ORIGINAL ARTICLE

Sonication of Removed Hip and Knee Prostheses for Diagnosis of Infection

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ABSTRACT

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BACKGROUND

Culturing of samples of periprosthetic tissue is the standard method used for the microbiologic diagnosis of prosthetic-joint infection, but this method is neither sensitive nor specific. In prosthetic-joint infection, microorganisms are typically present in a biofilm on the surface of the prosthesis. We hypothesized that culturing of samples obtained from the prosthesis would improve the microbiologic diagnosis of prosthetic-joint infection.

METHODS

We performed a prospective trial comparing culture of samples obtained by sonication of explanted hip and knee prostheses to dislodge adherent bacteria from the prosthesis with conventional culture of periprosthetic tissue for the microbiologic diagnosis of prosthetic-joint infection among patients undergoing hip or knee revision or resection arthroplasty.

RESULTS

We studied 331 patients with total knee prostheses (207 patients) or hip prostheses (124 patients); 252 patients had aseptic failure, and 79 had prosthetic-joint infection. With the use of standardized nonmicrobiologic criteria to define prosthetic-joint infection, the sensitivities of periprosthetic-tissue and sonicate-fluid cultures were 60.8% and 78.5% (P<0.001), respectively, and the specificities were 99.2% and 98.8%, respectively. Fourteen cases of prosthetic-joint infection were detected by sonicate-fluid culture but not by prosthetic-tissue culture. In patients receiving antimicrobial therapy within 14 days before surgery, the sensitivities of periprosthetic tissue and sonicate-fluid culture were 45.0% and 75.0% (P<0.001), respectively.

CONCLUSIONS

In this study, culture of samples obtained by sonication of prostheses was more sensitive than conventional periprosthetic-tissue culture for the microbiologic diagnosis of prosthetic hip and knee infection, especially in patients who had received antimicrobial therapy within 14 days before surgery.

IN THE UNITED STATES, 638,000 PATIENTS underwent hip or knee replacement in 2003.[1] Although they may improve the quality of life, these procedures are associated with complications, including aseptic failure and prosthetic-joint infection.[2] It is important to distinguish prosthetic-joint infection from other causes of joint failure, because its management is different.[3] Nonmicrobiologic methods developed for diagnosing native-joint infection use different criteria from those used to diagnose prosthetic-joint infection.[4] Microbiologic diagnosis of prosthetic-joint infection may also require different criteria from those used for the microbiologic diagnosis of native-joint infection.

Most clinicians and laboratory workers culture periprosthetic tissue (hereafter referred to as "tissue") for microbiologic diagnosis of prosthetic-joint infection. This method was not developed for the diagnosis of prosthetic-joint infection, and its sensitivity and specificity for this diagnosis are imperfect. Specificity is an issue because the associated microbes are often skin flora that may be contaminants. Sensitivity is also an issue; typically, multiple (as many as six[5]) tissue samples are cultured. It has been suggested that multiple samples should be obtained because the numbers of organisms are small. It is possible that there are substantial numbers of organisms associated with the infected joint that are not concentrated in the periprosthetic tissue.

Organisms associated with prosthetic-joint infection are found attached to the prosthesis, where they often form biofilms.[6] This observation suggests that obtaining a sample from the prosthesis might improve the diagnosis of prosthetic-joint infection. Tunney et al. used bath sonication to dislodge adherent bacteria from explanted prosthetic hips,[7,8] but they did not evaluate the use of this method for the diagnosis of prosthetic-joint infection. We performed a study to determine whether this approach would improve the diagnosis of prosthetic-joint infection.[9] Although the method of Tunney et al. improved bacterial recovery, it lacked specificity because the prosthetic components were placed in bags that leaked.[9] We modified this approach by processing removed implants in solid containers, reducing the number of culture plates, and adding a vortexing step before sonication; the last modification was based on unpublished experiments demonstrating that vortexing increases the concentration of air bubbles and thus enhances the cavitation effect of subsequent sonication.

We report the results of a prospective trial comparing this new diagnostic approach with conventional tissue culture for the microbiologic diagnosis of prosthetic-joint infection. We found that the new approach improves sensitivity without compromising specificity.

