CURRENT CONCEPTS REVIEW

The Function of Sonication in the Diagnosis of Periprosthetic Joint Infection After Total Knee Arthroplasty

E. Carlos Rodriguez-Merchan, MD, PhD[1]

Research performed at the Department of Orthopaedic Surgery, La Paz University Hospita-IdiaPaz, Madrid, Spain

Received: 14 November 2019 *Accepted: 14 November 2020*

Abstract

Periprosthetic joint infection (PJI) following total knee arthroplasty (TKA) is a serious adverse event. Culturing of samples of periprosthetic tissue is the standard technique utilized for the microbiological diagnosis of PJI. However, this technique is neither sensitive nor specific since in PJI the microorganisms are usually in a biofilm on the surface of the prosthesis. The objective of this paper is to know the role of sonication in the diagnosis of PJI after TKA. Sonication consists in taking samples of bacteria from biofilms adhered to the prosthetic surface. The reported sensitivity for the diagnosis of PJI of the periprosthetic tissue cultures and sonicate fluid cultures is 54% and 75%, apiece. The specificity is 98% and 87%, respectively. In conclusion, the sonication technique is a dependable test for the diagnosis of PJI after TKA with a greater sensitivity and specificity than the conventional periprosthetic tissue cultures. Sonication of polyethylene liners, rather than the whole prosthesis, has been reported to be sufficient for diagnosis of prosthetic joint infection.

Level of evidence: III

Keywords: Periprosthetic joint infection, Sonication, Total knee arthroplasty

Introduction

Periprosthetic joint infection (PJI) following total knee arthroplasty (TKA) is a serious adverse event. At 1 month, the infection frequency of the surgical site (SSI) is 1.1%, while the frequency of deep infection is 0.1%. The frequency of PJI during the life of the patient after a TKA ranges between 0.7 and 4.6%. Compared with individuals operated on for TKA without PJI Individuals, in individuals with PJI the length of hospitalization is longer (5.3 vs. 3 days), and they need more readmissions (3.6 vs. 0.1) and more hospital visits (6.5 vs. 1.3).[1] The average annual cost of patients with PJI operated from TKA is higher ($ 116,383 on average) than in patients operated on for TKA without PJI ($ 28,249 on average). Hospital costs are between 2 and 24 times greater in individuals with PJI than in those without PJI. PJI after TKA represents a great trouble for patients, orthopedic surgeons and health economy.[1]

Culturing of samples of periprosthetic tissue is the standard technique utilized for the microbiological diagnosis of PJI. However, this technique is neither sensitive nor specific since in PJI the microorganisms are usually in a biofilm on the surface of the prosthesis.[2] According to Portillo et al, cultures have limited sensitivity in the diagnosis of PJI, especially in low-grade infections.[3] Serum markers, such as erythrocyte sedimentation rate (ESR) and the C reactive protein (CRP), are valuable noninvasive tools for diagnosing PJI. Nevertheless, there is no serum biomarker that in solitude has good sensitivity and specificity. Therefore, the aforementioned serum biomarkers are usually combined with more invasive synovial tests. The clinical suspicion and the assessment of the aforementioned biomarkers are essential for the diagnosis of PJI, although we still do not know a serum

Corresponding Author: E. Carlos Rodriguez-Merchan, Department of Orthopedic Surgery, La Paz University Hospital, Madrid, Spain
Email: ecrmerchan@hotmail.com

