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ORIGINAL PAPER

Sonication of explants enhances the diagnostic accuracy of synovial fluid and tissue cultures and can help determine the appropriate antibiotic therapy for prosthetic joint infections

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Abstract

Purposes This study aimed to evaluate the sensitivity and specificity of the sonication cultures according to the International Consensus Meeting 2018 criteria and to evaluate the effect of sonication on the antibiotic treatment of patients.

Methods Sixty-four patients who were scheduled for revision hip or knee arthroplasties were included in the study. Aspiration fluid, tissue, and sonication cultures were performed from all patients and compared in terms of sensitivity, specificity, positive predictive value (PPV), negative predictive value (NPV), and overall accuracy. Other targets of the study were to investigate the rate of change in the antibiotic treatment.

Results The sensitivity, specificity, PPV, NPV, and overall accuracy of the fluid culture obtained by the sonication method were 71.4%, 96.6%, 96.2%, 73.7%, and 82.8%, respectively. The sensitivity, specificity, PPV, NPV, and overall accuracy of the fluid culture obtained after tissue sampling were 68.6%, 100%, 100.0%, 72.5%, and 82.8%, respectively. There was no statistically significant difference between the sonication method and tissue culture in terms of sensitivity and specificity ($p = 1.0$). The sensitivity, specificity, PPV, NPV, and overall accuracy of the fluid culture obtained by the aspiration method were 28.6%, 93.1%, 83.3%, 51.9%, and 57.8%, respectively. Treatment change was applied in 10 (15.6%) patients.

Conclusion Our prospectively collected data revealed that sonication of the explants alone did not increase the sensitivity, and we found that sonicate culture sometimes changed the antibiotic therapy strategy in patients with periprosthetic joint infection because different microorganisms were detected.

Trial registration: This study was prospectively registered in a public trials registry (https://clinicaltrials.gov/, NCT04304885)

Keywords Sonication · Sensitivity · Accuracy · Revision · Periprosthetic joint infection · Aseptic · Tissue culture

Level of evidence: II, diagnostic

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Introduction

Periprosthetic joint infection (PJI) is a serious complication that compromises patient outcomes and satisfaction and increases morbidity and mortality after total joint replacement (TJR) [1–4]. Using data from the National (Nationwide) Inpatient Sample (NIS) of the USA, Kurtz et al. reported that the incidence of PJI ranged from 2.0 to 2.4% after both total hip arthroplasty (THA) and total knee arthroplasty (TKA) [1, 3, 4]. A prior infection is the most important cause of revision arthroplasty failure [5]. Although recent studies have shown that the annual frequency of PJI is not rising, classical microbiological methods continue to be used to isolate causative microorganisms and to suggest antibiotic treatments. Although the Musculoskeletal Infection Society (MSIS) and/or the International Consensus Meeting (ICM) criteria ensure very accurate PJI diagnosis, some responsible microbes are not cultured (culture-negative PJI) [6]. This may suggest that the joint is aseptic; antibiotic therapy (if prescribed) may be ineffective. Recently, polymerase chain reaction (PCR) and next-generation sequencing (NGS) have been used to detect possibly causative microorganisms. However, such tests are not always available and may be costly, susceptible to irrelevant factors, and may falsely detect microbes in sterile joints [7].

It is essential to improve culture sensitivity. We have used sonication to expose microbes in implant biofilms [8]. This process is controversial: some studies have reported improved diagnostic sensitivities [8, 9], while others have not [10]. Additionally, to date no standard sonication method is available [11]. Any effect of sonicate culture data on the choice of antibiotic therapy remains unclear. In this prospective study, we hypothesized that the diagnostic accuracy afforded by sonication fluid culture would be higher than those of synovial fluid or periprosthetic tissue cultures and that the findings would significantly influence the choice of antibiotic therapy in patients with hip or knee PJI. We explored the sensitivity, specificity, positive predictive value (PPV), negative predictive value (NPV), and overall accuracy afforded by sonicate culture and whether such culture affected PJI treatment strategies.

