Strategies in prevention and treatment of prosthetic joint infections

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SECTION

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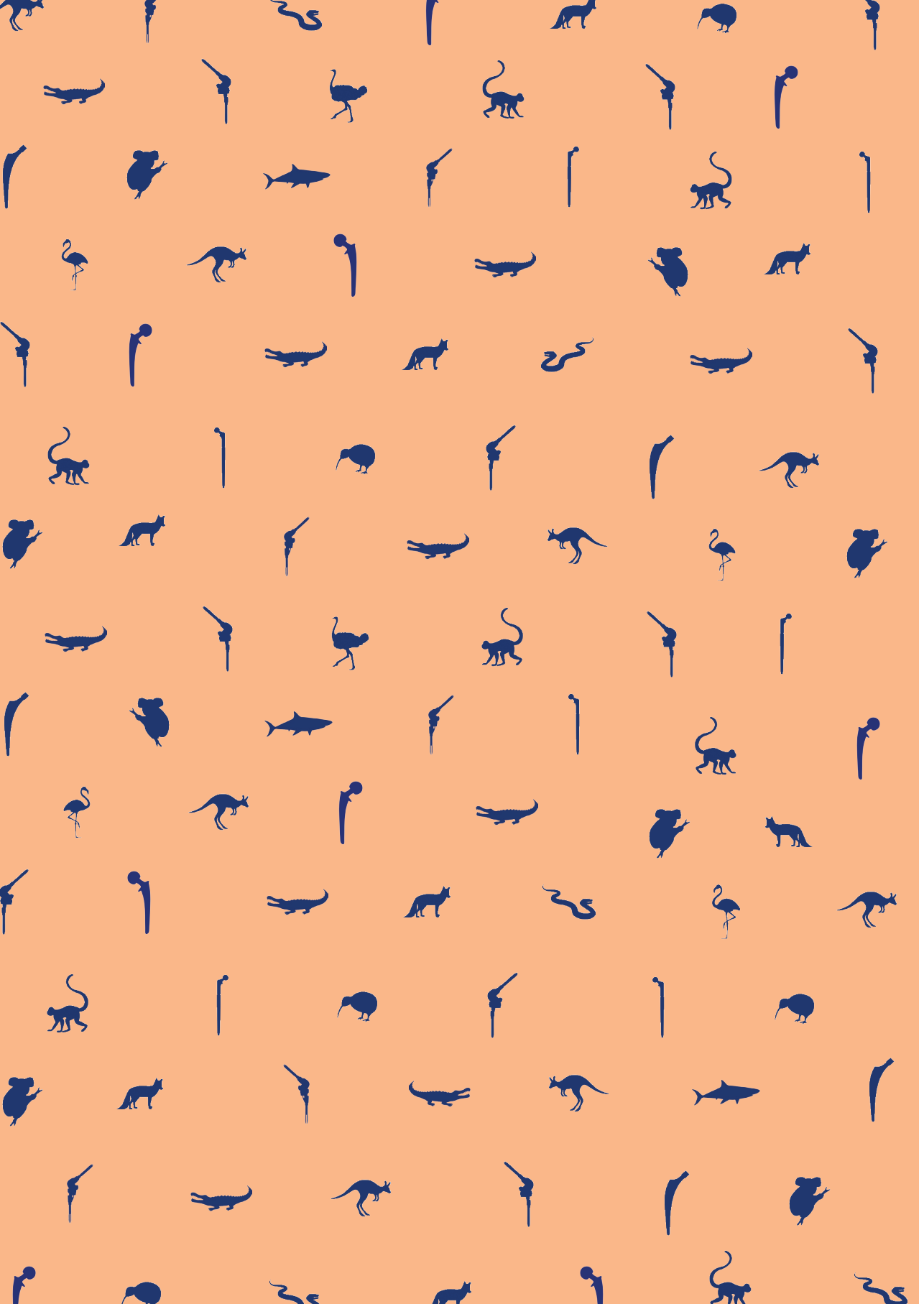

CHAPTER

4

Hip and Knee Section, Treatment, Algorithm: Proceedings of International Consensus on Orthopaedic Infections

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QUESTION 1:

Should early postoperative infection and acute hematogenous infection be treated and managed differently?

Recommendation:

There is no evidence to support the notion that early postoperative infection and acute hematogenous infection should be treated differently as long as the onset of symptoms is < 4 weeks (favourable <7 days). Implants are well-fixed, no sinus tract exists, and the isolated infecting organism is sensitive to an antimicrobial agent.

