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ORIGINAL ARTICLE

Evaluation of the use of sonication of retrieved implants for the diagnosis of prosthetic joint infection in a routine setting

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Abstract

In order to evaluate the usefulness of sonication of retrieved implants for the diagnosis of prosthetic joint infection (PJI) in a large group of patients in a routine setting, we designed a 3-year retrospective study. Patients were classified into two groups: those meeting the clinical criteria of PJI and those that did not (control group). Two hundred patients and 276 samples were included. The types of infection were early ($n = 44$), delayed ($n = 53$), positive intraoperative cultures ($n = 13$) and late-acute ($n = 8$). The culture sensitivities of sonicate fluid, periprosthetic tissue, synovial fluid and combination of periprosthetic tissue and/or synovial fluid were 69.5, 52.8, 54.8 and 60.2%, respectively. The specificities were 97.6, 90.3, 93.0 and 89.9%, respectively. Sonicate fluid culture of implants was more sensitive than peri-implant tissue, synovial fluid and combination of periprosthetic tissue and/or synovial fluid for all infection types, though it was especially useful in delayed infection: 91.3% vs. 60.0% ($p = 0.0015$), 63.2% ($p = 0.0005$) and 66.7% ($p = 0.0001$), respectively. When sonicate fluid culture of implants was performed in addition to conventional cultures, the sensitivity increased significantly in total (from 60.2 to 77.1%) and delayed PJI (from 45.1 to 71.7%). On the other hand, for early PJI, sonicate fluid culture of prosthesis was not superior to conventional diagnostic methods.

Introduction

Prosthetic joint infection (PJI) is a serious and devastating consequence of orthopaedic surgery. Although incidence is currently lower than 5% [1], this rate is expected to climb in the coming years [2] due to the increasing number of orthopaedic surgeries being performed. PJI diagnosis is based on clinical findings, analytical parameters, laboratory results from peripheral blood and synovial fluid, histological studies, imaging tests and microbiological techniques [3]. Traditional microbiologic methods consist of culture of synovial fluid and periprosthetic tissue. Sonication of retrieved prostheses for the diagnosis of PJI was first reported by Trampuz et al. in 2007 [4]. Since then, this technique, which uses ultrasound to release biofilm-forming bacteria from the implant surface [5, 6], has been demonstrated to be especially useful for the diagnosis of PJI [4, 7]. In recent years, many experimental studies have indicated that sonication of retrieved implants produces positive outcomes in terms of sensitivity (Sn) and specificity (Sp). Indeed, a meta-analysis published in 2014 which collected data from 12 studies showed Sn = 80% and Sp = 95% [8]. These data were very similar to those published by Liu et al. in another meta-analysis from 2017 [9].

However, most published studies have small sample sizes, except a few works [4, 7, 10]. But, especially, they are performed under experimental conditions, before the diagnostic method is incorporated in the routine care setting [11–21]. The aim of this work was to compare the usefulness of sonicate fluid culture (SFC) from explanted implants with conventional techniques [peri-implant tissues culture (PITC), synovial fluid culture and culture of periprosthetic tissue and/or synovial fluid] for the diagnosis of PJI in a large group of patients in a routine care setting.

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Materials and methods

Study design and patients

A retrospective study was carried out between January 2011 and June 2014 at Fundación Jiménez Díaz hospital. All patients with prostheses submitted for microbiological cultures were included in the study. They were classified into two groups: those with clinical criteria of PJI and those not meeting such criteria (control group). PJI was suspected when at least one of the following commonly accepted criteria [22] was met: (1) sinus drainage; (2) presence of acute inflammation identified by histopathologic examination; (3) presence of macroscopic purulence around the implant; (4) presence of two or more positive cultures from high-quality samples (synovial fluid, periprosthetic tissue, blood cultures); or (5) presence of acute or chronic pain in the absence of a mechanical problem AND at least one altered blood parameter [including erythrocyte sedimentation rate (ESR), C-reactive protein (CRP) or synovial cell count].

PJIs were classified as early (< 3 months), delayed (3–12 or 24 months) or late-acute (occurring > 12–24 months after surgery). Some infected patients were also classified as unexpected positive intraoperative cultures.

Microbiological procedures

Samples were removed after prosthetic joint implant surgery in the orthopaedic surgery department of the hospital and then sent to the microbiology laboratory. For those cases where no immediate processing was available, prostheses were maintained at 4 °C during 24 h. There, they were processed for culture according to the sonication protocol used in our hospital [20, 23].

