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QUESTION 6: What intraoperative metrics can be utilized at the time of intended reimplantation to help decision-making and reduce the risk of subsequent recurrence?

RECOMMENDATION: Intraoperatively, frozen section and leukocyte esterase (LE) strip test can be used as decision-making metrics for reimplantation.

LEVEL OF EVIDENCE: Limited

DELEGATE VOTE: Agree: 66%, Disagree: 25%, Abstain: 9% (Super Majority, Weak Consensus)

RATIONALE

The intraoperative decision-making process for reimplantation must be based on metrics that are fast (due to time constraints), accurate to reduce the risk of recurrence and reliable so that such metrics can be reproduced in many scenarios.

Frozen Section (FS)

Intraoperative FSs have been used as a fast and accurate indicator of infection during reimplantation due to high specificity. Most of the studies recommend withholding reimplantation in the presence of positive results. Nonetheless there is a debate regarding optimal cutoff for the number of polymorphonuclear cells (PMNs) per high-power field and whether this should be a quantitative or qualitative analysis. The primary reason FS is not universally accepted as a decision-making marker is its reliability. FS continues to have a low sensitivity (between 25 - 50%) in the presence of infection [1–5]. FS is also dependent on a highly specialized pathologist with experience, which is evident in a study published by George et al. where even in the presence of a highly trained pathologist, the sensitivity only reached 50% [5]. Gram and fungal stains have very low sensitivity [6–8], and therefore are not recommended.

Leukocyte Esterase (LE)

The LE strip test has the advantages of being a fast, accurate and reliable test. This is supported by several recently published studies and a meta-analysis [9–22]. These publications show that LE has a sensitivity that ranges from 49% up to 95%, and a specificity that ranges from 82 - 100%. Some papers also have shown a positive predictive value (PPV) from 71.5 to 100%.

One of the limitations observed with LE, being a colorimetric assay, was the potential for inaccurate readings in the presence of a bloody sample. A recent study by Li X et al. [23] showed that when a bloody sample is centrifuged, the LE continues to have excellent sensitivity and specificity (92 and 93.1% respectively), making it still a very reliable test for intraoperative decision-making. Another concern when LE started to be widely used was its accuracy in the presence of adverse local tissue reactions (ALTR), namely metallosis. Tischler et al. [12] demonstrated that LE combined with PMN % was reliable in ruling out infection in 92.9% of the cases evaluated.

Alpha-Defensin

The alpha-defensin test as a reliable synovial biomarker for the diagnosis of infection was introduced by Deirmengian et al. [14] Since then, newer techniques have been developed which achieve similar results in a faster fashion. Alpha-defensin lateral-flow immunoassays [24–31]are faster and have a sensitivity that ranges from 64.7 - 94.5%, a specificity with a range of 87 - 99.6%, a positive predictive value (PPV) from 74.6 - 98.1%, and a negative predictive value (NPV) from 83.7 - 98.2%. However, a few studies [29,30] have demonstrated that the immunoassay test performed in the laboratory setting is more accurate than the lateral-flow technique, and provides sensitivity ranges from 83.6 - 97.1%, specificity ranges of 97 - 100%, PPV ranges from 94.9 - 100%, and NPV ranges from 89.9 - 98.2%.

As with LE, other factors can impact the accuracy of Alpha-defensin testing. The specificity and PPV can decrease in the presence of ALTR [24] and crystal deposition arthroplasties [31].

Interleukins

Another lateral-flow immunoassay technique being used for the diagnosis of PJI involves interleukins, specifically Interleukin-6 (IL-6). This intraoperative test allows for a rapid assessment of the cytokines within the synovial fluid. This technique is already in use with an acceptable specificity but relatively low sensitivity. However, when IL-6 is measured in the lab with radioimmunoassay techniques, it is more accurate [32].

Despite having these time-tested and novel techniques, the surgeon continues to rely on a combination of preoperative testing, intraoperative clinical judgment and the interpretation of these intraoperative metrics to decide whether it is safe to proceed with reimplantation and avoid the risk of PJI recurrence.

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QUESTION 7: What is the diagnostic accuracy of a frozen section (FS) during reimplantation surgery? What thresholds should be used in this context?

RECOMMENDATION: Adequate peer-reviewed literature exists to support either of two diagnostic thresholds for supporting the diagnosis of periprosthetic infections of the hip and knee: 5 neutrophils (PMNs) in each of at least 5 high power (400X) microscopic fields (HPF), or 10 PMNs in each of at least 5 HPFs.

LEVEL OF EVIDENCE: Moderate

DELEGATE VOTE: Agree: 83%, Disagree: 10%, Abstain: 7% (Super Majority, Strong Consensus)

RATIONALE

A common method of treating periprosthetic infection of the hip or knee is two-stage exchange [1], but it can be difficult to determine if and when the infection has been adequately treated and the infected joint is ready to receive a new implant. The tests commonly used to help diagnose infection at revision arthroplasty, such as serologic tests, microbiologic culture, and the cell count with differential of aspirated joint fluid may have been influenced by the previous surgery as well as an antibiotic-containing spacer and may not have the same predictive value as when they are applied at revision arthroplasty [2].

One of the few tests that can be performed during a reimplantation or revision arthroplasty operation is the interpretation of a FS of