Methods

Study design

This prospective study was approved by our institution's Clinical Research Ethics Committee (54,022,451–050.05.04). The protocol of the study was designed to conform to the principles of the Declaration of Helsinki [12] and has been prospectively registered to the international registry system (NCT04304885, https://clinicaltrials.gov/). Informed consent form was obtained from all patients.

Participants

Subjects included patients who were scheduled for revision hip or knee arthroplasties for septic or aseptic reasons and those with periprosthetic fractures or instability. Any patients with early or acute infections exhibiting symptoms within four weeks of the index procedure were excluded. All participants scheduled for revision TJR for any reason were pre-operatively evaluated in terms of possible PJI using the ICM 2018 criteria [13, 14].

Sample size

Based on previous research, the sensitivity of conventional culture is 45–94% and that of sonicate fluid culture is 58–97% [15–18]. We assumed that the 20% difference was important; to prove this, the minimum number of participants was set at 59 (affording an 80% power at a significance level of 0.05).

Specimens

We determined the leukocyte and granulocyte proportions in synovial fluid aspirates, the leukocyte esterase levels, and culture status. Synovial fluid was inoculated (0.1-mL aliquots) onto 5% (w/v) sheep blood and EMB agar plates and chocolate medium (Standard Media, Turkey) for aerobic bacteria cultivation. Schaedler sheep blood (5% w/v) agar (Standard Media) and thioglycolate broth were used to culture anaerobic bacteria (for 14 days) with the aid of an Anoxomat anaerobic system. Synovial fluid volumes > 0.5 mL were added to BACTEC Peds Plus/F bottles and incubated for five days in the BACTEC FX incubator (BD Diagnostic Systems) [19].

Intra-operative periprosthetic tissue samples were collected from three to five different areas exhibiting the most prominent inflammatory changes, homogenized in 3-mL quantities of brain–heart infusion broth for one minute, and the homogenates were inoculated (0.5-mL aliquots) in the same manner as synovial fluid. All plates were incubated at 35 °C aerobically or anaerobically for 14 days in a 5% (v/v) CO_2 incubator. Subcultures were performed if any cloudiness was observed in thioglycollate cultures after 24 h.

Explanted prosthetic components were placed in straight-sided, wide-mouthed polypropylene containers previously autoclaved for 15 minutes at 132 °C and 27 psi under sterile conditions. The explants were processed within one hour

by our microbiology laboratory. One hundred milliliters of Ringer's solution were added to each container. The container was then vortexed for 30 s using a Vortex-Genie and sonicated (40 ± 2 kHz; power density 0.22 ± 0.04 W/cm^2, delivered by a calibrated hydrophone; J.P. Selectra, Spain) in an ultrasound bath for five minutes, followed by additional vortexing for 30 s. This sonication method is known to preserve microbial viability [20]. The sonicate fluid was plated onto aerobic and anaerobic sheep blood agar plates (0.5-mL aliquots) and incubated in the same manner as the tissue cultures. Microorganisms were counted and identified using routine microbiological techniques. A total of 80 mL of sonication fluid was centrifuged at 2600 rpm for 15 minutes, and the residue was Gram-stained. If at least five colony-forming units of the same organism were evident on both plates, we assumed that culture sensitivity and specificity were optimal.

The material of the explanted prosthesis components was recorded and evaluated in terms of aseptic and septic groups. All cultures proceeded for at least 14 days to detect slow-growing bacteria. The culture results of the three different methods were recorded separately for each patient. The culture reports of the conventional methods were given to a blinded infectious disease specialist who was asked to prescribe antibiotic therapy for all patients. The culture results of sonicate fluid was then added to the initial culture reports of the patients, and the same blinded infectious disease specialist was asked to redetermine antibiotic therapy for all patients using the combined culture reports. Changes in antibiotic therapy was noted for each patient. The final decisions were put into practice.

Outcomes

Primary outcome

The pre-specified primary outcome was a comparison of the culture results of sonication fluid to the conventional methods in terms of sensitivity, specificity, PPV, NPV, and overall accuracy according to the ICM 2018 criteria [13].

Secondary outcome measures

One secondary outcome measure was the extent of changes in antibiotic treatment determined according to the conventional cultures and the combined cultures for the aseptic and septic groups. Another secondary outcome measures were the sensitivity and specificity of the combined culture results. We also compared the sensitivity and specificity of sonicate fluid culture and tissue culture for patients who received pre-operative antibiotic therapy.