Periprosthetic tissues (3–6 samples) and/or synovial fluid inoculated in blood culture bottles (BacT/Alert system, bioMérieux, Marcy l'Etoile, France) were also processed and cultured in the same media as SFC (Tryptic soy-5% sheep blood agar, Chocolate agar, MacConkey agar, Schaedler-5% sheep blood agar for anaerobic cultures, Sabouraud Chloramphenicol agar, all from bioMérieux, Marcy l'Etoile, France), including also mycobacterial cultures (Löwenstein–Jensen and Coletsos slants and BacT/Alert mycobacterial liquid culture system, bioMérieux, Marcy l'Etoile, France) for peri-implant biopsies.

Clinical data

The study was approved by the Ethics in Research Committee of Fundación Jiménez Díaz Hospital. The clinical charts of the patients included were reviewed and data were analysed following a predefined protocol.

Statistical analysis

A statistical study to compare Sn, Sp, positive predictive value (PPV) and negative predictive value (NPV) for SFC of implants, PITC, synovial fluid culture and periprosthetic tissue and/or synovial fluid culture was performed. Values were calculated with two by two contingency tables considering the presence of positive culture, in patients with and without PJI. The sensitivities of the different methods were compared using the Chi-square test and Fisher's exact test, comparing only those cases that had both diagnostic tests performed. *p*-Values < 0.05 were considered statistically significant. Analysis was carried out using Epi Info 3.5.4 software (CDC, Atlanta, GA, USA).

Results

A total of 276 prostheses/prosthesis components from 200 patients were studied. Seventy-five were male and 125 female, and the mean age was 70.9 years (24–98). One hundred and eighteen patients were diagnosed as infected and 82 did not have infection (considered the control group). The most frequent type was delayed infection ($n = 53$), followed by early infection ($n = 44$), unexpected positive cultures ($n = 13$) and late-acute infection ($n = 8$).

In addition to SFC, PITC was also performed in 171 patients, and synovial fluid culture was carried out in 125 cases.

Types of prosthesis included hip ($n = 133$), total knee ($n = 119$), shoulder ($n = 16$) and partial hip ($n = 8$). Of the 276 samples, 181 had been obtained from patients with clinical criteria of PJI, while 95 originated from patients not meeting these criteria.

Early infection ($n = 44$)

With a mean age of 70.6 years and a majority of women ($n = 28$), the type of explanted prosthesis was: total hip ($n = 22$), knee ($n = 14$), partial hip ($n = 6$) and shoulder ($n = 2$).

Regarding the symptoms, pain and purulent discharge from surgical wound were the most frequent ones ($n = 23$ and 22, respectively), followed by wound dehiscence ($n = 5$) and synovial fluid effusion ($n = 4$). Two patients were finally diagnosed with luxation and two with prosthesis loosening. The CRP value was obtained only from 29 patients (mean of 10.1 mg/dL).

When analysing patient treatment, differences appeared among pharmacologic and surgical management. All cases ($n = 44$) received antimicrobial therapy after surgery, while only seven patients received it before surgery. Regarding surgical treatment, the kind of surgery performed was: DAIR (debridement, antibiotics and implant retention) with polyethylene replacement ($n = 34$), one-stage revision ($n = 8$), two-

stage revision with a spacer of vancomycin and gentamicin ($n = 1$) and girdlestone arthroplasty ($n = 1$).

Data on culture of sonicated prostheses in comparison with periprosthetic tissue and/or synovial fluid culture for patients with early PJI are shown in Table 1. Every negative result from peri-implant biopsies and/or synovial fluid culture in patients with clinical criteria of early PJI was regarded as a false-negative of these techniques.

Delayed infection ($n = 53$)

With a mean age of 70.1 years, 29 patients were women and 24 were men. For this infection type, the removed prostheses were: total hip ($n = 24$), knee ($n = 25$), shoulder ($n = 3$) and partial hip ($n = 1$).

In delayed infection, the main symptom was pain (present in 54 of 63 patients), prosthetic loosening ($n = 25$) and luxation ($n = 5$). Fistula ($n = 5$) and synovial fluid effusion ($n = 1$) were less common. The CRP value was also altered as in early PJI, but, in this case, it was lower; it was taken from 13 patients (mean of 5.35 mg/dL).

