;17:380e3. https://doi.org/10.1016/j.anaerobe.2011.03.013.

[25] Tunney MM, Dunne N, Einarsson G, McDowell A, Kerr A, Patrick S. Biofilm formation by bacteria isolated from retrieved failed prosthetic hip implants in an in vitro model of hip arthroplasty antibiotic prophylaxis. J Orthop Res 2007;25:2e10. https://doi.org/10.1002/jor.20298.

[26] Griffin JW, Guillot SJ, Redick JA, Browne JA. Removed antibiotic-impregnated cement spacers in two-stage revision joint arthroplasty do not show biofilm formation in vivo. J Arthroplasty 2012;27:1796e9. https://doi.org/10.1016/j.arth.2012.06.019.

[27] Ma D, Shanks RMQ, Davis CM, Craft DW, Wood TK, Hamlin BR, et al. Viable bacteria persist on antibiotic spacers following two-stage revision for periprosthetic joint infection. J Orthop Res 2018;36:452e8. https://doi.org/10.1002/jor.23611.

[28] Morley JR, Blake SM, Hubble MJW, Timperley AJ, Gie GA, Howell JR. Preservation of the original femoral cement mantle during the management of infected cemented total hip replacement by two-stage revision. J Bone Joint Surg Br 2012;94:322e7. https://doi.org/10.1302/0301-620X.94B3.28256.

[29] Leijtens B, Sadeghi N, Schreurs BW, Rijnen WH. Cement-within-cement revision of infected total hip replacement; disappointing results in 10 retrospective cases. Hip Int 2016;26:67e72. https://doi.org/10.5301/hipint.5000310.

[30] Bjarnsholt T, Alhede M, Jensen PØ, Nielsen AK, Johansen HK, Homøe P, et al. Antibiofilm properties of acetic acid. Adv Wound Care (New Rochelle) 2015;4:363e72. https://doi.org/10.1089/wound.2014.0554.

[31] d'Astorg H, Amzallag J, Poignard A, Roudot Thoraval F, Allain J. Peri-acetabular cement extrusion in the course of total hip replacement: incidence and consequences. An analysis from 269 consecutive cemented total hips. Orthop Traumatol Surg Res 2011;97:608e14. https://doi.org/10.1016/j.otsr.2011.04.007.

[32] Mirza YH, Tansey R, Sukeik M, Shaath M, Haddad FS. Biofilm and the role of antibiotics in the treatment of periprosthetic hip and knee joint infections. Open Orthop J 2016;10:636e45. https://doi.org/10.2174/1874325001610010636.

[33] Chou ACC, Mahadev A. The use of C-reactive protein as a guide for transitioning to oral antibiotics in pediatric osteoarticular infections. J Pediatr Orthop 2016;36:173e7. https://doi.org/10.1097/BPO.0000000000000427.

[34] Siliski JM, Scott RD. Obturator-nerve palsy resulting from intrapelvic extrusion of cement during total hip replacement. Report of four cases. J Bone Joint Surg Am 1985;67:1225e8.

[35] Jerosch J. Femoral nerve palsy in hip replacement due to pelvic cement extrusion. Arch Orthop Trauma Surg 2000;120:499e501.

[36] Oleksak M, Edge AJ. Compression of the sciatic nerve by methylmethacrylate cement after total hip replacement. J Bone Joint Surg Br 1992;74:729e30.

[37] Nonomura M, Kanaoka T, Soeda A, Matsuo M. A case of a methylmethacrylate foreign body in the bladder wall. Int J Urol 1994;1:278e80.

[38] Middleton RG, Reilly DT, Jessop J. Occlusion of the external iliac vein by cement. J Arthroplasty 1996;11:346e7.

[39] Ottolenghi CE. Massive osteo and osteo-articular bone grafts. Technic and results of 62 cases. Clin Orthop Relat Res 1972;87:156e64.

[40] Mankin HJ, Doppelt S, Tomford W. Clinical experience with allograft implantation. The first ten years. Clin Orthop Relat Res 1983:69e86.

[41] Lord CF, Gebhardt MC, Tomford WW, Mankin HJ. Infection in bone allografts. Incidence, nature, and treatment. J Bone Joint Surg Am 1988;70:369e76.

[42] Mankin HJ, Hornicek FJ, Raskin KA. Infection in massive bone allografts. Clin Orthop Relat Res 2005:210e6.

[43] Tomford WW, Thongphasuk J, Mankin HJ, Ferraro MJ. Frozen musculoskeletal allografts. A study of the clinical incidence and causes of infection associated with their use. J Bone Joint Surg Am 1990;72:1137e43.