METHODS

STUDY POPULATION

A total of 404 patients undergoing removal of a total knee or hip prosthesis for aseptic failure or presumed infection at the Mayo Clinic, in Rochester, Minnesota, were enrolled between August 12, 2003, and December 13, 2005. Patients were excluded if obvious contamination occurred in the operating room, the prosthesis did not fit in the container provided for it, or only one tissue sample was cultured. The study was determined by the institutional review board of the Mayo Clinic to be exempt from the requirement for informed consent; only patients who provided written authorization for the use of their health records (as provided by Minnesota Statute 144.335) were enrolled in the study.

DIAGNOSIS OF PROSTHETIC-JOINT INFECTION

In accordance with standard criteria,[10] a diagnosis of prosthetic-joint infection was made if at least one of the following was present: visible purulence in the synovial fluid or surrounding the prosthesis, acute inflammation on histopathological examination of permanent tissue sections (as determined by the clinical pathologist), or a sinus tract communicating with the prosthesis. Aseptic failure was defined as failure of a prosthesis in the absence of any of these criteria. Previous antimicrobial therapy was defined as receipt of antimicrobial agents during the 14 days before removal of the prosthesis. A clinical pathologist who was unaware of the clinical history or other test results reviewed histopathological specimens that could not be clearly classified as showing or not showing acute inflammation.

SPECIMEN COLLECTION

Preoperatively, synovial fluid was aspirated for leukocyte count, differential blood count, and culture at the surgeon's discretion. Intraoperatively, tissue with the most obvious inflammatory changes was

collected for microbiologic and histopathological studies. The prosthetic components (including polyethylene and polymethylmethacrylate, if present) were placed in 1-liter, straight-sided, wide-mouthed polypropylene jars (Nalgene) that had been autoclaved at 132°C and 27 psi for 15 minutes. The specimens were processed by the microbiology laboratory within 6 hours.

CONVENTIONAL MICROBIOLOGIC METHODS

Synovial fluid was inoculated in 0.1-ml aliquots onto aerobic blood agar, chocolate agar, and anaerobic blood agar and into thioglycollate broth (BD Diagnostic Systems). Residual synovial-fluid volumes of more than 0.5 ml were inoculated into a BACTEC Peds Plus/F bottle and incubated in a BACTEC 9240 instrument (BD Diagnostic Systems) for 5 days.[11] Tissue specimens were homogenized in 3 ml of brain–heart infusion broth for 1 minute, and the homogenate was inoculated in aliquots of 0.5 ml, as described for synovial fluid. Aerobic and anaerobic sheep-blood agar plates (BD Diagnostic Systems) were incubated at 35 to 37°C in 5 to 7% carbon dioxide aerobically and anaerobically for 5 days and 7 days, respectively. Cloudy thioglycollate broth was subcultured. Optimal culture sensitivity and specificity were achieved when two or more tissue specimens were considered positive for the same organism (Table 1).

SONICATION OF REMOVED PROSTHESES

Four hundred milliliters of Ringer's solution was added to each container. The container was vortexed for 30 seconds using a Vortex-Genie (Scientific Industries) and then subjected to sonication (frequency, 40±2 kHz; and power density, 0.22±0.04 W/cm^2, as determined with the use of a calibrated hydrophone [type 8103, Brüel and Kjær]), in an Aquasonic Model 750T ultrasound bath (VWR Scientific Products) for 5 minutes, followed by additional vortexing for 30 seconds (see Fig. 1 of the Supplementary Appendix, available with the full text of this article at www.nejm.org). The sonication method used has been shown to preserve microbial viability.[12] The resulting sonicate fluid was plated in 0.5-ml aliquots onto aerobic and anaerobic sheep-blood agar plates and incubated as described for tissue cultures. Microorganisms were enumerated and classified by routine microbiologic techniques. A total of 200 ml of sonicate fluid was centrifuged

at 2600 rpm for 15 minutes, and the sediment was Gram's stained. Optimal culture sensitivity and specificity were achieved if there were at least five colony-forming units of the same organism on either plate (Table 1).

STATISTICAL ANALYSIS

The baseline characteristics of the group with aseptic failure and the group with prosthetic-joint infection were compared by the Wilcoxon rank-sum or the chi-square test, as appropriate. The sensitivity and specificity of the different culture methods were compared by McNemar's test of paired proportions. A P value of less than 0.05 (for a two-sided test) was considered to indicate statistical significance. The sensitivity, specificity, positive predictive value, and negative predictive value of microbiologic cutoffs were calculated with two-by-two contingency tables. Ninety-five percent confidence intervals were calculated as exact binomial confidence intervals. The cutoff value of the number of colony-forming units for differentiating between prosthetic-joint infection and aseptic failure was determined by a previously described method.[13] The diagnostic accuracy of sonicate-fluid cultures was evaluated by constructing a receiver-operating-characteristic (ROC) curve. The area under the ROC curve was calculated as previously described.[14] Calculations were performed with the SAS statistical software package, version 8.2.

