Infected total hip replacements: assessment and management

ABSTRACT

Infected total hip replacements pose a diagnostic and management challenge. Careful history, clinical examination, blood tests, plain radiographs and hip aspiration are all part of the clinical assessment. International consensus on establishing the diagnosis helps surgeons to formulate management plans. Management strategies include debridement and prosthesis retention, single-stage revision, two-stage revision, suppressive antibiotic treatment and excision arthroplasty. This article reviews the clinical assessment, diagnosis, principles of surgical management and outcomes of revision surgery of infected total hip replacements.

Total hip replacement is one of the most successful and cost-effective orthopaedic procedures (Laupacis et al, 1993). The number of primary hip replacements performed continues to increase. The latest annual report of the National Joint Registry of England and Wales reported that 87 733 total hip replacements were performed in 2016 (National Joint Registry, 2017). The underlying diagnosis was osteoarthritis in most cases with a median age of 69 years at the time of surgery. Although total hip replacement is a highly successful operation with high patient satisfaction and improved outcomes, a wide range of complications can cause persistent pain and low satisfaction rate. Over a 13-year period, the National Joint Registry for England and Wales collected data on 890 681 recorded hip replacements and found the cumulative percentage probability of revision after primary hip replacement was 6.8% (National Joint Registry, 2017).

Approximately 1–2% of hip arthroplasties become infected (Pulido et al, 2008). This incidence is higher in patients with diabetes, rheumatological disease, obesity, coagulopathy, preoperative anaemia or sickle cell disease (Bongartz et al, 2008; Bozic et al, 2012). Additional risk factors include prolonged operative time and previous hip surgery. Wound healing complications, such as skin necrosis and postoperative haematoma, also make infection more likely (Pulido et al, 2008).

This article reviews infectious causes of painful or problematic hip replacements, clinical assessment and management. It focuses on the presenting symptoms, clinical assessment, management in the arthroplasty clinic, principles and outcomes of revision surgery.

Presenting symptoms and clinical assessment

History is perhaps the most important aspect of evaluating a painful hip replacement. Pain is the most common presenting symptom of a failing hip replacement. History begins with the underlying condition that led to the primary hip replacement, whether it was for osteoarthritis, rheumatoid arthritis, osteonecrosis or neck of femur fracture. Location, onset, character, severity, radiation, precipitating and relieving factors, and systemic symptoms are all valuable clues to establishing the cause of failure. Persistent pain without a pain-free interval since the initial surgery points towards infection or an overlooked underlying diagnosis such as spinal stenosis or radiculopathy. On the other hand, recent onset of 'start-up pain', e.g. pain on getting out of a chair and walking, around the thigh or groin, after years of a pain-free, well-functioning hip replacement would point towards mechanical loosening of the implants. Similarly, location of the pain is an important indicator of its origin – buttock pain or posterior thigh pain, particularly with radiation to the calf muscles, suggests a spinal cause. Pain originating from a hip replacement tends to be in the groin or acetabular region or in the anterior proximal thigh. Further, mechanical pain that increases with weight-bearing and mobilization and is relieved by rest is usually related to loosening.

Clinical examination of the patient includes lumbar spine, knee and specific hip examination focusing on gait, range of pain-free motion, and the presence of any swelling, erythema or sinus, although this is rarely seen. Pain elicited with active range of motion or at the extremes of rotation suggests component loosening. Pain with resisted ipsilateral straight leg raise suggests hip pathology while pain with ipsilateral or contralateral passive straight leg raise suggests a radiculopathy or lumbar spine pathology. This should be followed by a brief neurological examination of both lower extremities to rule out a spinal pathology or neuropathy. An abnormality of the peripheral pulses may suggest vascular claudication as a source of pain.

Further specialist assessment of the hip includes assessment of the leg length, e.g. progressive shortening of the leg may indicate femoral component subsidence or acetabular component migration. An apparent discrepancy may, on the other hand, indicate an abduction or adduction contracture of the hip, pelvic obliquity, or lumbar scoliosis

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as a result of degenerative disc disease. Finally, the integrity of the abductor complex which plays a crucial role in hip stability, function and operative planning should be assessed by Trendelenburg testing (Hardcastle and Nade, 1985).