[44] Berry DJ, Chandler HP, Reilly DT. The use of bone allografts in two-stage reconstruction after failure of hip replacements due to infection. J Bone Joint Surg Am 1991;73:1460e8.

[45] Ilyas I, Morgan DAF. Massive structural allograft in revision of septic hip arthroplasty. Int Orthop 2001;24:319e22. https://doi.org/10.1007/s002640000200.

[46] Wang JW, Chen CE. Reimplantation of infected hip arthroplasties using bone allografts. Clin Orthop Relat Res 1997:202e10.

[47] Hsieh P-H, Shih C-H, Chang Y-H, Lee MS, Yang W-E, Shih H-N. Treatment of deep infection of the hip associated with massive bone loss: two-stage revision with an antibiotic-loaded interim cement prosthesis followed by reconstruction with allograft. J Bone Joint Surg Br 2005;87:770e5. https://doi.org/10.1302/0301-620X.87B6.15411.

[48] Alexeeff M, Mahomed N, Morsi E, Garbuz D, Gross A. Structural allograft in two-stage revisions for failed septic hip arthroplasty. J Bone Joint Surg Br 1996;78:213e6.

[49] Lee PTH, Clayton RA, Safir OA, Backstein DJ, Gross AE. Structural allograft as an option for treating infected hip arthroplasty with massive bone loss. Clin Orthop Relat Res 2011;469:1016e23. https://doi.org/10.1007/s11999-010-1673-1.

[50] Traore A, Tribak K, Be J, Cauter MV, Mobiot-Aka C, Traore YS, et al. Proximal femoral allograft in two-stage revision for failed septic hip arthroplasty. Open J Orthop 2015;05:379. https://doi.org/10.4236/ojo.2015.512051.

[51] Loty B, Postel M, Evrard J, Matron P, Courpied JP, Kerboull M, et al. One stage revision of infected total hip replacements with replacement of bone loss by allografts. Study of 90 cases of which 46 used bone allografts. Int Orthop 1992;16:330e8.

[52] Lange J, Troelsen A, Thomsen RW, Søballe K. Chronic infections in hip arthroplasties: comparing risk of reinfection following one-stage and two-stage revision: a systematic review and meta-analysis. Clin Epidemiol 2012;4:57e73. https://doi.org/10.2147/CLEP.S29025.

[53] Tsahakis PJ, Beaver WB, Brick GW. Technique and results of allograft reconstruction in revision total knee arthroplasty. Clin Orthop Relat Res 1994:86e94.

[54] Wilde AH, Schickendantz MS, Stulberg BN, Go RT. The incorporation of tibial allografts in total knee arthroplasty. J Bone Joint Surg Am 1990;72:815e24.

[55] Stockley I, McAuley JP, Gross AE. Allograft reconstruction in total knee arthroplasty. J Bone Joint Surg Br 1992;74:393e7.

[56] Harris AI, Poddar S, Gitelis S, Sheinkop MB, Rosenberg AG. Arthroplasty with a composite of an allograft and a prosthesis for knees with severe deficiency of bone. J Bone Joint Surg Am 1995;77:373e86.

[57] Mow CS, Wiedel JD. Structural allografting in revision total knee arthroplasty. J Arthroplasty 1996;11:235e41.

[58] Engh GA, Herzwurm PJ, Parks NL. Treatment of major defects of bone with bulk allografts and stemmed components during total knee arthroplasty. J Bone Joint Surg Am 1997;79:1030e9.

[59] Ghazavi MT, Stockley I, Yee G, Davis A, Gross AE. Reconstruction of massive bone defects with allograft in revision total knee arthroplasty. J Bone Joint Surg Am 1997;79:17e25.

[60] Clatworthy MG, Ballance J, Brick GW, Chandler HP, Gross AE. The use of structural allograft for uncontained defects in revision total knee arthroplasty. A minimum five-year review. J Bone Joint Surg Am 2001;83-A:404e11.

[61] English H, Timperley AJ, Dunlop D, Gie G. Impaction grafting of the femur in two-stage revision for infected total hip replacement. J Bone Joint Surg Br 2002;84:700e5.

[62] Dennis DA. The structural allograft composite in revision total knee arthroplasty. J Arthroplasty 2002;17:90e3.

[63] Garino JP. The use of impaction grafting in revision total knee arthroplasty. J Arthroplasty 2002;17:94e7.

[64] Hockman DE, Ammeen D, Engh GA. Augments and allografts in revision total knee arthroplasty: usage and outcome using one modular revision prosthesis. J Arthroplasty 2005;20:35e41. https://doi.org/10.1016/j.arth.2004.09.059.