RESULTS

STUDY POPULATION

A patient was excluded from the study if a prosthesis component was obviously contaminated in the operating room (3 patients), if a prosthesis component did not fit into the container (9 patients), or if only one tissue sample was submitted for culture (61 patients). Of the remaining 331 patients, 207 had knee prostheses and 124 had hip prostheses; 252 had aseptic failure and 79 had prosthetic-joint infection (Table 2). The groups were similar in age, sex ratio, and distribution of the type of joint.

MICROBIOLOGIC RESULTS

The sensitivity of sonicate-fluid culture (78.5%) was superior to that of tissue culture (60.8%, P<0.001) and not significantly different from that of synovial-fluid culture (56.3%, P=0.058); the specifici-

Table 1. Comparison of Microbiologic Tests for the Diagnosis of Prosthetic-Joint Infection.

Test	Patients with Prosthetic-Joint Infection (N=79)	Patients with Aseptic Failure (N=252)	Sensitivity	Specificity	Positive Predictive Value	Negative Predictive Value
	no. of patients with positive specimens*		*% (95% confidence interval)*			
Synovial-fluid culture	18/32	2/108	56.3 (37.7–73.6)	98.1 (93.5–99.8)	90.0 (68.3–98.8)	88.3 (81.2–93.5)
Periprosthetic-tissue culture†						
≥1 positive culture	58	23	73.4 (62.3–82.7)	90.9 (86.6–94.1)	71.6 (60.5–81.1)	91.6 (87.4–94.7)
≥2 positive cultures	48	2	60.8 (49.1–71.6)	99.2 (97.2–99.9)	96.0 (86.3–99.5)	89.0 (84.7–92.4)
Sonicate-fluid culture†‡						
≥1 CFU	64	28	79.0 (68.5–87.3)	88.5 (83.9–92.2)	68.8 (58.4–78.0)	93.9 (88.9–95.8)
≥2 CFU	63	8	79.7 (69.2–88.0)	96.8 (93.8–98.6)	88.7 (79.0–95.0)	93.8 (90.2–96.4)
≥3 CFU	63	5	79.7 (69.2–88.0)	98.0 (95.4–99.4)	92.6 (83.7–97.6)	93.9 (90.3–96.5)
≥4 CFU	62	5	78.5 (67.8–86.9)	98.0 (95.4–99.4)	92.5 (83.4–97.5)	93.6 (89.9–96.2)
≥5 CFU	62	3	78.5 (67.8–86.9)	98.8 (96.6–99.8)	95.4 (87.1–99.0)	93.6 (90.0–96.2)
≥6 CFU	62	3	78.5 (67.8–86.9)	98.8 (96.6–99.8)	95.4 (87.1–99.0)	93.6 (90.0–96.2)
≥7 CFU	60	3	75.9 (65.0–84.9)	98.8 (96.6–99.8)	95.2 (86.7–99.0)	92.6 (89.2–95.7)
≥8 CFU	59	3	74.7 (63.6–83.8)	98.8 (96.6–99.8)	95.2 (86.5–99.0)	92.6 (88.8–95.4)
≥9 CFU	58	3	73.4 (62.3–82.7)	98.8 (96.6–99.8)	95.1 (86.3–99.0)	92.2 (88.4–95.1)
≥10 CFU	57	3	72.2 (60.9–81.7)	98.8 (96.6–99.8)	95.0 (86.1–99.0)	91.9 (88.0–94.8)
≥25 CFU	55	2	69.6 (58.2–79.5)	99.2 (97.2–99.9)	96.5 (87.9–99.6)	91.2 (87.2–94.3)
≥50 CFU	54	1	68.4 (56.9–78.4)	99.6 (97.8–100.0)	98.2 (90.3–100.0)	90.9 (86.9–94.1)
Gram's staining of sonicate fluid	34/76	0/250	44.7 (33.3–56.6)	100.0 (98.5–100.0)	100.0 (89.7–100.0)	85.6 (81.1–89.4)

