

HK24: Is there a difference in the diagnostic yield of synovial fluid versus periarticular tissues for isolation of infective organisms causing periprosthetic joint infection?

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Response/Recommendation: Yes. Periarticular tissues have a higher yield for the isolation of infective organism(s). Despite the latter, analysis of synovial fluid for various parameters, including culture, plays a critical role, and hence both fluid and periarticular tissue samples should be obtained in the setting of periprosthetic joint infection (PJI).

Level of Evidence: Moderate

Rationale:

Identification of the causative organism(s) in the setting of periprosthetic joint infection (PJI) is crucial for both diagnosis and treatment. Accurate organism identification is necessary for targeted antibiotic therapy and impacts treatment outcomes(1–6). Despite various recently proposed techniques and advanced technologies, conventional culture techniques of synovial fluid (SF) and/or intraoperative periarticular tissue samples remain the most widely used method for organism isolation in PJI.

It is inherently difficult to provide evidence-based recommendations regarding the yield of SF and tissue sample culture results, as there is major heterogeneity within the literature regarding how PJI was defined, study protocols, and statistical analysis. Many institutions have wide variability among culture techniques, sample handling, and sampling protocols. Synovial fluid samples are generally sent for one culture, while periarticular tissues are often sent in multiples. Conventional wisdom proposes that combining multiple tissue samples will improve sensitivity and decrease specificity. Given this, combining multiple tissue samples will improve the culture yield and provide a greater opportunity for a positive result. Additionally, it has been demonstrated that SF samples culture planktonic bacteria more commonly present in acute infections or in PJI secondary to high virulence organisms, versus tissue or sonication cultures which are more likely to capture sessile and biofilm-protected organisms (7,8).

A review of the literature suggests that periprosthetic tissue cultures appear to have greater diagnostic sensitivity (65 to 94%) compared to synovial fluid (45 to 75%) (9–12) however, there are conflicting reports. A recent study by Boyle et al. examined 363 PJI patients, as defined by the most recent ICM criteria, and found 76.8% concordance between preoperative SF samples and intraoperative tissue culture at the time of revision surgery. Only seven (1.9%) SF samples were polymicrobial compared to 35 (9.6%) intraoperative tissue samples. These findings highlight the importance of tissue culture for identifying causative organisms, particularly in the setting of polymicrobial PJI. Organism type did play a role in the concordance rate, with MSSA and MRSA being most likely to be identified with SF samples while *C. acnes* and polymicrobial infections were more likely to be identified with periarticular tissue sampling (13).

In the setting of chronic or indolent PJI, SF samples alone are less likely to identify the causative organism and can often provide false negative results (14). This is supported by recent literature indicating that SF culture poorly identifies slow-growing gram-positive anaerobic bacteria such as *C. acnes* (15,16). Interestingly, Font-Viscarra et al. examined 87 PJIs and compared the frequency of positive cultures between SF samples with periprosthetic tissue and swab samples. They found SF samples to be culture-positive in 90% of cases compared to 82% of tissue samples. The authors partially attributed this to the use of SF sample incubation in blood culture flasks, a notion supported in the literature (17).

Conversely, Schulz et al. (18) evaluated 167 PJI patients who had either a preoperative SF sample or an intraoperative tissue sample with a positive culture. In this study, 66% of synovial fluid cultures identified the causative organism. This was found to be significantly lower compared to intraoperative cultures identifying an organism in 92% of cases. As expected, intraoperative specimens were more likely to identify polymicrobial infections. Chronic infections were more likely to have an organism detected from intraoperative tissue samples rather than synovial fluid, again a common theme seen in the literature. Bjerkan et al. (20) evaluated 18 PJI cases, with SF culture positive in 12, while tissue specimens were culture positive in 16 of the samples ($P = 0.008$), indicating the improved yield of periarticular tissue sampling.

Several studies have evaluated concordance rates between preoperative SF samples and intraoperative samples (Table 1). Tetreault et al. (19) performed a randomized controlled trial of 65 PJI patients who had preoperative culture-positive aspirations and provided prophylactic pre-incisional antibiotics to one group while the other group received antibiotics after tissue samples were collected. The concordance rates between preoperative and intraoperative cultures were 82 and 81% in the pre-incision antibiotic and post-sample antibiotic groups, respectively. Though this highlights that antibiotic use may not impact yield, there is still a difference in organism identification from SF alone and intraoperative tissue. Barker et al. (21) similarly aimed to identify the accuracy of SF aspirations in the setting of PJI. The authors concluded that the post-test probability of synovial fluid culture was not reliable, again highlighting the need for multiple tissue samples.

Also, Huang et al. evaluated 49 PJI patients. They found that SF identified an organism via culture in 61.2% of PJI cases. However, 79.6% of these cases yielded a positive culture when combining synovial tissue and sonicate fluid samples. This again highlights the importance of sampling periarticular tissues for organism identification. Interestingly, next-generation sequencing (NGS), a novel technique that is gaining traction in the world of PJI, identified an organism in 95.6% of PJI patients (22). These findings are similar to those reported in other NGS-related PJI studies, indicating the possible utility of this technology in identifying organisms from both SF and tissue samples in PJI patients(23–26).

In conclusion, both synovial fluid and tissue specimens are helpful in identifying infective organisms in the setting of PJI. Combining multiple periarticular tissues with synovial fluid obtained intraoperatively provides an increased yield overall and is helpful with organism identification in patients who have PJI, particularly in cases of **slow-growing** organisms and polymicrobial infections. More novel techniques, such as tissue and implant sonication, as well as metagenomic sequencing, may provide additional utility in identifying causative pathogens; however, the limited availability and lack of consensus limit their use at this time.

Table 1. Studies in the literature report concordance between preoperative synovial fluid culture results and intraoperative tissue sample results.

Study and Publication Year	Definition of Infection	Concordance rate (%)	Synovial fluid positive culture (%)	Periarticular tissue positive culture (%)
Shanmugasundaram et al. (2014) (27)	Surgeon Discretion	75 (THA) 78.6 (TKA)	44.4 THA 45.2 TKA	85 THA 79.3 TKA
Lindberg-Larsen et al. (2017)(28)	Surgeon Discretion	66		
Declercq et al. (2020) (29)	Sinus tract or 2+ cultures	68.2	77.6	87
Rockov et al. (2020)(30)	MSIS 2011	78.1		
Boyle et al. (2021)(13)	MSIS 2011	76.6		
Schulz et al. (2021)(18)	MSIS based	52.1		

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