Only seven patients received antibiotic treatment before surgery and all 53 patients received it in the postoperative stage. Unlike early infection, in cases of delayed infection, two-stage revision was the most widely used measure ($n = 28$), followed by one-stage revision ($n = 16$) and, finally, DAIR with polyethylene replacement ($n = 9$).

Data on the culture of sonicated prostheses in relation to PITC and/or synovial fluid culture for patients with delayed PJI are shown in Table 2.

Late-acute infection ($n = 8$)

This infection was found in five women and three men, and the mean age was 80.6 years old. In six cases, the kind of implant was total knee and in two cases total hip. The symptoms were pain ($n = 7$), spill ($n = 3$), prosthesis loosening ($n = 2$) and purulent discharge from surgical wound ($n = 1$). The proportion of polymorphs was slightly higher and that of lymphocytes lower than reference values (76.6% and 14.5%, respectively). The CRP value was taken from six patients (mean of 20.9 mg/dL).

Three patients received antibiotic therapy before surgery and all of them received it afterwards. Two-stage revision was carried out in four patients, replacement of polyethylene in three and one-stage revision in one patient.

Due to the low number of patients with late-acute infection, we did not calculate for statistically significant associations.

Table 1 Comparison of cultures of sonicated implants and periprosthetic tissue and/or synovial fluid in patients with early prosthetic join infection (PJI; $n = 44$)

Culture results	Number of patients	Type of culture	Microorganism (number of patients)
Sonication fluid +, periprosthetic tissue and/or synovial fluid +	31	Monomicrobial	*Staphylococcus aureus* (14)
			Klebsiella spp. (3)
			Enterobacter cloacae (2)
			Coagulase-negative staphylococci (2)
			Escherichia coli (1)
			Morganella morganii (1)
			Proteus mirabilis (1)
			Providencia stuartii (1)
			Pseudomonas aeruginosa (1)
		Polymicrobial	*Enterococcus faecalis*, *Escherichia coli* and *Proteus mirabilis* (1)
			Enterococcus faecalis and *Pseudomonas aeruginosa* (1)
			Klebsiella pneumoniae, *Proteus mirabilis* and *Staphylococcus aureus* (1)
			Klebsiella pneumoniae and *Pseudomonas aeruginosa* (1)
			Morganella morganii and *Pseudomonas aeruginosa* (1)
Sonication fluid +, periprosthetic tissue and/or synovial fluid −	4	Monomicrobial	*Escherichia coli* (1)
			Enterobacter cloacae (1)
			Pseudomonas fluorescens (1)
			Serratia marcescens (1)
Sonication fluid −, periprosthetic tissue and/or synovial fluid +	5	Monomicrobial	*Pseudomonas aeruginosa* (1)
			Staphylococcus aureus (2)
			Staphylococcus epidermidis (2)
Sonication fluid −, periprosthetic tissue and/or synovial fluid −	4		

Table 2 Comparison of cultures of sonicated implants and periprosthetic tissue and/or synovial fluid in patients with delayed PJI ($n = 63$)

Culture results	Number of patients	Type of culture	Microorganism (number of patients)
Sonication fluid +, periprosthetic tissue and/or synovial fluid +	24	Monomicrobial	*Staphylococcus aureus* (9)
			Staphylococcus epidermidis (3)
			Coagulase-negative staphylococci* (2)
			Enterobacter cloacae (1)
			Escherichia coli (1)
			Klebsiella pneumoniae (1)
			Pseudomonas aeruginosa (1)
			Staphylococcus lugdunensis (1)
		Polymicrobial	*Enterococcus faecalis* and *Propionibacterium acnes* (1)
			Enterococcus faecalis and *Staphylococcus epidermidis* (1)
			Proteus vulgaris and *Pseudomonas aeruginosa* (1)
			S. epidermidis and other CNS (2)
Sonication fluid +, periprosthetic tissue and/or synovial fluid −	12		*S. epidermidis* (3)
			Acinetobacter baumannii (1)
			Coagulase-negative staphylococci* (3)
			Propionibacterium acnes (1)
		Monomicrobial	*Escherichia coli* (1)
			Klebsiella pneumoniae (1)
			Ralstonia pickettii (1)
		Polymicrobial	*Enterobacter cloacae* and *Proteus mirabilis* (1)
Sonication fluid −, periprosthetic tissue and/or synovial fluid +	2	Monomicrobial	*Propionibacterium acnes* (1)
			Micrococcus luteus (1)
Sonication fluid −, periprosthetic tissue and/or synovial fluid −	15		

*Other than *Staphylococcus epidermidis*

Unexpected positive cultures ($n = 13$)

Eight men and five women were included in this category. The mean age was 64.1 years old and the infected prostheses were total hip ($n = 4$), knee ($n = 8$) and partial hip ($n = 1$). The symptoms and signs include pain ($n = 11$), loosening ($n = 6$), synovial fluid effusion ($n = 1$) and luxation ($n = 1$). Only in one patient was CRP performed (value 2.6 mg/dL).