* Where the denominator is shown, data were not available for all study patients.
† The number of cultures positive for the same microorganism is given.
‡ The number of colony-forming units (CFUs) per agar plate growing on either aerobic or anaerobic plates (whichever yielded higher counts) is given. According to the receiver-operating-characteristic analysis, the inflection point (i.e., the optimal cutoff) was 1 CFU or more. However, 5 CFU or more was selected as the ideal cutoff, because high specificity was considered more important than an optimal trade-off between sensitivity and specificity.

ties of sonicate-fluid culture, tissue culture, and synovial-fluid culture were 98.8%, 99.2%, and 98.1%, respectively. Fourteen cases of prosthetic-joint infection were detected by sonicate-fluid culture but not by tissue culture (see Table 1 of the Supplementary Appendix). The sensitivity of tissue culture increased from 50.0% to 54.1% to 66.7% to 72.7% as the number of specimens collected increased from two or three to four or five or more.

The number of organisms detected in sonicate-fluid culture was greater in patients with prosthetic-joint infection than in those with aseptic failure (P<0.001) (Fig. 1); the area under the ROC curve for the number of organisms detected in sonicate-fluid culture was 0.89 (95% confidence interval [CI], 0.85 to 0.93). Of the 62 patients with

positive sonicate-fluid cultures, the infection would have been missed in 7 had only aerobic culture been performed and in 3 had only anaerobic culture been performed.

The sensitivity and specificity of sonicate-fluid culture after Gram's staining were 44.7% and 100.0%, respectively; findings on Gram's staining correlated with sonicate-fluid culture results in all cases. One patient with prosthetic-joint infection had positive sonicate fluid on Gram's staining and negative sonicate-fluid and tissue cultures; this patient had received previous antimicrobial therapy.

Of the 48 patients with prosthetic-joint infection and positive tissue cultures, 4 had cultures that were positive as a result of growth from broth

Table 2. Characteristics of the Patients.

Characteristic	Patients with Aseptic Failure (N = 252)	Patients with Prosthetic-Joint Infection (N = 79)
Age — yr		
Median	70	68
Range	34–88	36–87
Sex — no. (%)		
Male	113 (45)	44 (56)
Female	139 (55)	35 (44)
Reason for primary arthroplasty — no. (%)		
Osteoarthritis	173 (69)	49 (62)
Inflammatory joint disorder*	25 (10)	6 (8)
Bone fracture or trauma	20 (8)	6 (8)
Congenital abnormalities	9 (4)	5 (6)
Avascular bone necrosis	8 (3)	3 (4)
Bone neoplasia	4 (2)	1 (1)
Other†	13 (5)	9 (11)
Risk factors for prosthetic-joint infection — no. (%)		
Diabetes mellitus	20 (8)	9 (11)
Long-term use of corticosteroids‡	7 (3)	5 (6)
Site of arthroplasty — no. (%)		
Knee	154 (61)	53 (67)
Hip	98 (39)	26 (33)
Visible purulence — no./total no. (%)§		
Synovial fluid	0/92	10/18 (56)
Implant site	0	56 (71)
Acute inflammation in tissue — no./total no. (%)§	0/244	51/61 (84)
Presence of sinus tract — no. (%)§	0	31 (39)
Preoperative laboratory findings — no./total no. (%)		
Blood leukocyte count >10×10⁹/liter¶	13/224 (6)	13/72 (18)
Erythrocyte sedimentation rate >30 mm/hr¶	22/192 (11)	44/64 (69)
Serum C-reactive protein >1.0 mg/dl¶	30/186 (16)	51/64 (80)
Synovial-fluid leukocyte count >1700/µl‖	13/80 (16)	17/18 (94)
Synovial-fluid differential >65% neutrophils‖	6/80 (8)	16/17 (94)