Level of Evidence: Moderate
Delegate Vote: Agree: 94%, Disagree: 5%, Abstain: 1% (Super Majority, Strong Consensus)

Rationale:

Early postoperative infection is usually defined as infection occurring within 3 weeks of index arthroplasty, although some authorities state that any infection within 3 months (90 days) of the index arthroplasty should be considered acute.[1] Hematogenous infections associated with a remote source are often classified as late infections, which can occur 1 to 2 years after arthroplasty.[2] Acute hematogenous infection is defined as infections with no more than 3 weeks of symptoms.[3] According to the Clinical Practice Guidelines by the Infectious Diseases Society of America, patients who have a well-fixed, functioning prosthesis without a sinus tract, infection occurring within 30 days of index arthroplasty or <3 weeks of onset of infectious symptoms, and having an organism susceptible to oral antimicrobial agents, should be candidates for debridement and implant retention (DAIR).[4] The International Consensus Meeting 2013 also proposed that DAIR should be considered in patients with infection occurring within 3 months of the index arthroplasty, with less than 3 weeks of symptoms in early postoperative infections, and those with symptoms less than 3 weeks in late hematogenous infection.[3] When these criteria are met, DAIR is a reasonable option for early postoperative or acute hematogenous infection. However, because of the relatively high failure rate of DAIR in some reports and the fact that mature biofilm on an implant surface forms within a few days, some studies have suggested that the DAIR should be restricted to patients with less than 5 days of infection symptoms.[5]

One prospective study demonstrated that 52% of acute hematogenous infections failed at 2-year follow-up following DAIR.[6] Treatment failure rates were 57.8% in

staphylococcal infection, 14.3% in streptococcal infections, and no failures were seen in gram-negative periprosthetic joint infection (PJI).[6] A second comparative study reported that the success rates after DAIR in hip and knee PJI may be significantly increased if treatment was initiated within 2 days of symptoms.[7] In the latter study, DAIR showed overall success rate of 82.1% for early infections and 57.1% for acute hematogenous infections. Patients with acute hematogenous infections had an 8-fold higher chance of failure. Given the higher failure rate in the acute hematogenous group, the authors suggested that treatment parameters for these infections required additional studies with higher patient numbers.[7] A recent study evaluating the outcome of DAIR showed no statistically significantly different treatment outcomes between early postoperative infection (15%) versus acute hematogenous infection (21%).[8] Modular components were exchanged in only 70% of the included patients in the latter study. Systemic host grade A (McPherson classification) was a strong predictor of treatment success.[8]

Several systematic reviews suggest that interventions in both early postoperative and acute hematogenous infections should be timely and aggressive (with exchange of modular parts), as each additional day of waiting lowers the odds for a successful outcome.[9-12] A recent meta-analysis reported the significant determinants of successful outcome following DAIR.[12] Time from onset of symptoms or index arthroplasty (<7 days) and the exchange of modular components were the most significant factors influencing outcome. In the latter meta-analysis, the authors detected that the reported success of DAIR has increased since 2004.[12] The exact reason for this improvement in outcome is not known but may relate to a publication in 2004 by Zimmerli et al which established an algorithm for DAIR.[10] The algorithm may have encouraged the orthopaedic community to change their indications for DAIR, attempt to optimize patients before DAIR by modifying risk factors for failure, and possibly altering the administration of antimicrobial regimen. Virulent organisms causing PJI are also predictors for treatment failure following DAIR, according to some studies. Staphylococcus aureus and methicillin-resistant S. aureus have been reported to result in a higher failure rate following DAIR when compared with gram-negative pathogens.[9,13] In addition, infections with methicillin-resistant Staphylococcus epidermidis and Vancomycin-resistant enterococci have been associated with inferior outcome following DAIR.[9,10] In contrast, in a study on early postoperative and acute hematogenous infections caused by S. aureus, this difference could not be shown.[14]

Acute hematogenous infection might be a marker of poor general health as almost half of the patients in one study had some critical medical comorbidity that may

have predisposed them to developing infection in the first instance.[15] Relatively high mortality rates around 20% after 2 years have been reported for patients with acute hematogenous infections, which could be attributed to higher rates of systemic sepsis at presentation in this patient population.[14,15]

In conclusion, DAIR is a viable option and a reasonable first therapeutic approach for patients with early postoperative and acute hematogenous infections. However, some studies have reported a high failure rate of this surgical treatment and a relatively high early mortality rates after DAIR for acute hematogenous infections compared with acute postoperative infections. These differences might be related to differences in the patho-etiology of these infections and the influence of the intrinsic host factors on the outcome. Therefore, studies focusing on improving treatment outcomes after acute hematogenous infections are desperately needed.

