

## 3.2. TREATMENT: MULTIDISCIPLINARY ISSUES

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**QUESTION 1:** Should periprosthetic joint infection (PJI) cases be referred to a regional center to improve the outcome of treatment and decrease cost?

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RECOMMENDATION: Yes, for probable better outcome and greater efficiency.

LEVEL OF EVIDENCE: Consensus

DELEGATE VOTE: Agree: 92%, Disagree: 6%, Abstain: 2% (Super Majority, Strong Consensus)

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### RATIONALE

PJI significantly increases the utilization of hospital and physician resources compared to primary cases or aseptic revisions [1]. There is evidence to support that primary total joint replacements performed in a specialized center may have lower complications and lower reoperations than those performed in non-specialized centers [2]. This experience should be extrapolated for the treatment of PJIs. It is reasonable to assume that treatment of patients with PJI in tertiary centers provides access to a multidisciplinary group of healthcare providers [3]. This is important, as management of patients with PJI usually requires interaction with a large group of healthcare providers such as infectious disease specialists, pharmacists, plastic surgeons, rehabilitation experts and so on. It has been demonstrated that the work of a multidisciplinary team using well-established protocols may achieve excellent results in management of a complex group of patients including those with PJI [4]. Moreover, an infected total knee arthroplasty (TKA) performed primarily at an arthroplasty center may have better clinical outcome after PJI treatment compared to those cases performed primarily in another type of hospital [5].

When treating a previously-failed PJI case, the place where the subsequent treatment is taken over may be even more important. A recent study evaluated the frequency, associated factors and mortality of amputation and arthrodesis after a failed treatment for infected TKA [6]. The results of this study suggest that recommending centers with a high volume of joint arthroplasties may be a way to reduce the risk of salvage procedures.

In agreement with our recommendations, it has been observed that referrals to tertiary centers to treat PJI have increased [7]. These cases may also generate a financial incentive for the accepting institution [7].

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**QUESTION 2:** What intraoperative findings during surgical management of orthopaedic infections need to be communicated with the infectious disease (ID) specialist?

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RECOMMENDATION: Intraoperative findings that contribute to the diagnosis of periprosthetic joint infection (PJI) must be communicated to the ID specialist. The presence of a sinus tract (major diagnostic criteria) or any other valuable objective data such as cell count, neutrophil differential, frozen section, as well as the result of the point of care diagnostic tests, such as leukocyte esterase and lateral flow alpha-defensin need to be communicated to the ID specialist. The extent of infection, in terms of involvement of soft tissues and bone, any hardware retained and the antibiotic type and dose used in the cement spacer are also useful information that should be detailed in the operative report for communication with the ID specialist.

LEVEL OF EVIDENCE: Consensus

## RATIONALE

For the purposes of this review, information or data that could be obtained during the course of the surgery and that could impact or influence the surgeon's or infectious disease specialist's decision-making, were categorized into two groups: surgeon findings or observations and intraoperative tests. The recommendations below presume that the surgeon is already documenting/communicating the precise surgery performed (e.g., debridement with retention of prosthesis vs. resection arthroplasty vs. first-stage of two-stage revision) and any plans for future surgery.

The area with the least evidence to support recommendations was that of surgeon observations. Intraoperative findings observed by the surgeon that could impact the decision-making of either the surgeon or infectious disease specialist would seem to be reasonable information to relay to the ID specialist. However, the objectivity and standardization of these findings are highly variable. A prior study compared the clinical acumen of the orthopaedic surgeon to the addition of further advanced testing in diagnosing PJI and found that the addition of intraoperative visual inspection and histopathology improved the accuracy of the surgeon's preoperative diagnosis, though there was no description of discrete or objective definitions of the intraoperative visual inspection [1].