* Inflammatory joint disorder includes rheumatoid arthritis, psoriasis, and systemic lupus erythematosus.
† Other reasons for primary arthroplasty include poliomyelitis, polymyalgia rheumatica, osteochondritis dissecans, chondromalacia, hemophilia, monoclonal gammopathy, previous septic arthritis, gout, and unknown reasons.
‡ Long-term use is defined as more than 25 mg of a prednisone equivalent per day for at least the past month.
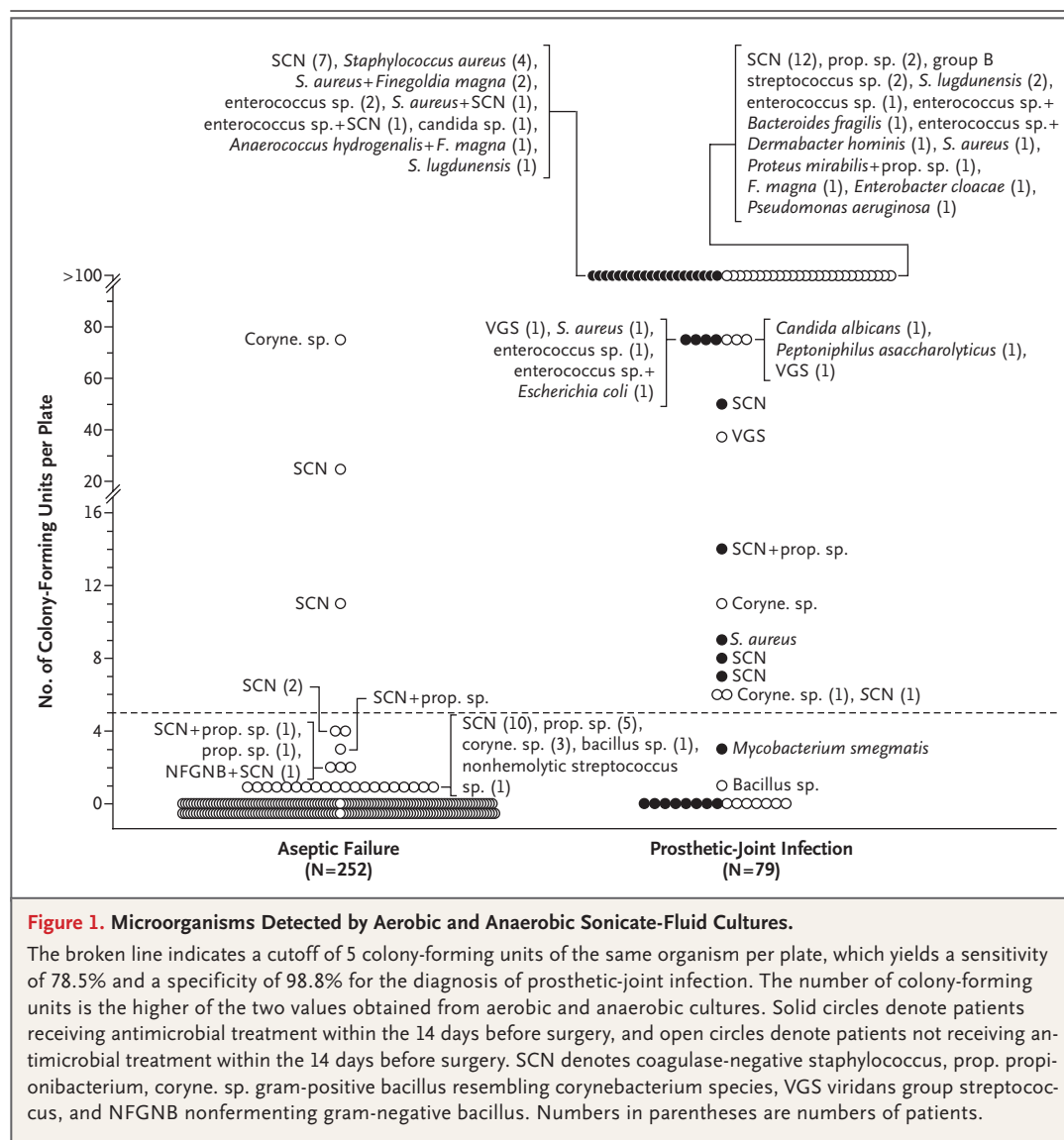§ This characteristic is considered to be a diagnostic criterion for prosthetic-joint infection.
¶ The cutoff is taken from Bernard et al.[15]
‖ The cutoff is taken from Trampuz et al.,[4] although that study excluded patients with underlying inflammatory joint diseases or connective-tissue diseases and evaluated only knee arthroplasties.

only of coagulase-negative staphylococci, viridans group streptococci, *Propionibacterium acnes*, or yeast; the bacteria were detected in sonicate-fluid culture. Of the patients with aseptic failure, two had positive tissue cultures, both for coagulase-negative staphylococci. Three patients with aseptic failure had positive sonicate-fluid cultures: two were positive for coagulase-negative staphylococci

Figure 1. Microorganisms Detected by Aerobic and Anaerobic Sonicate-Fluid Cultures.