[65] Bush JL, Wilson JB, Vail TP. Management of bone loss in revision total knee arthroplasty. Clin Orthop Relat Res 2006;452:186e92. https://doi.org/10.1097/01.blo.0000229360.04620.93.

[66] Backstein D, Safir O, Gross A. Management of bone loss: structural grafts in revision total knee arthroplasty. Clin Orthop Relat Res 2006;446:104e12. https://doi.org/10.1097/01.blo.0000214426.52206.2c.

[67] Lotke PA, Carolan GF, Puri N. Impaction grafting for bone defects in revision total knee arthroplasty. Clin Orthop Relat Res 2006;446:99e103. https://doi.org/10.1097/01.blo.0000214414.06464.00.

[68] Bezwada HP, Shah AR, Zambito K, Cerynik DL, Johanson NA. Distal femoral allograft reconstruction for massive osteolytic bone loss in revision total knee arthroplasty. J Arthroplasty 2006;21:242e8. https://doi.org/10.1016/j.arth.2005.06.005.

[69] Engh GA, Ammeen DJ. Use of structural allograft in revision total knee arthroplasty in knees with severe tibial bone loss. J Bone Joint Surg Am 2007;89:2640e7. https://doi.org/10.2106/JBJS.F.00865.

[70] Rudelli S, Uip D, Honda E, Lima AL. One-stage revision of infected total hip arthroplasty with bone graft. J Arthroplasty 2008;23:1165e77. https://doi.org/10.1016/j.arth.2007.08.010.

[71] Burnett RS, Keeney JA, Maloney WJ, Clohisy JC. Revision total knee arthroplasty for major osteolysis. Iowa Orthop J 2009;29:28e37.

[72] Lyall HS, Sanghrajka A, Scott G. Severe tibial bone loss in revision total knee replacement managed with structural femoral head allograft: a prospective case series from the Royal London Hospital. Knee 2009;16:326e31. https://doi.org/10.1016/j.knee.2009.02.007.

[73] Bauman RD, Lewallen DG, Hanssen AD. Limitations of structural allograft in revision total knee arthroplasty. Clin Orthop Relat Res 2009;467:818e24. https://doi.org/10.1007/s11999-008-0679-4.

[74] Lombardi AV, Berend KR, Adams JB. Management of bone loss in revision TKA: it's a changing world. Orthopedics 2010;33:662. https://doi.org/10.3928/01477447-20100722-37.

[75] Richards CJ, Garbuz DS, Pugh L, Masri BA. Revision total knee arthroplasty: clinical outcome comparison with and without the use of femoral head structural allograft. J Arthroplasty 2011;26:1299e304. https://doi.org/10.1016/j.arth.2010.12.003.

[76] Wang J-W, Hsu C-H, Huang C-C, Lin P-C, Chen W-S. Reconstruction using femoral head allograft in revision total knee replacement: an experience in Asian patients. Bone Joint J 2013;95-B:643e8. https://doi.org/10.1302/0301-620X.95B5.29915.

[77] Vasso M, Beaufils P, Cerciello S, Schiavone Panni A. Bone loss following knee arthroplasty: potential treatment options. Arch Orthop Trauma Surg 2014;134:543e53. https://doi.org/10.1007/s00402-014-1941-8.

[78] Chun CH, Kim JW, Kim SH, Kim BG, Chun KC, Kim KM. Clinical and radiological results of femoral head structural allograft for severe bone defects in revision TKA–a minimum 8-year follow-up. Knee 2014;21:420e3. https://doi.org/10.1016/j.knee.2013.04.012.

[79] Beckmann NA, Mueller S, Gondan M, Jaeger S, Reiner T, Bitsch RG. Treatment of severe bone defects during revision total knee arthroplasty with structural allografts and porous metal cones-a systematic review. J Arthroplasty 2015;30:249e53. https://doi.org/10.1016/j.arth.2014.09.016.

[80] Mancuso F, Beltrame A, Colombo E, Miani E, Bassini F. Management of metaphyseal bone loss in revision knee arthroplasty. Acta Biomed 2017;88:98e111.

[81] Sandiford NA, Misur P, Garbuz DS, Greidanus NV, Masri BA. No difference between trabecular metal cones and femoral head allografts in revision TKA: minimum 5-year follow-up. Clin Orthop Relat Res 2017;475:118e24. https://doi.org/10.1007/s11999-016-4898-9.

[82] Mortazavi SM, Molligan J, Austin MS, Purtill JJ, Hozack WJ, Parvizi J. Failure following revision total knee arthroplasty: infection is the major cause. Int Orthop 2011;35:1157e64. https://doi.org/10.1007/s00264-010-1134-1.