The presence of a sinus tract, one of the major diagnostic criteria of PJI, may be confirmed during the course of a surgery and should be relayed to the ID specialist [2]. The presence of purulence is one visual finding that had long been held as an important intraoperative finding that suggested infection [3] and was supported as a minor criteria in the definition of infection by the workgroup of the Musculoskeletal Infection Society (MSIS) [4]. Due to concerns about the subjectivity of the finding of purulence and the confusing picture that exists in the setting of other causes of cloudy synovial fluid, including metallosis and corrosion, purulence was removed from the minor diagnostic criteria by the International Consensus Meeting (ICM), when they revised the MSIS criteria. Alijanipour et al. [5] evaluated in their study whether purulence was a reliable marker of infection and found a sensitivity, specificity, positive and negative predictive values of 0.82, 0.32, 0.91 and 0.17, respectively. They noted that purulence was not correlated with higher culture positivity, but associated with higher synovial white blood cell (WBC) counts.

Recently, a publication by Parvizi et al. [6] entitled, "The 2018 Definition of Periprosthetic Hip and Knee Infection: An Evidence Based and Validated Criteria," established a diagnostic algorithm, emphasizing the role of intraoperative findings that are determinant for diagnosis of PJI. The recent criteria do include purulence as a minor criterion. The other tests have also been assessed using the preprobability testing and assigned a diagnostic score.

As the diagnosis of PJI is made usually by relying on a combination of tests, it is critical that the intraoperative findings related to its diagnosis are communicated with the ID specialist. For example, the presence of a sinus tract (major diagnostic criteria) should be confirmed intraoperatively and communicated to the ID specialist.

Other intraoperative findings that may also provide insight into the condition of the joint and influence treatment includes the soft tissue quality or condition, bone quality or condition, implant stability and the amount or type of hardware that was removed or retained. The ID specialists may alter the course and duration of the antibiotic treatment based on these findings. It is critical that the surgeon informs the ID specialist about any hardware that may have been retained. The latter, in particular, influences the course of treatment of the patient [7–10].

The second category of data that is obtained during the course of the procedure and should be communicated to the ID specialist are the results of intraoperative tests. If an intraoperative aspiration of the joint is performed and/or frozen section of the intraoperative samples are analyzed, the result of such findings should also be communicated to the ID specialist. These studies may impact the decision-making and help confirm the diagnosis. However, the results of these studies are not immediately available in the medical record or may not be recorded anywhere else, other than the surgeon's report. Intraoperative frozen histopathology represents one such study. Typical workflow entails a sample being sent to the pathology lab during the course of the surgery and often the result is telephoned into the surgical theater, with a formal written report to follow, sometimes days later. Given the potential importance of those findings on the decision-making and impact it may have on treatment [11–14], the results from this study should be communicated to the ID consultant. In addition to communicating the histology results, it is important to document the anatomic area from which the specimen was taken. Similarly, tissue samples sent for culture should be clearly labeled so that the ID specialist can understand which pathogens were found (e.g., superficial or deep, bone or synovium).

Other intraoperative tests may be valuable in the diagnosis and treatment decision-making for periprosthetic infections and the results should also be available to the ID consultant. Buttaro et al. [15] reported that synovial C-reactive protein (SCRP) had comparable diagnostic value compared to frozen sections. This was confirmed by Saleh et al. [16] who reported a high diagnostic value with SCRP, but also demonstrated diagnostic value testing for leukocyte esterase (LE), interleukin-6 (IL-6), interleukin-1 $\beta$ ,  $\alpha$  defensin, and interleukin-17 biomarkers. Given the comparable findings in the literature combined with both the relatively inexpensive and immediate point of care (POC) results, Saleh et al. [16] recommend the use of LE testing as a first-line assessment when the diagnosis of PJI is questionable. Another POC test includes the lateral flow IL-6 device, which has shown promising results in the PJI population. Kasperek et al. [17] reported on a POC lateral flow test for  $\alpha$  defensin and suggest that although it lacks the accuracy of the lab-based  $\alpha$  defensin, it is comparable to evaluating frozen sections. However, they note that it has limited use in cases involving metallosis and further suggest that it may not be used in isolation to rule out PJI [17]. These findings were further supported by a recent review where the authors recommend that care must be taken when interpreting the results of the lateral flow  $\alpha$  defensin test for the diagnosis of PJI intraoperatively [18]. As new POC tests are developed, or current ones are improved upon, the surgeon's intraoperative decision-making combined with these POC biomarker assays may prove to enhance the care that adult reconstruction patients are given, especially in the setting of revision total joint arthroplasty.