No patient received antibiotics after surgery until cultures were available, and only one patient received antibiotic therapy before surgery. Eleven patients underwent one-stage exchange and two of them had a two-stage exchange procedure.

Table 3 Data used to calculate the statistical parameters of all microbiological procedures for the diagnosis of early, delayed and total PJI

	Early PJI	Delayed PJI	Total infection	No infection
Culture of sonicated implant +	35	36	82	2
Culture of sonicated implant −	9	17	36	80
Total	44	53	118	82
Culture of periprosthetic tissue +	26	23	56	6
Culture of periprosthetic tissue −	9	28	50	59
Total	35	51	106	65
Culture of synovial fluid +	23	12	40	3
Culture of synovial fluid −	7	18	33	49
Total	30	30	73	52
Culture of periprosthetic tissue and/or synovial fluid +	36	26	70	8
Culture of periprosthetic tissue and/or synovial fluid −	8	27	48	74
Total	44	53	118	82

Table 4 Statistical parameters of all microbiological procedures (expressed in %)

	Sonication fluid	Periprosthetic tissue	Synovial fluid	Periprosthetic tissue and/or synovial fluid
Sn	69.5	52.8	54.8	60.2
Sp	97.6	90.8	94.2	90.2
PPV	97.6	90.3	93.0	89.8
NPV	69.0	54.1	59.8	61.2

As in the case of late-acute infections, the low number of cases implies that no statistics were performed for these cases.

Patients without infection ($n = 82$)

Fifty-eight women and 24 men comprised the control group, with a mean age of 69.1 years old. The kind of prosthesis removed was: total knee ($n = 51$), total hip ($n = 28$) and shoulder ($n = 3$).

Sixty-three patients complained of pain and 50% were diagnosed with aseptic loosening. Four cases were due to a luxation and two to fractures. A low number of patients received antibiotic treatment before or after the surgery (3 and 24, respectively). The most frequent surgical measure was one-stage revision ($n = 66$), followed by polyethylene replacement ($n = 11$) and two-stage revision ($n = 5$).

Statistical analysis

The data used to calculate the statistical parameters of Sn, Sp, PPV and NPV for early, delayed and total PJI are shown in Table 3 and the final results appear in Table 4.

For all infections, all statistical parameters improved with SFC of implants compared to the other techniques. The best improved values were Sp and PPV. However, the values of Sn and NPV were not high.

No significant differences were found between specificities. However, there were statistical associations between sensitivities in delayed and total infection. In delayed PJI, the value of Sn of SFC of prostheses experienced the greatest improvement (68.6%) with regard to culture of peri-implant biopsy (45.1%, $p = 0.001$), culture of synovial fluid (40%, $p = 0.0005$) and even culture of periprosthetic tissue and/or synovial fluid (49.1%, $p = 0.0001$). In total infection, SFC of implants was more sensitive than periprosthetic tissue culture: 67.9 vs. 45.1%, respectively ($p = 0.001$).

In addition, when SFC of prostheses was incorporated into the culture of periprosthetic tissue and/or synovial fluid, the number of patients diagnosed increased for all types of infection (Table 5). In early PJI, Sn increased from 76.6 to 87.2% without and with sonication, respectively, in delayed PJI from 46 to 69.8% and in total infection from 58.5 to 77.1%.

In the group of infected patients who received antimicrobial therapy before surgery ($n = 18$), the sensitivity of all types of diagnosis decreased in relation to those patients who did not receive therapy. Data from which values of sensitivity were calculated are shown in Table 6 and final results in Table 7. However, no significant associations were found. Although SFC of implants was the technique which diagnosed the most patients among the group who received antibiotics before surgery (66%), no statistical relations were discovered.