Results

In total, 64 patients were included in the study (Table 1). Patients were excluded if the prosthetic components became contaminated in the operating room ($n = 4$) or did not fit into the component containers ($n = 6$). The groups were equally distributed in terms of the implant material removed from the patients ($p = 0.9$). The mean age of the patients was 65.9 ± 11.6 (range 42–90) years, and 53.1% were women. Among them, 27 (42.2%) underwent TKA and 37 (57.8%) THA. According to the ICM 2018 criteria, 35 (54.7%) joints were diagnosed as septic and the remaining 29 (45.3%) as aseptic. The mean body mass index was 31.3 ± 7.5 (range 18.5–45.3) kg/m^2, and the interquartile range (IRQ) of the

Table 1 Demographic data of patients

Variables	Aseptic cases ($n = 29$)	Septic cases ($n = 35$)	Total ($n = 64$)
Mean age, years	64.9 ± 13.4	67.9 ± 7.6	65.9 ± 11.6
Sex, *n* % female	15 (51.7%)	19 (54.3%)	34 (53.1%)
Mean BMI, kg/m^2	31.6 ± 8.2	30.9 ± 7.0	31.3 ± 7.5
ASA, IQR	2 (1–3)	2 (1–3)	2 (1–3)
Materials			
Cobalt chrome and titanium alloys	12	15	27
Polyethylene	9	10	19
Ceramic	8	10	18
Time between first and last surgeries, years	2.0 ± 2.2	9.9 ± 8.8	7.2 ± 8.1
History of antibiotic use before surgery within 2 weeks	1 (3.5%)	10 (28.6%)	11 (17.2%)
Previous number of surgeries, IQR	2 (1–3)	2 (1–3)	2 (1–3)

BMI, body mass index; *ASA*, American Society of Anesthesiologists; *IQR*, interquartile range

American Society of Anesthesiologists (ASA) score was 2 (1–3). The IQR of previous surgeries was 2 (1–3). The time between the first and the index surgery was 7.2 ± 8.1 years (range 0.4–26 years). Ten (28.6%) of the patients who underwent surgery to treat PJI and 1 (3.5%) patient who underwent surgery to treat aseptic failure were using antibiotics within two weeks before surgery.

Table 2 lists the patients who yielded positive cultures; patients are listed separately by septic and aseptic groups. The sensitivity of the sonicate fluid culture was 71.4% and the specificity was 96.6%. The sensitivity of tissue culture was 68.6% and the specificity was 100%. There was no statistically significant difference between these two culture methods. ($p = 1.0$) The method with the lowest sensitivity was the joint aspiration fluid culture; the sensitivity was 28.6% and the specificity was 93.1%. The sensitivity was significantly less for culture of synovial fluid aspirate than culture of sonication fluid ($p = 0.01$) and tissue ($p = 0.03$). The highest culture sensitivity (94.3%) and high specificity (89.7%) were obtained when the three methods were combined. Table 3 lists all diagnostic results.

In patients receiving pre-operative antimicrobial therapy, the sensitivities and specificities were 70.0% and 100% for tissue culture and 80.0% and 100% for sonicate fluid (Table 3). No differences were observed between the two methods in terms of sensitivity ($p = 0.5$). Although tissue cultures and sonication fluid cultures were positive in three of 35 patients in the septic group, the culture results differed. In one of these patients, a fungus (*Candida albicans*) was isolated from tissue culture, and an additional bacterium (*Acinetobacter baumannii*) was isolated from sonicate fluid. Eight cases were positive on sonicate fluid culture but negative on periprosthetic tissue and aspiration fluid cultures. In total, 11 PJI patients were sonicate fluid culture-positive for microbes not isolated on periprosthetic tissue or aspiration fluid culture. Thus,