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### QUESTION 3: What quality of life (QOL) measures should be used when determining the functional outcomes of periprosthetic joint infection (PJI) treatment?

**RECOMMENDATION:** Currently, there are no QOL measures specific to determining outcome in PJI. However, when determining the outcomes of any arthroplasty related procedure, the current recommendations are to use both a general well-being/QOL measure (i.e., Patient-Reported Outcomes Measurement Information System (PROMIS) Global 10, Short Form 36 (SF-36), the Veterans RAND 6-Item Health Survey (VR-12), EuroQol five-dimensional (EQ-5D)) and a joint/disease specific (i.e., Western Ontario McMaster Osteoarthritis Index (WOMAC), Hip Disability and Osteoarthritis Outcome Score (HOOS Jr) or Knee Injury and Osteoarthritis Outcome Score (KOOS Jr)) patient-reported outcome measure. Supplemental information such as surgeon-reported outcome measures, an activity-specific score and satisfaction surveys may be helpful. However, the ideal combination has yet to be determined and validated for patients treated for PJI.

**LEVEL OF EVIDENCE:** Consensus

**DELEGATE VOTE:** Agree: 96%, Disagree: 1%, Abstain: 3% (Unanimous, Strongest Consensus)

### RATIONALE

One of the most severe complications after total joint arthroplasty (TJA) is a PJI [1]. Infections can present in many forms and their treatment can be just as variable (i.e., debridement, antibiotics and implant retention, one-stage exchange, two-stage exchange, resection arthroplasty, arthrodesis or amputation). Regardless of the approach, the goal of treatment is to improve the patient's overall and joint specific health. Outcome measures provide measurements of these domains to assess the effectiveness of an intervention [2]. However, there is no specific instrument of quality of life to evaluate patients with PJI at this time. Until such a tool is developed, the question becomes which of the existing measures should be applied to measure functional outcomes in this unique patient population.

**TABLE 1. Summary of PJI treatment studies using outcome measures**

Author	Year	Outcome Measure	Design	Treatment
Younger [13]	1997	SF36, HHS, Satisfaction Questionnaire	Retrospective	Two-stage
Hsieh [14]	2004	WOMAC, HHS	Prospective	Two -stage

Wang [4]	2004	SF12, KSS	Prospective	Knee, two-stage
Meek [15]	2004	SF12, WOMAC, Oxford, Patient Satisfaction	Retrospective	Knee spacer
Klinger [16]	2006	SF36, KOOS	Retrospective	Knee, arthrodesis
Masri [17]	2007	WOMAC, HHS	Retrospective	Two-stage
Scharfenberger [18]	2007	SF36, WOMAC, HHS	Retrospective	Hip, two-stage
Parvizi [1]	2008	SF36	Retrospective	Two-stage
Cahill [5]	2008	SF36, WOMAC, Satisfaction Questionnaire	Prospective	Hip, knee
Biring [19]	2009	SF12, WOMAC, UCLA Activity Scale, Oxford 12, Satisfaction Questionnaire	Retrospective	Hip, two-stage
Romanò [6]	2010	SF12, WOMAC, HHS	Prospective	Hip, two-stage
Boettner [3]	2011	SF36, HHS	Retrospective	Hip
Leung [20]	2011	SF12, WOMAC, UCLA Activity Scale, Oxford, Satisfaction Questionnaire	Retrospective	Hip, two-stage
Kappler [21]	2012	SF12, WOMAC	Retrospective	Two-stage
van Diemen [22]	2013	HOOS, mHHS	Retrospective	Hip
Sabry [23]	2013	SF12, mHHS	Retrospective	Two-stage
Aboltins [24]	2013	HHS, SF12	Prospective	Hip, case control
Barbarić [25]	2014	SF36, WOMAC, COOP/WONCA, FES-I	Retrospective	Two-stage
Helwig [26]	2014	SF12	Retrospective	Hip, knee
Helito [27]	2015	SF36	Retrospective	Knee, amputation
Nuñez [28]	2015	SF36, WOMAC	Prospective	Knee, DAIR