Radiographic and biochemical assessment

Anteroposterior radiographs of the pelvis cantered over the pubis and lateral radiograph of the hip are needed for all patients with painful hip replacement. Since Sir John Charnley pioneered hip replacements in the 1960s, a variety of hip replacement implants and systems have been used – cemented, uncemented and hybrid implants (*Figure 1*). Radiographic features that suggest loosening and potentially chronic infection include subsidence or migration of the components, and progressive lucent lines around the prosthesis which are best detected on serial radiographs (*Figure 2*) (McBride and Prakash, 2011). However, patients with acute or postoperative infections may lack any radiographical features to suggest infection.

Biochemical laboratory tests that are useful in diagnosing infection include elevated serum C-reactive protein level, erythrocyte sedimentation rate and white cell count. Peripheral white cell count is rarely elevated in late chronic infection and is not a sensitive screening tool. Erythrocyte sedimentation rate greater than 30 mm/h and C-reactive protein level greater than 10 mg/litre are reasonably sensitive and specific for the diagnosis of infection. However, in asymptomatic patients following hip replacements, the erythrocyte sedimentation rate may take up to 1 year to return to normal, whereas the C-reactive protein level normalizes within 3–4 weeks (Parvizi et al, 2013).

Diagnosis and classification

There are three main mechanisms by which infections occur:

1. Direct contamination of the wound at time of surgery
2. Haematogenous spread of distant bacterial colonization or infection from a separate site
3. Reactivation of latent hip infection in a previously septic joint (Shirwaiker et al, 2015).

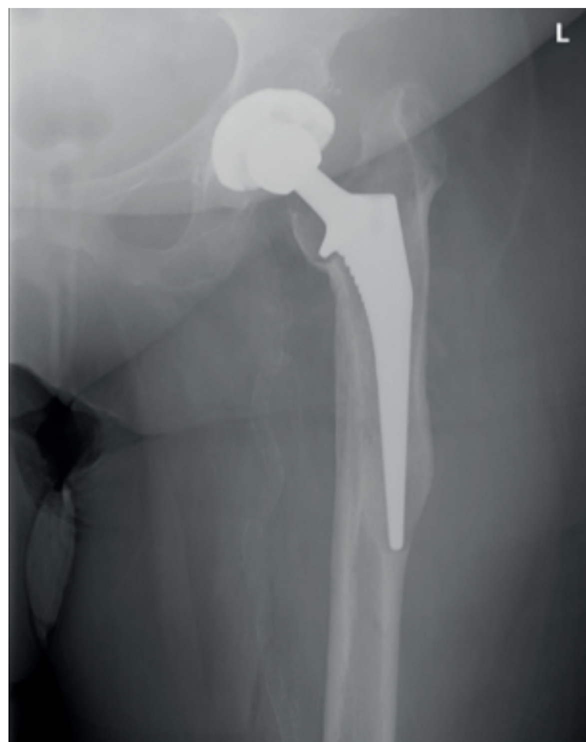

Figure 2. Radiograph of clinically infected left hip replacement demonstrating an uncemented prosthesis with radiographic evidence of loosening. The femoral component has subsided and eroded the lateral femoral cortex.

Most total hip infections are caused by Gram-positive organisms, particularly coagulase-negative staphylococci and *Staphylococcus aureus* (Parvizi et al, 2013, 2017; Gbejuade et al, 2015; Gundtoft et al, 2017). Meticillin resistance has become common in many centres, and the elaboration of glycocalyx by Staphylococcus and Pseudomonas is a marker for higher virulence as it plays an important role in forming a biofilm (a structured

Figure 1. Examples of different hip replacements. **a.** Cemented Charnley hip replacement. **b.** Modern cemented prosthesis. **c.** Uncemented prosthesis.

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aggregation of microbial cells encased in a self-produced matrix and adherent to implant surfaces and interfaces). This biofilm shields the organisms and increases their resistance to antibiotics (Gbejuade et al, 2015). Gram-negative organisms are encountered more frequently in haematogenous infections, particularly those arising from the urinary tract. On the other hand, patients with draining sinuses often have mixed growth (Kliushin et al, 2017).