QUESTION 2:

Should operative treatment differ in patients with systemic sepsis in the setting of PJI?

Recommendation:

Yes. Patients with systemic sepsis in the setting of PJI should have surgical bioburden reduction, either with implant retention or resection of components (if indicated and safe), along with concurrent antimicrobial therapy. Reimplantation should be delayed until sepsis is resolved.

Level of Evidence:	Limited
Delegate Vote:	Agree: 79%, Disagree: 19%, Abstain: 2% (Super Majority, Strong Consensus)

Rationale:

Infection of total joint arthroplasty is a known and devastating complication all surgeons seek to avoid. Despite best efforts, prosthetic joints can be seeded from local and systemic sources.[16-24] Although periprosthetic joint infection (PJI) usually presents without systemic signs of pyrexia, chills, and other symptoms, occasional PJI may result in systemic sepsis when the blood culture may also be positive for infection. In the context of systemic sepsis, hematogenous spread is the definitive mechanism by which PJI develops in previously well patients. Orthopaedic infections appear to be caused by the same common group of bacterial pathogens. In this group, the majority are gram-

positive cocci, namely, Staphylococcus aureus and Staphylococcus epidermidis. There is the ever present threat of methicillin-resistant S. aureus as a difficult PJI infection to remove. Moreover, the growing number of vancomycin-resistant enterococcus and other serious Gram-negative bacteria are also a concern. Gram-negative bacteria are associated with more severe episodes of sepsis because of the production and release of lipopolysaccharides (endotoxin).

Highlighted across several studies is the concept of the arthroplasty surface acting as a unique microbial substratum.[25] Gallo et al reported the affinity of S epidermidis to attach to the polyethylene surfaces as opposed to S. aureus preference for bare metal. In each of the papers examined by Gallo et al, the presence of biofilm on the wearing or corroded surfaces of the implants was a key factor in the bacterial resistance to host and antimicrobial attack. A paper referenced in the Gallo et al review by Gristina, characterized the colonization of the prosthesis as a "race for the surface".[25,26] This concept is apt at highlighting the need for pathogens to colonize, undeterred by local and host factors.

These concepts are of pivotal importance when examining the published material reviewed here in the context of the original question "To evaluate whether operative treatment should differ in patients with systemic sepsis in the setting of prosthetic joint infection." As demonstrated in this review and supported by the significant cohort size, PJI can occur as a consequence of local or hematogenous colonization. Overall, severity of infection is higher with hematogenous spread, as is the difficulty in clearing the infection for subsequent implant revision.[27-29] Osteomyelitis before implantation of prosthetic joints indicates increased risk as reported by Jerry et al.[19] The nearly 5-fold increase in recurrence rates seen in patients with prior bone infection serves as a significant warning to surgeons to adequately debride as much contaminated surface as is feasible to allow for control of infection and subsequent implantation.[19]

Based on the articles included in this review, there is no evidence to suggest that the implantation of prosthetic joints during an episode of sepsis is advisable. Often, however, joint arthroplasty procedures will need to be performed to alleviate the tremendous pain associated with infective destruction of a joint surface. Each of the included studies recommended a staged approach to surgical management of PJI with the most common approach being 2-staged revision. There is very limited evidence to support retention of implants if a curative outcome is the main objective of the treatment. Also, there is a lack of evidence to suggest initiating antibiotic therapy to counter the systemic sepsis before the first stage revision surgery. Although

identification and eradication of clinically obvious secondary foci, similar to indwelling catheters and skin, soft tissue, respiratory, and genitourinary infections could be of vital importance for controlling the PJIs and preventing subsequent relapse. Therefore, similar to PJIs without systemic sepsis, a combination of effective debridement and concurrent intravenous antimicrobial therapy is the current best practice standard of care. The main limitation associated with the effective execution of this thorough and proven care strategy seems to be the accurate diagnosis of the complete clearance of infection to restore aseptic status to the patient.

It must be noted that, as of the completion of this review, there are no studies that directly evaluate whether operative treatment should differ in patients with systemic sepsis in the setting of prosthetic joint infection. There are a number of closely related papers quoted previously, but that is the limit of current knowledge. It is, however, our opinion that patients with systemic sepsis exhibiting constitutional symptoms are at serious risk and should be treated urgently. The best option of treatment is bioburden reduction which involves extensive soft tissue debridement and removal of infected prostheses.