Table 2 Results of different cultures

Case classification according to ICM 2018	No. of patients	Organism (no. of patients)
Prosthetic joint infection	35	
Concordant positive sonicate fluid and periprosthetic tissue cultures	14	MRSA (2)
		MSSA (3)
		MRCS (2)
		MSCNS (3)
		Enterococcus faecalis (1)
		Morganella morganii + *Escherichia coli* (1)
		Klebsiella pneumoniae (2)
Discordant positive sonicate fluid and periprosthetic tissue cultures	3	*Candida albicans* + *Acinetobacter baumannii* (1)
		Cutibacterium acnes + MSCNS (1)
		Cutibacterium acnes + group B *Streptococcus* sp. (1)
Positive sonicate fluid and negative periprosthetic tissue cultures	8	MSCNS (2)
		MRCNS (1)
		Group B *Streptococcus* sp. (1)
		Ralstonia pickettii (1)
		Cutibacterium acnes (2)
		Cronobacter sakazakii (1)
Negative sonicate fluid and positive periprosthetic tissue cultures	7	*Cutibacterium acnes* (2)
		MSCNS (2)
		MRCNS (2)
		Bacillus cereus (1)
Positive aspiration fluid and negative periprosthetic tissue and sonicate fluid cultures	1	MRCNS (1)
Culture-negative PJI	2	
Aseptic failure	29	
Positive sonicate fluid and negative periprosthetic tissue cultures	1	*Escherichia coli* (1)
Negative sonicate fluid and positive periprosthetic tissue cultures	0	
Negative sonicate fluid and periprosthetic tissue cultures	28	

MSSA, methicillin-sensitive *Staphylococcus aureus*; *MRSA*, methicillin-resistant *Staphylococcus aureus*; *MRCNS*, methicillin-resistant coagulase-negative *Staphylococcus*; *MSCNS*, methicillin-sensitive coagulase-negative *Staphylococcus*

Table 3 Microbiologic tests for the diagnosis of prosthetic joint infection

Test	Sensitivity	Specificity	Positive predictive value	Negative predictive value	Accuracy
	% (95% confidence interval)				
Synovial fluid culture	28.6% (14.7%–46.3%)	93.1% (77.2%–99.2%)	83.3% (54.3%–95.5%)	51.9% (46.2%–57.7%)	57.8% (44.8%–70.1%)
Periprosthetic tissue culture	68.6% (50.7%–83.2%)	100% (88.1%–100%)	100%	72.5% (61.8%–81.1%)	82.8% (71.3%–91.1%)
Sonication fluid culture	71.4% (53.7%–89.3%)	96.6% (82.3%–99.9%)	96.2% (78.27%–99.4%)	73.7% (62.3%–82.6%)	82.8% (71.3%–91.1%)
Combined culture	94.3% (80.9%–99.3%)	89.7% (72.7%–97.8%)	91.7% (79.0%–97.0%)	92.9% (77.1%–98.1%)	92.2% (82.7%–97.4%)
Periprosthetic tissue culture*	70.0% (34.8%–93.3%)	100.00% (2.5%–100%)	100%	25.0% (11.5%–46.2%)	72.7% (39.0%–93.9%)
Sonication fluid culture*	80.0% (44.4%–97.5%)	100.00% (2.5%–100%)	100%	33.3% (12.7%–63.3%)	81.8% (48.2%–97.7%)

*Periprosthetic tissue and sonication fluid culture of patients receiving preoperative antimicrobial therapy

the antibiotic therapies were changed or supplemented in nine of the 11 PJI patients on the basis of the microbiological culture antibiogram sensitivities (Table 4). Among patients who underwent aseptic revision, antibiotic treatment was offered to only one (3.5%) patient with a positive sonicate fluid culture. The proportions of treatment changes differed statistically between aseptic and septic cases ($p = 0.001$). The planned treatments of 10 (15.6%) patients were changed on the basis of the sonicate fluid culture results.