While acute postoperative infections with leaky wounds are easily diagnosed, chronic or latent infections can present a diagnostic challenge to differentiate infections from aseptic loosening or other causes of painful hip replacements. Following history, examination, blood tests and radiographs in the arthroplasty clinic, hip aspiration is the next step if infection is suspected. This is done under local anaesthetic and fluoroscopy guidance, often in the operating theatre to ensure sterility with a full surgical scrub and preparation. Any fluid aspirated is then sent for microbiology assessment including Gram staining, crystals, culture and sensitivities.

Diagnostic criteria from the international consensus on periprosthetic joint infections are used worldwide (Parvizi et al, 2013). There are two major and six minor criteria:

Major criteria (diagnosis can be made when one major criteria exists):
1. Sinus tract communicating with prosthesis
2. Pathogen isolated by culture from two separate tissue or fluid samples from the affected joint.

Minor criteria (diagnosis can be made when at least four of the following six minor criteria exist):
1. Elevated erythrocyte sedimentation rate (>30 mm/h) or C-reactive protein level (>10 mg/litre)
2. Elevated synovial white cell count (>1100 cells/ul for knees, >3000 cells/ul for hips)
3. Elevated synovial levels of polymorphonuclear neutrophils (>80% for hips)
4. Purulence in the affected joint
5. Pathogen isolation in one culture
6. Five or more polymorphonuclear neutrophils per high-power field in five high-power fields at x400 magnification (intraoperative frozen section of periprosthetic tissue).

Research has identified alpha defensin-1, a synovial fluid peptide produced by neutrophils in response to infected joint replacements, which showed 100% sensitivity and 95% specificity. This test is currently used in a complementary role to the criteria of the international consensus (Bingham et al, 2014; Deirmengian et al, 2015; Suda et al, 2017).

Preventative measures

Since Lidwell et al's (1982) benchmark trial on reducing the risk of periprosthetic joint infections, numerous guidelines have been drawn up in an attempt to reduce the risk of infection. Most recently, Parvizi et al (2017) published guidelines derived from the World Health Organization and the Centers for Disease Control and Prevention evidence-based guidelines for the prevention of surgical site infections, the Society for Healthcare Epidemiology of America and the National Institute for Health and Care Excellence guidelines. These cover a wide spectrum of measures during the patient's journey from being listed for surgery to postoperative wound care, including:
1. Preoperative measures: nasal decolonization, skin cleansing and advice on the use of immunosuppressive medications in patients with inflammatory arthropathies
2. Perioperative measures: the importance of glycaemic control and antibiotic prophylaxis
3. Intraoperative measures: the use of laminar flow theatres, orthopaedic space suits, operating theatre traffic, surgical site preparation, skin sealant and drapes, normothermia and oxygenation, antibiotic-impregnated bone cement, wound irrigation and wound dressings
4. Postoperative measures: minimizing the need for blood transfusions and dealing with wound complications.

Management

There are five main options for managing infected hip replacements:

Debridement, antibiotics, irrigation and retention of prosthesis

Surgical debridement and prosthetic retention, with exchange of modular components, is indicated for acute infection in the immediate postoperative period or for late acute haematogenous infection of a well-fixed and functional prosthesis. Early surgical debridement is crucial as this strategy is not successful if performed more than 2–3 weeks after symptom onset. The reported success rate ranges from 14–100% and is difficult to assess because of variability in time to treatment, microorganism, subsequent antibiotic treatment, quality of the debridement, status of implant fixation, condition of the surrounding soft tissues and criteria for success. For an acute postoperative infection, debridement, antibiotics, irrigation and retention of prosthesis has in a success rate of around 75%, but for chronic infections the failure rate is very high (Kuiper et al, 2013; Tsang et al, 2017).