QUESTION 3:

What should be done for patients with persistent wound drainage after total joint arthroplasty? What are the indications for surgical intervention?

Recommendation:

Management of draining wounds after total hip or knee arthroplasty consists of 2 main steps; nonoperative and operative. The nonoperative measures include modification of venous thromboembolism prophylaxis, nutritional supplementation, dressing measures (such as negative-pressure wound therapy), and restriction of range of motion. If draining continues for more than 7 days after implementing the nonoperative measures, operative interventions may be indicated including irrigation and debridement, synovectomy, and single-stage exchange. In certain situations, superficial wound washout may be indicated (Fig. 1).

Level of Evidence:	Limited
Delegate Vote:	Agree: 89%, Disagree: 8%, Abstain: 3% (Super Majority, Strong Consensus)

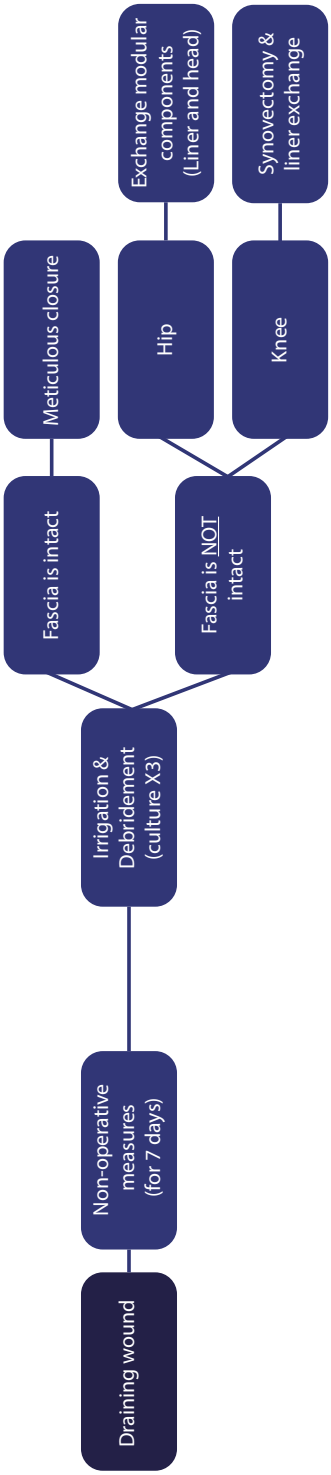

Figure 1: Management of draining wounds after total joint arthroplasty.

Rationale:

Drainage after total hip and knee arthroplasty increases the risk of subsequent superficial or deep infection. Studies have shown that the risk of deep infection increases by 29% after total knee arthroplasty (TKA) and 42% after total hip arthroplasty (THA) with each additional day of drainage.[30]

DEFINITION

Persistent wound drainage (PWD) by definition is an area of drainage greater than 2x2 cm on the incisional gauze that persists over 72 hours postoperatively.[31] Drainage can be due to hematoma, seroma, fat necrosis, or defects in arthrotomy closure.[32]

Nonoperative Measures

Ceasing Anticoagulation Agents Anticoagulation agents for venous thromboembolism prophylaxis have been shown to affect PWD after total hip and knee arthroplasty. Low-molecular-weight heparin leads to higher rates of prolonged wound drainage after THA and TKA compared with aspirin and warfarin.[30] Fondaparinux had fewer wound complications but no difference in infection after TKA compared with aspirin, low-molecular-weight heparin or warfarin.[33] Dabigatran was found to have an increased rate of wound drainage and increased length of stay after TKA and THA.[34] Therefore, one of the first steps in patients with PWD is to cease the anticoagulation medications, if possible.

Negative-Pressure Wound Therapy

Negative-pressure wound therapy (NPWT) applied to closed incisions after TKA or THA has been shown to reduce the rate of superficial wound infection.[35] In patients undergoing primary total hip or knee arthroplasty, NPWT has been shown to reduce postsurgical wound exudate, number of dressing changes, a trend toward reduced length of stay, and a trend toward reduced postop surgical wound complications.[36] Using ultrasound to measure volume, NPWT has been shown to reduce the size of postop seromas when compared to a standard dressing.[37] NPWT applied 3-4 days after THA for persistent drainage resulted in drainage resolution in 76% while 24% required further surgery.[38] As part of local wound care in the first 7 days of PWD, we recommend using incisional NPWT systems.