Discussion

The most important strength of this study is its prospective design. We also used a new PJI diagnostic algorithm [13] of high sensitivity and specificity, and we evaluated cultures from synovial fluid, intra-articular tissue, and sonicate fluid when evaluating sensitivity and specificity. We found no statistically significant differences between tissue and sonicate fluid cultures, although the sensitivity of the sonicate culture method was somewhat higher than that of the tissue method. Another important finding of this study was

Table 4 Patients with changed treatment

Case classification according to ICM 2018	Organism (no. of patients)		
	Same treatment[a] (*n*)	Different treatment[b] (*n*)	Antibiotics
Prosthetic joint infection			
Discordant positive sonicate fluid and periprosthetic tissue cultures		Candida albicans + *Acinetobacter baumannii* (1)	Flukonazol + ceftazidime/avibactam
	Cutibacterium acnes + MSCNS (1)		Ampicillin/sulbactam
	Cutibacterium acnes + Group B *Streptococcus* sp. (1)		Ampicillin/ulbactam
Positive sonicate fluid and negative periprosthetic tissue cultures		MSCNS (2)	Ampicillin/sulbactam
		MRCNS (2)	Teicoplanin or vancomycin
		Ralstonia pickettii (1)	Ciprofloxacin
		Cutibacterium acnes (2)	Ampicillin/sulbactam
		Cronobacter sakazakii (1)	Trimethoprim/sulfamethoxazole
Aseptic failure			
Positive sonicate fluid and negative periprosthetic tissue cultures		*Escherichia coli* (1)	Ampicillin/sulbactam

[a]Same treatment, if the same antibiotics were suggested to the patient for different microorganisms; [b]different treatment, if different antibiotics for different microorganisms were suggested to the patient or patients who will receive antibiotic therapy based on sonication culture results only

MRCNS, methicillin-resistant coagulase-negative *Staphylococcus*; *MSCNS*, methicillin-sensitive coagulase-negative *Staphylococcus*

that the accuracies of two diagnostic methods were similar. After sonicate fluid culture, 15.6% of the antibiotic treatment regimens were changed and thereby may increase the therapeutic success rate.

In a recently published retrospective study, Hoekstra et al. found that the sensitivities of periprosthetic tissue and sonicate cultures were 94.3% and 80.5%, respectively. Although the sensitivity and specificity of sonicate cultures were lower than those of tissue cultures, 9% of the patients were treated to eliminate microbes isolated from only sonicate cultures. Such culture was considered to be a useful diagnostic tool in clinical practice because it resulted in significant changes in treatment [15]. Another important result of the present study is that the combined use of sonicate, synovial fluid, and tissue cultures afforded 94.3% sensitivity and 89.7% specificity.

The consensus is that isolation of phenotypically identical microorganisms from more than one culture is the gold standard for the diagnosis of PJI: the antibiograms of such cultures are used to choose effective antibiotics [13]. However, isolation of all infecting microorganisms may not be always possible, and the results of the present study demonstrate that sonicate culture may play effective roles in both PJI diagnosis and treatment in such situations.

The sonication method is technically simple and can be performed in most microbiology laboratories. As intraoperative tissue cultures alone may exhibit high rates of contamination and false positives [21], alternative methods such as sonication of explants have been proposed to confirm that only PJI organisms are isolated [22, 23]. Tani et al. prospectively compared the sensitivities and specificities of cultures obtained from sonicated explants and conventional periprosthetic tissue cultures in patients with PJI and aseptic loosening undergoing hip and knee revisions [24]. The sensitivity of sonicate culture was higher than that of conventional culture (77.0% vs. 55.7%). Some studies have suggested that sonication of the prosthesis may increase the diagnostic capacity of the PCR test in patients with culture-negative PJI [25–27]. However, the statistical significance afforded by this method remains controversial. A recent meta-analysis of nine studies that used PCR to evaluate sonicate fluid revealed that the PJI diagnostic values were clinically acceptable, with a sensitivity of 75% [28]. However, no statistically significant difference was apparent compared to conventional culture. The culture sensitivity of fluids obtained by sonication was similar to that of PCR. Qu et al. conducted a meta-analysis of studies comparing tissue, synovial fluid, and sonicate fluid cultures and concluded that tissue samples afforded the maximum sensitivity but sonicate fluid afforded the highest specificity [29]. Other reports have claimed that tissue PCR is less sensitive than tissue culture [26, 30]. Sebastian et al. found that implant sonicate cultures increased the diagnostic sensitivity for PJI from 66.7% to 92.5% [9]. Trampuz et al. published a remarkable prospective case series using sonicate cultures to diagnose PJI [8]. The sensitivity of sonicate fluid culture was 78.5%, which was significantly higher than those of synovial fluid culture (56.3%) and tissue culture (60.8%). Thus, although some studies have supported the idea that sonicate culture is superior to tissue culture, other studies have not. The discrepancies may be attributable to several factors. It appears that no standardized definition of PJI was used in many studies; the application of different criteria may have led to underestimation of septic case numbers.