Single-stage revision

This includes surgical debridement, removal of the infected prosthesis and re-implanting a new prosthesis at the same settings. This strategy may have lower morbidity and costs, and reduce the technical difficulties associated with delayed reconstruction. Prerequisites for a successful single-stage revision includes a healthy patient, a single infecting organism with low virulence and known sensitivity to antibiotics, and minimal bone loss. Most series have reported a success rate of up to 80%. However, with emerging antibiotic resistance and the need for complex reconstruction techniques with significant bone loss, the use of a single-stage revision strategy is limited (Castellani et al, 2017; Parisi et al, 2017).

Two-stage revision

Two-stage revision is the traditional strategy in managing infected hip replacements. This involves a thorough surgical debridement of soft tissues, removal of all components and cement, and insertion of especially devised spacers made

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of cement beads impregnated with heat-stable antibiotics prepared to achieve high elution rates of antibiotics as a vehicle for local delivery (*Figure 3*). Systemic intravenous antibiotics as guided by cultures and sensitivities of organisms from deep tissue samples obtained at the time of surgery are given for 6 weeks. Patients can mobilize with crutches and weight bear as tolerated. Once inflammatory markers (C-reactive protein, erythrocyte sedimentation rate, white cell count) normalize, a second stage is planned (usually within 8–12 weeks) where a definitive prosthesis and hip reconstruction is undertaken. This could be achieved using standard implants (*Figure 3b*) or a more complex mega-prosthesis (*Figure 3c*) depending on the bone loss and integrity of soft tissues. Success rates (no recurrence of infection) are as high as 95% (Biring et al, 2009; Sanchez-Sotelo et al, 2009; Romano et al, 2012; Berend et al, 2013; Castellani et al, 2017).

Suppressive treatment with long-term antibiotics

This is only indicated for elderly frail, low-demand patients who are not fit for surgical intervention, have reasonably fixed implants, and infection with a low virulence organism that is sensitive to oral antibiotics (Wouthuyzen-Bakker et al, 2017).

Resection arthroplasty (Girdleston procedure)

This is a last resort for medically and functionally compromised patients who have high anaesthetic and operative risk for either single- or two-stage revision procedures or those with recurrent infections who have failed two-stage revisions. As a salvage procedure this includes surgical debridement, removal of all components in an attempt to achieve pain relief and control infection with no plans for subsequent implantation (Malcolm et al, 2015).

Outcomes

The choice of single- or two-stage revision for prosthetic joint infection of the hip remains controversial. Surgeons balance multiple factors when pursuing a particular strategy based on patient factors, their own skills and expertise, available resources, and the infecting organism. There is no level 1 evidence comparing these approaches. The INFORM trial (Strange et al, 2016) (ISRCTN10956306) is recruiting patients for the first multicentre randomized controlled trial comparing single- *vs* two-stage revisions for infected hip replacements. Current evidence is based on observational studies that have assessed re-infection outcomes following one-stage or two-stage surgical revisions, with inconsistent results. Differences between cohorts of patients where either of these approaches is used makes direct comparison difficult.

Wolf et al (2011), in their systematic review of 11 two-stage studies (321 patients) and eight one-stage studies (576 patients), reported an increased re-infection rate after one-stage (12.3%) *vs* two-stage revision (6.5%) of infected total hip replacements, but a higher mortality rate with two-stage revision. In a review by Lange et al (2012), which included 36 studies of either one-stage (375 patients) or two-stage revision (929 patients), the estimated absolute risk of reinfection was 13.1% (95% confidence interval 10.0–17.1%) in the one-stage cohort and 10.4% (95% confidence interval 8.5–12.7%) in the two-stage cohort. Functional outcomes have not been evaluated as widely as reinfection rates. Leonard et al (2014) assessed functional outcomes and found only small case series with small numbers of patients. There was a trend toward better functional outcomes in single-stage surgery, but this reached significance in only one study.

Conclusions

Infected total hip replacements pose a diagnostic and management challenge with an incidence of approximately 1–2% . Careful history, clinical examination, blood tests, plain radiographs and hip aspiration are all part of the clinical assessment. International consensus on establishing the diagnosis helps surgeons to formulate management plans. Management strategies include debridement and prosthesis retention, single-stage or two-stage revision, suppressive antibiotics treatment and excision arthroplasty.