The broken line indicates a cutoff of 5 colony-forming units of the same organism per plate, which yields a sensitivity of 78.5% and a specificity of 98.8% for the diagnosis of prosthetic-joint infection. The number of colony-forming units is the higher of the two values obtained from aerobic and anaerobic cultures. Solid circles denote patients receiving antimicrobial treatment within the 14 days before surgery, and open circles denote patients not receiving antimicrobial treatment within the 14 days before surgery. SCN denotes coagulase-negative staphylococcus, prop. propionibacterium, coryne. sp. gram-positive bacillus resembling corynebacterium species, VGS viridans group streptococcus, and NFGNB nonfermenting gram-negative bacillus. Numbers in parentheses are numbers of patients.

and one for a gram-positive bacillus resembling corynebacterium species.

DISCORDANT CULTURES

Fourteen patients with prosthetic-joint infection had positive sonicate-fluid cultures and negative tissue cultures (see Table 1 of the Supplementary Appendix). Among the six patients in this group who also had positive synovial-fluid cultures, the microbiologic findings of sonicate-fluid and synovial-fluid cultures were concordant. Review of the medical records of the other eight patients found that in seven of these patients, the same microorganism that was identified in sonicate-fluid culture had been identified in a culture pre-

viously obtained from the site of the arthroplasty performed at another institution before surgery. Of the 17 study patients with prosthetic-joint infection and negative sonicate-fluid cultures, all had negative tissue cultures.

Among patients with prosthetic-joint infection, the microbiologic findings of sonicate-fluid or tissue culture were concordant with those of synovial-fluid culture when both cultures were positive. The microbiologic findings of sonicate-fluid and tissue culture were concordant when both cultures were positive, with the following exceptions. In five cases, one organism was detected by tissue culture and *Escherichia coli*, propionibacterium species, *Dermabacter hominis*, coagulase-negative

staphylococci, or *Staphylococcus aureus* was also detected by sonicate-fluid culture. In one case, group B streptococcus species was detected by tissue culture and enterococcus species and coagulase-negative staphylococci were detected by sonicate-fluid culture. In another case, two organisms were detected by sonicate-fluid and tissue culture and, in addition, coagulase-negative staphylococci was detected by tissue culture. In three cases, one organism was detected by sonicate-fluid culture and coagulase-negative staphylococci, corynebacterium species, or *Finegoldia magna* was detected by tissue culture. In one case, sonicate-fluid culture yielded corynebacterium species, whereas tissue culture yielded yeast (Table 3).

PREVIOUS ANTIMICROBIAL THERAPY

The sensitivity of tissue and sonicate-fluid culture was reduced in patients receiving antimicrobial therapy (Fig. 2). For tissue culture, the sensitivity decreased from 76.9% to 47.8% to 41.2% as the antimicrobial-free interval before surgery decreased from greater than 14 days, to 4 to 14 days, to 0 to 3 days, respectively (P for trend <0.001). For sonicate-fluid culture, the sensitivity was 82.1%, 87.0%, and 58.8% for the same time intervals, respectively (P for trend=0.12). Sonicate-fluid culture was more sensitive than tissue culture when antimicrobial agents were discontinued within 14 days before surgery (75% vs. 45%, P<0.001).

SINGLE POSITIVE CULTURES

Among the 252 patients with aseptic failure, 21 (8.3%) had single positive tissue cultures. Among the 79 patients with prosthetic-joint infection, 10 (12.7%) had single positive tissue cultures. If one or more positive cultures were considered to represent a positive tissue-culture result, the sensitivity of tissue culture would not be significantly different from that of sonicate-fluid culture (73.4% vs. 78.5%, P=0.21); however, the specificity (90.9% vs. 98.8%) would be compromised (P<0.001). Furthermore, in 4 of 10 cases of prosthetic-joint infection, the microorganism detected in the single positive tissue culture did not correlate with the microorganism detected in the sonicate-fluid cultures, a result suggesting the possibility of contamination of tissue.

Even if the one case of positive sonicate-fluid culture but negative tissue culture not considered by the treating clinician to be prosthetic-joint infection were excluded and any tissue culture positive for *S. aureus*, enterococcus species, or yeast were considered positive (see Table 1 of the Supplementary Appendix), the sensitivity of sonicate-fluid cultures would remain superior to that of tissue cultures (P=0.01).