Because the diagnosis of periprosthetic joint requires a complex approach, sometimes orthopedic implant infection is controversial even after bacterial isolation [7, 13, 29, 31]. So, germ on an implant is not necessarily correlated with clinical infection. Although this study was prospective in design, it had certain limitations, and our findings should be interpreted accordingly. First, we could not send all removed implants to the laboratory for sonication because some were longer than the sterile containers, especially certain revision stems. One of other potential contamination problems of sonicated implants is their handling. Second, the sonicated implants were not made of the same materials. We did not investigate the biofilm-forming properties of polyethylene, ceramics, titanium, or cobalt–chromium. This remains a subject for future work. Finally, because our study focused on the culture results of different methods, we did not explore whether sonicate culture influenced infection-free survival after the revised TJR, treatment success, or patient satisfaction.

Conclusion

Our prospectively collected data revealed that sonication of the explants alone did not increase the sensitivity or specificity of infectious microbe isolation from prosthetic joints. Rather, culture sensitivity was increased when all of the synovial fluid, periprosthetic tissue, and explant sonicate were cultured and the results were combined. Most importantly, we found that sonicate culture sometimes changed the antibiotic therapy strategy in patients with PJI because different microorganisms were detected.

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Author contribution All authors were fully involved in the study and preparation of the manuscript.

Data availability The datasets generated during and analyzed during the current study are available from the corresponding author on reasonable request.

Declarations

Ethics approval This study has institutional ethical approval (54022451-050.05.04).

Consent to participate Informed consent form to participate was obtained from all patients.

Consent for publication Informed consent form to publish was obtained from all patients.

Conflict of interest The authors declare no competing interests.