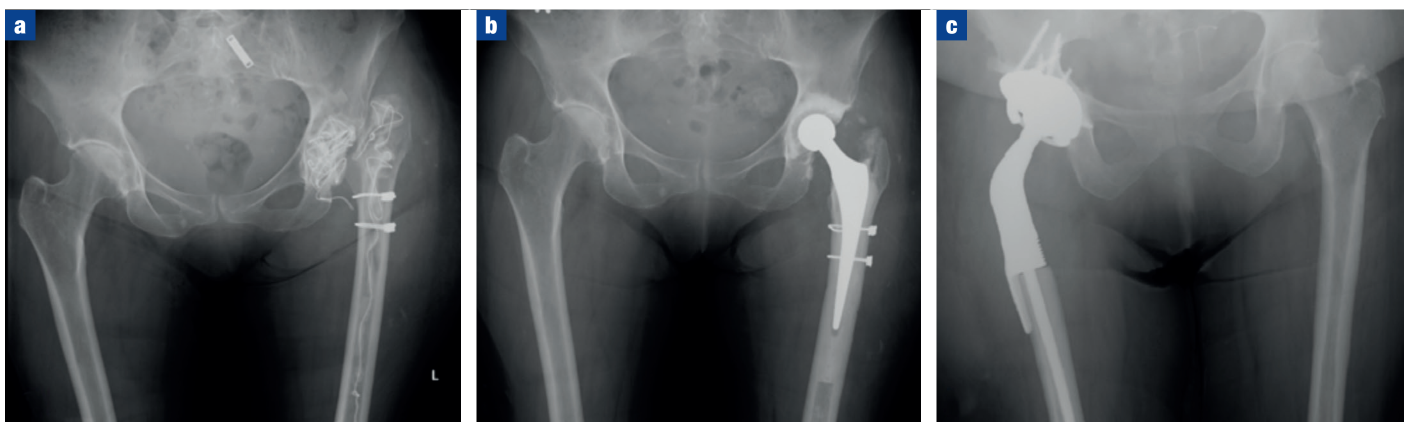

Figure 3. An infected total hip replacement managed with two-stage revision. **a.** Anteroposterior radiograph with left hip first stage revision which includes surgical debridement, removal of prosthesis and inserting an antibiotic-loaded cement spacer in both the acetabulum and femoral canal for local delivery of antibiotics. **b.** Anteroposterior radiograph following second-stage revision of the same patient which involved removal of the spacer and reconstructing the hip using a fully cemented prosthesis. **c.** Another patient who underwent second-stage revision who required more complex reconstruction techniques using proximal femoral replacement implants.

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Patient and surgeon factors and available resources all play a role in applying these strategies. Level 1 evidence on the effectiveness of single- *vs* two-stage revisions is lacking, but two-stage revision remains the most successful strategy in eradicating chronic infection and restoring function. **BJHM**

Conflict of interest: none.

KEY POINTS

- Total hip replacement is one of the most successful and cost-effective interventions in orthopaedic surgery, but the incidence of infection after hip replacement is about 1–2%.
- History, examination, bloods, plain radiographs and hip aspiration are all tools to aid the diagnosis.
- Surgical management is through revision surgery and antibiotics, traditionally via a two-stage approach of debridement and use of antibiotic-loaded cement spacer followed by definitive re-implantation once infection eradicated.
- In patients with no immunocompromise and a low virulence organism, single-stage revision with immediate exchange of implants may be adequate.

Berend KR, Lombardi AV Jr, Morris MJ, Bergeson AG, Adams JB, Sneller MA (2013) Two-stage treatment of hip periprosthetic joint infection is associated with a high rate of infection control but high mortality. *Clin Orthop Relat Res* **471**(2): 510–518. https://doi.org/10.1007/s11999-012-2595-x

Bingham J, Clarke H, Spangehl M, Schwartz A, Beauchamp C, Goldberg B (2014) The alpha defensin-1 biomarker assay can be used to evaluate the potentially infected total joint arthroplasty. *Clin Orthop Relat Res* **472**(12): 4006–4009. https://doi.org/10.1007/s11999-014-3900-7