Nutrition

Malnourishment has several definitions. One of the most commonly used ones is serum transferrin <200 mg/dL, serum albumin <3.5 g/dL, or total lymphocyte count <1500/

mm3. Poor nutritional status is associated with a significant (up to 5-fold) increase in risk of wound complications after THA and TKA.[39-41] Malnourished patients are more likely to fail nonoperative treatment (odds ratio 18.29), as well as surgical debridement (35% vs 5%, P < .0003).[3] We strongly urge modifying the nutritional status of the patients before an elective arthroplasty procedure. In case of a PWD, postoperative nutritional supplements can help improving the wound healing process.

Surgical Intervention

Surgical intervention for drainage should be considered after 5-7 days of PWD.[30-32] Saleh et al conducted a 20-year surveillance study and concluded that patients with longer 5 days of drainage have 12.7 times higher likelihood to develop surgical site infection in comparison with those who had less drainage time.[31] Therefore, we recommend proceeding with surgical intervention if the PWD continues for more than 7 days.

The first step of the surgical intervention is irrigation and debridement (I&D) and obtaining at least 3 intraoperative cultures. Irrigation is recommended to be performed with at least 9 L of an irrigation solution, such as normal saline or an aqueous iodophor solution. At this point, if the fascia is found to be intact we recommend meticulous closure. However, if the fascia is not intact, modular components should be exchanged.[30,32] Studies have shown promising results with single I&D. Jaberi et al reported that in THA and TKA patients with PWD, drainage stopped in 76% of patients after single-stage I&D.[30] The remaining 24% required subsequent treatments such as repeat I&D, removal of implant, or long-term antibiotic administration.

QUESTION 4:

How should infected bilateral hip or knee arthroplasties be managed?

Recommendation:

The optimal surgical treatment for infected bilateral hip or knee arthroplasties is unknown. While revising the components likely provides improved outcomes over limited debridement with component retention, data do not preferentially support either a single-stage or 2-stage exchange revision arthroplasty.

Level of Evidence:	Limited
Delegate Vote:	Agree: 83%, Disagree: 11%, Abstain: 6% (Super Majority, Strong Consensus)

Rationale:

Infected bilateral hip or knee arthroplasties presents a rare treatment dilemma for both the patient and surgeon. The literature on this topic is limited, however, with only 2 small case series and at least 9 case reports describing multiple simultaneous periprosthetic joint infections.[16,20,42-56] Treatment options include debridement with component retention, single-stage revision, and two-stage revision surgery. The largest study by Wolff et al on infected bilateral total knee arthroplasty demonstrated improved outcomes with a simultaneous 2-staged revision when compared with irrigation, debridement, and prosthetic salvage.[45] Concerns exist about the morbidity of a 2-stage revision and the immobility and restricted weight bearing on both extremities during the antibiotic spacer period. A series of 16 bilateral infected arthroplasty patients by Zeller et al noted good results with single-stage exchange and another center reported 2 cases of successful treatment of bilateral infected total hip arthroplasty with a simultaneous single-stage revision.[46,56]

Surgical treatment of bilateral infected arthroplasties should consider factors such as the virulence of the organism, medical comorbidities, patient age, and functional status. For bilateral acute hematogenous infection, some authors performed an irrigation, debridement, and exchange of modular bearing surfaces followed by targeted antibiotic therapy, but these results were limited to case reports.[44,47-52,54,55] For chronic bilateral periprosthetic infections, these case reports described the same therapeutic management as is commonly favoured for unilateral infection: 2-stage revision with placement of an antibiotic impregnated cement spacer for a period of at least 6-8 weeks before reimplantation.[48,53,54] An interval of several days occurred between each side undergoing surgery in these series, while others performed simultaneous bilateral revision surgery. The decision whether to perform simultaneous bilateral revision surgery for periprosthetic joint infection should also consider the patient's medical comorbidities and functional status. With only small retrospective case series in the literature, we can issue a limited recommendation that revising the components likely results in improved outcomes; however, we do not have the data to recommend a single-stage or 2-stage revision procedure over the other.

We do however feel that performing resection arthroplasty of 2 joints under the same anaesthesia represents immense physiological insult to the patient and all efforts should be made to minimize the operative time and blood loss in these patients, if bilateral surgery is contemplated. The use of two expert teams to operate at the same time has been suggested by some investigators.

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