References

1. Kurtz S, Mowat F, Ong K, Chan N, Lau E, Halpern M (2005) Prevalence of primary and revision total hip and knee arthroplasty in the United States from 1990 through 2002. J Bone Joint Surg Am 87:1487–1497. https://doi.org/10.2106/JBJS.D.02441
2. Phillips JE, Crane TP, Noy M, Elliott TS, Grimer RJ (2006) The incidence of deep prosthetic infections in a specialist orthopaedic hospital: a 15-year prospective survey. J Bone Joint Surg Br 88:943–948. https://doi.org/10.1302/0301-620X.88B7.17150
3. Kurtz SM, Lau E, Schmier J, Ong KL, Zhao K, Parvizi J (2008) Infection burden for hip and knee arthroplasty in the United States. J Arthroplasty 23:984–991. https://doi.org/10.1016/j.arth.2007.10.017
4. Kurtz SM, Medel FJ, MacDonald DW, Parvizi J, Kraay MJ, Rimnac CM (2010) Reasons for revision of first-generation highly cross-linked polyethylenes. J Arthroplasty 25:67–74. https://doi.org/10.1016/j.arth.2010.04.018
5. Mortazavi SM, Schwartzenberger J, Austin MS, Purtill JJ, Parvizi J (2010) Revision total knee arthroplasty infection: incidence and predictors. Clin Orthop Relat Res 468:2052–2059. https://doi.org/10.1007/s11999-010-1308-6
6. Parvizi J, Gehrke T (2014) Definition of periprosthetic joint infection. J Arthroplasty 29:1331. https://doi.org/10.1016/j.arth.2014.03.009
7. Torchia MT, Amakiri I, Werth P, Moschetti W (2020) Characterization of native knee microorganisms using next-generation sequencing in patients undergoing primary total knee arthroplasty. Knee 27:1113–1119. https://doi.org/10.1016/j.knee.2019.12.013
8. Trampuz A, Piper KE, Jacobson MJ, Hanssen AD, Unni KK, Osmon DR, Mandrekar JN, Cockerill FR, Steckelberg JM, Greenleaf JF, Patel R (2007) Sonication of removed hip and knee prostheses for diagnosis of infection. N Engl J Med 357:654–663. https://doi.org/10.1056/NEJMoa061588
9. Sebastian S, Malhotra R, Sreenivas V, Kapil A, Chaudhry R, Dhawan B (2018) Sonication of orthopaedic implants: a valuable technique for diagnosis of prosthetic joint infections. J Microbiol Methods 146:51–54. https://doi.org/10.1016/j.mimet.2018.01.015
10. Yan Q, Karau MJ, Greenwood-Quaintance KE, Mandrekar JN, Osmon DR, Abdel MP, Patel R (2018) Comparison of diagnostic accuracy of periprosthetic tissue culture in blood culture bottles to that of prosthesis sonication fluid culture for diagnosis of prosthetic joint infection (PJI) by use of Bayesian latent class modeling and IDSA PJI criteria for classification. J Clin Microbiol 56:e00319-18. https://doi.org/10.1128/JCM.00319-18
11. Ascione T, Barrack R, Benito N, Blevins K, Brause B, Cornu O, Frommelt L, Gant V, Goswami K, Hu R, Klement MR, Komnos G, Malhotra R, Mirza Y, Munhoz Lima AL, Nelson C, Noor SS, O'Malley M, Oussedik S, Portillo ME, Prieto H, Saxena A, Sessa G (2019) General assembly, diagnosis, pathogen isolation - culture matters: Proceedings of International Consensus on Orthopedic Infections. J Arthroplasty 34:S197–S206. https://doi.org/10.1016/j.arth.2018.09.071
12. (2013) World Medical Association Declaration of Helsinki: ethical principles for medical research involving human subjects. Jama 310:2191–2194. https://doi.org/10.1001/jama.2013.281053
13. Parvizi J, Tan TL, Goswami K, Higuera C, Della Valle C, Chen AF, Shohat N (2018) The 2018 Definition of Periprosthetic Hip and Knee Infection: an evidence-based and validated criteria. J Arthroplasty 33(1309–1314):e1302. https://doi.org/10.1016/j.arth.2018.02.078
14. Shohat N, Bauer T, Buttaro M, Budhiparama N, Cashman J, Della Valle CJ, Drago L, Gehrke T, Marcelino Gomes LS, Goswami K, Hailer NP, Han SB, Higuera CA, Inaba Y, Jenny JY, Kjaersgaard-Andersen P, Lee M, Llinas A, Malizos K, Mont MA, Jones RM, Parvizi J, Peel T, Rivero-Boschert S, Segreti J, Soriano A, Sousa R, Spangehl M, Tan TL, Tikhilov R, Tuncay I, Winkler H, Witso E, Wouthuyzen-Bakker M, Young S, Zhang X, Zhou Y, Zimmerli W (2019) Hip and knee section, what is the definition of a periprosthetic joint infection (PJI) of the knee and the hip? Can the same criteria be used for both joints?: Proceedings of International Consensus on Orthopedic Infections. J Arthroplasty 34:S325–S327. https://doi.org/10.1016/j.arth.2018.09.045
15. Hoekstra M, Veltman ES, Nurmohamed R, van Dijk B, Rentenaar RJ, Vogely HC, van der Wal BCH (2020) Sonication leads to clinically relevant changes in treatment of periprosthetic hip or knee joint infection. J Bone Jt Infect 5:128–132. https://doi.org/10.7150/jbji.45006
16. Banousi A, Evangelopoulos DS, Stylianakis A, Fandridis E, Chatziioannou S, Sipsas NV, Pneumaticos SG (2020) A comparative study of heterogeneous antibiotic resistance of microbial populations in conventional periprosthetic tissue cultures and sonication fluid cultures of orthopaedics explanted prostheses. Eur J Orthop Surg Traumatol 30:1307–1318. https://doi.org/10.1007/s00590-020-02704-4
17. Renz N, Feihl S, Cabric S, Trampuz A (2017) Performance of automated multiplex PCR using sonication fluid for diagnosis of periprosthetic joint infection: a prospective cohort. Infection 45:877–884. https://doi.org/10.1007/s15010-017-1073-5
18. Piper KE, Jacobson MJ, Cofield RH, Sperling JW, Sanchez-Sotelo J, Osmon DR, McDowell A, Patrick S, Steckelberg JM, Mandrekar JN, Fernandez Sampedro M, Patel R (2009) Microbiologic diagnosis of prosthetic shoulder infection by use of implant sonication. J Clin Microbiol 47:1878–1884. https://doi.org/10.1128/JCM.01686-08
19. Hughes JG, Vetter EA, Patel R, Schleck CD, Harmsen S, Turgeant LT, Cockerill FR 3rd (2001) Culture with BACTEC Peds Plus/F bottle compared with conventional methods for detection of bacteria in synovial fluid. J Clin Microbiol 39:4468–4471. https://doi.org/10.1128/JCM.39.12.4468-4471.2001
20. Pitt WG, Ross SA (2003) Ultrasound increases the rate of bacterial cell growth. Biotechnol Prog 19:1038–1044. https://doi.org/10.1021/bp0340685
21. Barrack RL, Aggarwal A, Burnett RS, Clohisy JC, Ghanem E, Sharkey P, Parvizi J (2007) The fate of the unexpected positive intraoperative cultures after revision total knee arthroplasty. J Arthroplasty 22:94–99. https://doi.org/10.1016/j.arth.2007.03.029
22. Gbejuade HO, Lovering AM, Webb JC (2015) The role of microbial biofilms in prosthetic joint infections. Acta Orthop 86:147–158. https://doi.org/10.3109/17453674.2014.966290
23. Patel R, Alijanipour P, Parvizi J (2016) Advancements in diagnosing periprosthetic joint infections after total hip and knee arthroplasty. Open Orthop J 10:654–661. https://doi.org/10.2174/1874325001610010654
24. Tani S, Lepetsos P, Stylianakis A, Vlamis J, Birbas K, Kaklamanos I (2018) Superiority of the sonication method against