Röhner [29]	2015	KOOS, SF36, WOMAC, KSS, Lysholm	Retrospective	Knee, arthrodesis
Aboltins [30]	2016	SF12	Prospective	Hip, DAIR
Grammatopoulos [31]	2017	OHS	Retrospective	Hip, DAIR
Poulsen [32]	2018	EQ-5D, OHS	Retrospective	Hip, two-stage
Beaupre [33]	2017	WOMAC, RAND 36	Retrospective	Hip spacer

SF36, Short Form 36; HHS, Harris Hip Score; WOMAC, Western Ontario McMaster Osteoarthritis Index; SF12, Short Form 12; KSS, Knee Society Score; UCLA Activity Score, University of California Los Angeles Activity Score; HOOS, Hip Disability and Osteoarthritis Outcome Score; Mhhs, Modified Harris Hip Score; COOP/WONCA, Dartmouth Primary Care Cooperative Research Network/World Organization of National Colleges, Academies, and Academic Associates of General Practitioners/Family Physicians; FES-I, Falls Efficacy Scale – International; KOOS, Knee Injury and Osteoarthritis Outcome Score; Lysholm, Lysholm Knee Score Scale; OHS, Oxford Hip Score; EQ-5D, EuroQol five-dimensional; RAND, Research and Development Corp.

After a literature review, 26 studies were identified from 1997 to 2017 that addressed functional outcomes in the setting of PJI treatments (Table 1). The most commonly-used outcome measurements were WOMAC (13 studies), Short Form 36 (SF-36) (10 studies), and Short Form 12 (SF-12) (10 studies). Overall, 19/26 studies (73.1%) reported both an overall health measure in combination with a joint or disease-specific measure. No studies compared one outcome measure to another as a gold standard outcome measure for TJA/PJI does not exist [2]. When compared to aseptic revisions, septic revisions tended to have worse functional outcomes [3,4] but differences in mental, emotional or satisfaction outcomes were mixed [3–6].

Since no current literature or consensus has specifically addressed which outcome measures should be used in infection, the recommendations are extrapolated from TJA in general. Meetings have recently been held to address the heterogeneity in outcome measure reporting in TJA in general. The first was the Patient-Reported Outcomes Summit for Total Joint Arthroplasty convened by the American Association of Hip and Knee Surgeons (AAHKS) in 2015 [7]. The group recommended that either the PROMIS 10 or the VR-12 instruments be used to assess general health, in addition to KOOS Jr and HOOS Jr for disease specific health. These instruments were chosen because they have been validated and contain a minimal number of questions [7–9]. This has been followed by The International Consortium for Health Outcome Measurements (ICHOM) as well as the International Society of Arthroplasty Registries (ISAR). Both have endorsed a multidimensional strategy in order to evaluate the results after TJA, including: (1) a general health/QOL score, (2) an organ-specific score and (3) a satisfaction question [10–12].

In conclusion, QOL outcome measures should be recorded in the PJI population similar to general arthroplasty. There is no evidence to suggest which specific outcome is superior in PJI patients as none of them have been specifically validated. Guidelines from previous meetings and consensus literature support the use of a both a global health measure in addition to a joint/disease specific measure at minimum, but do not specifically recommend a particular measure for PJI patients. Adjunct tools such as a satisfaction questionnaire should also be considered.

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