DISCUSSION

More than a decade ago, the National Institutes of Health Consensus Development Conference statement on total hip replacement suggested that the diagnosis of infected implants was challenging because the diagnostic tests were inaccurate.[16] The results of our study show that culture of microorganisms from removed orthopedic implants is more sensitive than tissue culture. The technique is simple and can be performed in most microbiology laboratories (see Fig. 1 of the Supplementary Appendix). Furthermore, it yields viable microorganisms that can be subjected to antimicrobial-susceptibility testing. Our results emphasize the importance of performing both aerobic and anaerobic sonicate-fluid culture; 11% of positive cultures were obtained only on anaerobic plates and 5% of positive cultures only on aerobic plates. Improved detection of polymicrobial prosthetic-joint infection appears to be another advantage of sonicate-fluid culture.

This technique typically yields high numbers of organisms (at least 50 colony-forming units per plate). Explanted prostheses and tissue may be contaminated in the operating suite or during processing in the microbiology laboratory. Quantification of the number of microorganisms in sonicate fluid may help to distinguish infected from contaminated prostheses.

Preoperative administration of antimicrobial agents (including oral antimicrobial agents given for suppression of prosthetic-joint infection and discontinued before surgery) can affect the sensitivity of tissue and sonicate-fluid culture. Antimicrobial agents were stopped more than 14 days before surgery in 9 of 31 study patients with negative tissue cultures, 7 (77.8%) of whom also had negative sonicate-fluid cultures. This result suggests that stopping antimicrobial therapy 2 weeks before surgery, a common practice, may not result in ideal culture sensitivity. The optimal antimicrobial-free period required before revision or resection arthroplasty to obtain meaningful culture results remains to be determined. However, in patients receiving antimicrobial therapy within 14
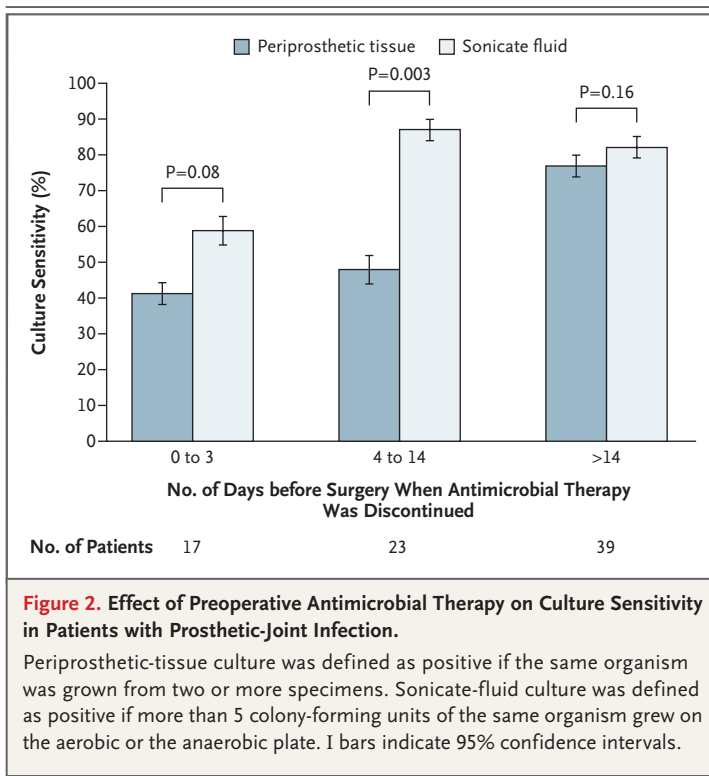
Table 3. Results of Sonicate-Fluid and Periprosthetic-Tissue Cultures.