Discussion

Traditional microbiological diagnosis of PJI has been based on culture of synovial fluid and peri-implant biopsies. Despite the notable improvement that these methods have introduced in this field, they have limitations. For example, it is known that culture of synovial fluid is not useful for the diagnosis of delayed PJI, where bacteria are embedded in the biofilm attached to the implant surface [3, 24, 25]. Within the effort to facilitate interpretation of periprosthetic cultures, Atkins et al. [26] established the criteria that are, nowadays, considered the gold standard in most reviews and guidelines [22, 27, 28].

Table 5 Data used to calculate the increase in the number of patients diagnosed with PJI when sonicate fluid culture (SFC) of the retrieved implant is added to conventional cultures (periprosthetic tissue and/or synovial fluid) for early, delayed and total PJI

	Early PJI ($n = 44$)	Delayed PJI ($n = 53$)	Total PJI ($n = 118$)
SFC +, conventional cultures +	31	24	60
SFC +, conventional cultures −	4	12	22
SFC −, conventional cultures +	5	2	9
SFC −, conventional cultures −	4	15	27

Table 6 Data used to calculate the sensitivity of all microbiological procedures (total infection) in patients who received antibiotic treatment before surgery and those who did not

	Antibiotics before the surgery	No antibiotics before the surgery	Total
Culture of sonicated implant +	12	70	82
Culture of sonicated implant −	6	30	36
Total	18	100	118
Culture of periprosthetic tissue +	8	48	56
Culture of periprosthetic tissue −	8	42	50
Total	16	90	106
Culture of synovial fluid +	5	35	40
Culture of synovial fluid −	6	27	33
Total	11	62	73
Culture of periprosthetic tissue and/or synovial fluid +	10	62	72
Culture of periprosthetic tissue and/or synovial fluid −	8	38	46
Total	18	100	118

The introduction of sonication of the retrieved implant represented a revolution in the microbiological diagnosis of PJI, because it improves, in all the studies, the sensibility of all other methods, especially for chronic/delayed infections [1, 8, 9, 29]. However, most studies performed the test under controlled conditions because they are the evaluation of an experimental method, including some performed by our group [11, 20, 23, 30].

Here, we demonstrated that SFC of retrieved implants showed better results than culture of conventional samples (peri-implant tissue, synovial fluid and even periprosthetic tissue and/or synovial fluid). SFC of implants was the method which diagnosed the most patients in all types of infection, followed by culture of periprosthetic tissue and/or synovial fluid. However, this increase is probably due to the improvement in delayed infections. In these cases, the improvement was detected when sonication was compared with PITC, culture of synovial fluid and culture of periprosthetic tissue and/or synovial fluid. Moreover, when sonication of explanted implants was performed in addition to periprosthetic tissue and/or synovial fluid culture, the number of patients diagnosed increased for all types of infection. In delayed and total PJI, this relation was statistically significant, while it was not for acute PJI. This could be explained by the fact that, in delayed infections, microorganisms are embedded on the surface of the implant, forming a biofilm, and the application of ultrasound might release them from the surface [7]. However, despite the improvement, SFC of implants produced four false-negative results in delayed infections. For all these reasons, we underscore the importance of performing both conventional techniques and sonication of retrieved prostheses.

Likewise, even with low values, Sn of PITC and synovial fluid culture were better for acute than for delayed infection, a result that is consistent with the findings of other authors [31, 32]. In other words, in early PJI, SFC of retrieved prostheses is not superior to conventional methods.

We found that, in every method Sn decreased when patients received antibiotic treatment before surgery, as many authors concluded [19, 33]. Trampuz et al. also found statistically significant differences in Sn of SFC of prostheses in patients who received antibiotics before surgery and those who did not [4]. However, we did not find them either when Sn of each method was compared between both groups or when Sn of SFC of prostheses was compared with those of the rest of the techniques. Probably the reason for this could be the low number of patients included in the group ($n = 18$).

In conclusion, the introduction of sonication in clinical microbiology routine improves the aetiological diagnosis of PJI, especially among chronic/delayed infections. Its introduction in the routine practice of a clinical laboratory is useful to improve the microbiological diagnosis of PJIs.

Table 7 Values of sensitivity of all microbiological procedures (total infection) in patients who received antibiotic treatment before surgery and those who did not

	Antibiotic treatment before surgery	No antibiotic treatment before surgery
Sonication fluid culture	66.7%	70%
Periprosthetic tissue culture	50%	53.3%
Synovial fluid culture	45.5%	56.5%
Periprosthetic tissue and/or synovial fluid culture	55.6%	62%

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Compliance with ethical standards

Conflict of interest No conflict of interest for any of the authors regarding this study.

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