Biring GS, Kostamo T, Garbuz DS, Masri BA, Duncan CP (2009) Two-stage revision arthroplasty of the hip for infection using an interim articulated Prostalac hip spacer: A 10- to 15-year follow-up study. *J Bone Joint Surg Br* **91-B**(11): 1431–1437. https://doi.org/10.1302/0301-620X.91B11.22026

Bongartz T, Halligan CS, Osmon DR et al (2008) Incidence and risk factors of prosthetic joint infection after total hip or knee replacement in patients with rheumatoid arthritis. *Arthritis Rheum* **59**(12): 1713–1720. https://doi.org/10.1002/art.24060

Bozic KJ, Lau E, Kurtz S, Ong K, Rubash H, Vail TP, Berry DJ (2012) Patient-related risk factors for periprosthetic joint infection and postoperative mortality following total hip arthroplasty in Medicare patients. *J Bone Joint Surg Am* **94**(9): 794–800. https://doi.org/10.2106/JBJS.K.00072

Castellani L, Daneman N, Mubareka S, Jenkinson R (2017) Factors associated with choice and success of one- versus two-stage revision arthroplasty for infected hip and knee prostheses. *HSS Jrnl* **13**(3): 224–231. https://doi.org/10.1007/s11420-017-9550-z

Deirmengian C, Kardos K, Kilmartin P, Gulati S, Citrano P, Booth RE Jr (2015) The Alpha-defensin test for periprosthetic joint infection responds to a wide spectrum of organisms. *Clin Orthop Relat Res* **473**(7): 2229–2235. https://doi.org/10.1007/s11999-015-4152-x

Gbejuade HO, Lovering AM, Webb JC (2015) The role of microbial biofilms in prosthetic joint infections. *Acta Orthop* **86**(2): 147–158. https://doi.org/10.3109/17453674.2014.966290

Gundtoft PH, Pedersen AB, Varnum C, Overgaard S (2017) Increased mortality after prosthetic joint infection in primary THA. *Clin Orthop Relat Res* **475**(11): 2623–2631. https://doi.org/10.1007/s11999-017-5289-6

Hardcastle P, Nade S (1985) The significance of the Trendelenburg test. *J Bone Joint Surg Br* **67**(5): 741–746.

Kliushin NM, Ermakov AM, Malkova TA (2017) Chronic periprosthetic hip infection: micro-organisms responsible for infection and re-infection. *Int Orthop* **41**(6): 1131–1137. https://doi.org/10.1007/s00264-016-3341-x

Kuiper JWP, Vos SJCJ, Saouti R et al (2013) Prosthetic joint-associated infections treated with DAIR (debridement, antibiotics, irrigation, and retention). *Acta Orthop* **84**(4): 380–386. https://doi.org/10.3109/17453674.2013.823589

Lange J, Troelsen A, Thomsen RW, Soballe K (2012) Chronic infections in hip arthroplasties: comparing risk of reinfection following one-stage and two-stage revision: a systematic review and meta-analysis. *Clin Epidemiol* **4**: 57–73. https://doi.org/10.2147/clep.s29025

Laupacis A, Bourne R, Rorabeck C et al (1993) The effect of elective total hip replacement on health-related quality of life. *J Bone Joint Surg* **75**(11): 1619–1626. https://doi.org/10.2106/00004623-199311000-00006

Leonard HAC, Liddle AD, Burke Ó, Murray DW, Pandit H (2014) Single- or two-stage revision for infected total hip arthroplasty? A systematic review of the literature. *Clin Orthop Relat Res* **472**(3): 1036–1042. https://doi.org/10.1007/s11999-013-3294-y

Lidwell OM, Lowbury EJ, Whyte W, Blowers R, Stanley SJ, Lowe D (1982) Effect of ultraclean air in operating rooms on deep sepsis in the joint after total hip or knee replacement: a randomised study. *BMJ* **285**(6334): 10–14. https://doi.org/10.1136/bmj.285.6334.10

Malcolm TL, Gad BV, Elsharkawy KA, Higuera CA (2015) Complication, survival, and reoperation rates following girdlestone resection arthroplasty. *J Arthroplasty* **30**(7): 1183–1186. https://doi.org/10.1016/j.arth.2015.02.011