Type of Infection and Culture Results	No. of Patients	Organism or Finding (No. of Patients)*
Prosthetic-joint infection	79	
Positive sonicate-fluid and negative periprosthetic-tissue cultures	14	SCN (5) *Staphylococcus aureus* (3) Enterococcus sp. (2) Viridans group streptococci (1) Propionibacterium sp. (1) Corynebacterium sp. (1) Candida sp. (1)
Positive sonicate-fluid and periprosthetic-tissue cultures	48	
Concordant†	37	SCN (18) *S. aureus* (4) *S. lugdunensis* (3) *S. aureus* + *Finegoldia magna* (2) Viridans group streptococci (2) Group B streptococcus sp. (1) Enterococcus sp. (1) Propionibacterium sp. (1) *Enterobacter cloacae* (1) *Pseudomonas aeruginosa* (1) *F. magna* (1) *Bacteroides fragilis* + enterococcus sp. (1) *Candida albicans* (1)
Discordant	11	
Additional organism detected by sonicate-fluid culture (sonicate-fluid culture/periprosthetic-tissue culture)	5	Enterococcus sp. + *Escherichia coli*/enterococcus sp. (1) SCN + *S. aureus*/SCN (1) *Proteus mirabilis* + propionibacterium sp./*P. mirabilis* (1) Enterococcus sp. + *Dermabacter hominis*/enterococcus sp. (1) Propionibacterium sp. + SCN/propionibacterium sp. (1)
Additional organism detected by periprosthetic-tissue culture (sonicate-fluid culture/periprosthetic-tissue culture)	4	*Peptoniphilus asaccharolyticus*/*P. asaccharolyticus* + corynebacterium sp. (1) Enterococcus sp./enterococcus sp. + SCN (1) *F. magna* + *Anaerococcus hydrogenalis*/*F. magna* + *A. hydrogenalis* + SCN (1) Group B streptococcus sp./group B streptococcus sp. + *F. magna* (1)
Different organisms detected (sonicate-fluid culture/periprosthetic-tissue culture)	2	SCN + enterococcus sp./group B streptococcus sp. (1) Corynebacterium sp./yeast (1)
Negative sonicate-fluid and positive periprosthetic-tissue cultures	0	
Negative sonicate-fluid and periprosthetic-tissue cultures	17	
Aseptic failure	252	
Positive sonicate-fluid and negative periprosthetic-tissue cultures	3	SCN (2) Corynebacterium sp. (1)
Positive sonicate-fluid and periprosthetic-tissue cultures	0	
Negative sonicate-fluid and positive periprosthetic-tissue cultures	2	SCN (2)
Negative sonicate-fluid and periprosthetic-tissue cultures	247	

* SCN denotes coagulase-negative staphylococcus.
† Concordant indicates that the organism was isolated from both sonicate-fluid and periprosthetic-tissue cultures.

Figure 2. Effect of Preoperative Antimicrobial Therapy on Culture Sensitivity in Patients with Prosthetic-Joint Infection.

Periprosthetic-tissue culture was defined as positive if the same organism was grown from two or more specimens. Sonicate-fluid culture was defined as positive if more than 5 colony-forming units of the same organism grew on the aerobic or the anaerobic plate. I bars indicate 95% confidence intervals.

infection, which occurred both in patients who used systemic antimicrobials in the 2 weeks before surgery and in those who did not. Possible reasons for these culture-negative cases include case misclassification, the presence of microorganisms that did not grow under the conditions studied (e.g., because of inappropriate mediums, inadequate incubation time,[17] or loss of viability during transport of the specimen), previous antimicrobial therapy, or release of antimicrobial agents from polymethylmethacrylate.[18] A multimodal approach to the diagnosis of prosthetic-joint infection, including clinical, microbiologic, and tissue histopathological findings, appears to be warranted.

It has been suggested that some cases of aseptic failure are missed cases of prosthetic-joint infection.[8] Despite improved sensitivity, the use of sonicate-fluid culture did not identify a substantial number of potentially infected cases among the patients with aseptic failure. This finding indicates either that bacteria are not involved in the pathogenesis of aseptic failure or that sonicate-fluid culture is inadequate to detect the microorganisms associated with aseptic failure if any are present. Given the limitations of the current microbiologic techniques for identifying the organisms that cause prosthetic-joint infection, this new technique warrants further study.

days before surgery, sonicate-fluid cultures were more sensitive than tissue cultures. We speculate that this is because planktonic bacteria present in tissue are more susceptible to antiinfective agents than are biofilm bacteria.

There are several important limitations to this study, including the lack of a gold-standard definition of prosthetic-joint infection. Processing explanted orthopedic components for culture in the laboratory takes approximately twice as long as processing tissue specimens; however, only a single specimen (i.e., the components of the explanted hip or knee prosthesis) is submitted to and processed in the laboratory, in contrast to the multiple tissue specimens typically submitted and processed. Our study was not designed to detect mycobacteria and fungi. Of three fungal infections, only one was detected by both sonicate-fluid and tissue cultures. When mycobacterial or fungal prosthetic-joint infection is suspected, special tissue cultures should be performed. Another limitation is that not all resected prosthesis components could be fitted into the containers provided.

Despite the use of the new technique, there remained culture-negative cases of prosthetic-joint

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