conventional periprosthetic tissue cultures for diagnosis of prosthetic joint infections. Eur J Orthop Surg Traumatol 28:51–57. https://doi.org/10.1007/s00590-017-2012-y
25. Hischebeth GTR, Gravius S, Buhr JK, Molitor E, Wimmer MD, Hoerauf A, Bekeredjian-Ding I, Randau TM (2017) Novel diagnostics in revision arthroplasty: implant sonication and multiplex polymerase chain reaction. J Vis Exp. https://doi.org/10.3791/55147
26. Rak M, KavcIc M, Trebse R, Co RA (2016) Detection of bacteria with molecular methods in prosthetic joint infection: sonication fluid better than periprosthetic tissue. Acta Orthop 87:339–345. https://doi.org/10.3109/17453674.2016.1165558
27. Huang Z, Wu Q, Fang X, Li W, Zhang C, Zeng H, Wang Q, Lin J, Zhang W (2018) Comparison of culture and broad-range polymerase chain reaction methods for diagnosing periprosthetic joint infection: analysis of joint fluid, periprosthetic tissue, and sonicated fluid. Int Orthop 42:2035–2040. https://doi.org/10.1007/s00264-018-3827-9
28. Liu K, Fu J, Yu B, Sun W, Chen J, Hao L (2018) Meta-analysis of sonication prosthetic fluid PCR for diagnosing periprosthetic joint infection. PLoS ONE 13:e0196418. https://doi.org/10.1371/journal.pone.0196418
29. Qu X, Zhai Z, Li H, Li H, Liu X, Zhu Z, Wang Y, Liu G, Dai K (2013) PCR-based diagnosis of prosthetic joint infection. J Clin Microbiol 51:2742–2746. https://doi.org/10.1128/JCM.00657-13
30. Ryu SY, Greenwood-Quaintance KE, Hanssen AD, Mandrekar JN, Patel R (2014) Low sensitivity of periprosthetic tissue PCR for prosthetic knee infection diagnosis. Diagn Microbiol Infect Dis 79:448–453. https://doi.org/10.1016/j.diagmicrobio.2014.03.021
31. Kobayashi N, Procop GW, Krebs V, Kobayashi H, Bauer TW (2008) Molecular identification of bacteria from aseptically loose implants. Clin Orthop Relat Res 466:1716–1725. https://doi.org/10.1007/s11999-008-0263-y