McBride TJ, Prakash D (2011) How to read a postoperative total hip replacement radiograph. *Postgrad Med J* **87**(1024): 101–109. https://doi.org/10.1136/pgmj.2009.095620

National Joint Registry (2017) NJR 14th Annual Report. www.njrcentre.org.uk/njrcentre/Reports,PublicationsandMinutes/Annualreports/tabid/86/Default.aspx (accessed 30 January 2018)

Parisi TJ, Konopka JF, Bedair HS (2017) What is the long-term economic societal effect of periprosthetic infections after THA? A Markov analysis. *Clin Orthop Relat Res* **475**(7): 1891–1900. https://doi.org/10.1007/s11999-017-5333-6

Parvizi J, Gehrke T, Chen AF (2013) Proceedings of the International Consensus on Periprosthetic Joint Infection. *Bone Joint J* **95-B**(11): 1450–1452. https://doi.org/10.1302/0301-620x.95b11.33135

Parvizi J, Shohat N, Gehrke T (2017) Prevention of periprosthetic joint infection: new guidelines. *Bone Joint J* **99-b**(4 Suppl B): 3–10. https://doi.org/10.1302/0301-620x.99b4.bjj-2016-1212.r1

Pulido L, Ghanem E, Joshi A, Purtill JJ, Parvizi J (2008) Periprosthetic joint infection: the incidence, timing, and predisposing factors. *Clin Orthop Relat Res* **466**(7): 1710–1715. https://doi.org/10.1007/s11999-008-0209-4

Romano CL, Romano D, Albisetti A, Meani E (2012) Preformed antibiotic-loaded cement spacers for two-stage revision of infected total hip arthroplasty. Long-term results. *Hip Int* **22**(Suppl 8): S46–S53. https://doi.org/10.5301/hip.2012.9570

Sanchez-Sotelo J, Berry DJ, Hanssen AD, Cabanela ME (2009) Midterm to long-term followup of staged reimplantation for infected hip arthroplasty. *Clin Orthop Relat Res* **467**(1): 219–224. https://doi.org/10.1007/s11999-008-0480-4

Shirwaiker RA, Springer BD, Spangehl MJ et al (2015) A clinical perspective on musculoskeletal infection treatment strategies and challenges. *J Am Acad Orthop Surg* **23** (Suppl): S44–S54. https://doi.org/10.5435/JAAOS-D-14-00379

Strange S, Whitehouse MR, Beswick AD et al (2016) One-stage or two-stage revision surgery for prosthetic hip joint infection – the INFORM trial: a study protocol for a randomised controlled trial. *Trials* **17**(1): 90. https://doi.org/10.1186/s13063-016-1213-8

Suda AJ, Tinelli M, Beisemann ND, Weil Y, Khoury A, Bischel OE (2017) Diagnosis of periprosthetic joint infection using alpha-defensin test or multiplex-PCR: ideal diagnostic test still not found. *Int Orthop* **41**(7): 1307–1313. https://doi.org/10.1007/s00264-017-3412-7

Tsang SJ, Ting J, Simpson A, Gaston P (2017) Outcomes following debridement, antibiotics and implant retention in the management of periprosthetic infections of the hip: a review of cohort studies. *Bone Joint J* **99-b**(11): 1458–1466. https://doi.org/10.1302/0301-620x.99b11.bjj-2017-0088.r1

Wolf CF, Gu NY, Doctor JN, Manner PA, Leopold SS (2011) Comparison of one and two-stage revision of total hip arthroplasty complicated by infection: a Markov expected-utility decision analysis. *J Bone Joint Surg Am* **93**(7): 631–639. https://doi.org/10.2106/JBJS.I.01256

Wouthuyzen-Bakker M, Nijman JM, Kampinga GA, van Assen S, Jutte PC (2017) Efficacy of antibiotic suppressive therapy in patients with a prosthetic joint infection. *J Bone Joint Infect* **2**(2): 77–83. https://doi.org/10.7150/jbji.17353

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