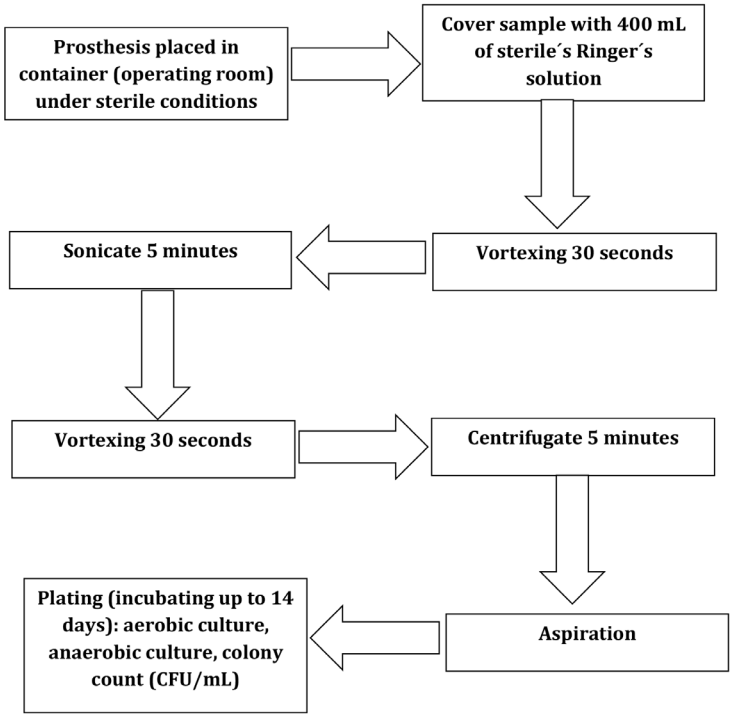

Figure 1. Diagram of prosthesis sonication protocol (CFU = colony-forming units; ML = milliliters).

marker that can be considered the gold standard of the diagnosis of PJI.[4]

Sonication of the implants retrieved during revision surgery of TKA is the best option currently available to detect the microorganisms that colonize the implant. It would be good if the sonication was incorporated in a generalized way to the new protocols of diagnosis of infection after TKA, since it could help the early and precise detection of said infection.[5] Sonication consists in taking samples of bacteria from biofilms adhered to the prosthetic surface. After removing the prosthesis during the revision arthroplasty, it is placed in a container with 400 ml of Ringer's solution and subjected to a combination of vortexing and sonication. Then, the bacteria obtained by the sonication process are incubated and cultured [Figure 1].

Results of literature review

A narrative review of the literature on the topic the function of sonication in the diagnosis of PJI after TKA was performed. A Cochrane Library and PubMed (MEDLINE) exploration associated with the topic was carried out. The solely language explored was English. Abstracts of scientific meeting and other sources of proof were not included. The chief criteria for choice were papers that were devoted to the sunction of sonication in PJI. shows the strategies utilized (PubMed /Medline and Cochrane Library) [Figure 2]. The explorations were dated from the beginning of the exploration devices (PubMed and Cochrane Library) until 6 February 2019.

How useful is sonication?

In 2006 Trampuz et al published the first study found in the literature on sonication in PJI.[6] These authors analyzed by means of sonication in polyethylene bags the prostheses removed in 24 individuals diagnosed with PJI of the hip and knee. The sensitivity for the diagnosis of PJI of the periprosthetic tissue cultures and sonicate fluid cultures was 54% and 75%, respectively. The specificity was 98% and 87%, respectively.

With the utilization of standardized nonmicrobiologic guidelines to define PJI, the sensitivities of periprosthetic-tissue and sonicate-fluid cultures were 60.8% and 78.5%, apiece, and the specificities were 99.2% and 98.8%, apiece.[2]

The results of sonication culture were set against the conventional tissue culture by Holinka et al.[7] The sensitivity of sonication fluid culture was 83.3%, of single positive tissue culture was 72.2% and 61.1% when two or more cultures caused the same microorganism.

According to van Diek et al sonication is a very specific evaluation for diagnosis of PJI.[8] Nonetheless, because of the low sensitivity, a negative sonication test does not eliminate the existence of PJI. Thus, sonication is not adequate for screening of microorganisms during revision surgery.

Tani et al stated that sonication represents a dependable method to make the diagnosis of PJI with a higher sensitivity and specificity than the conventional periprosthetic tissue cultures.[9]

In 2018 Park et al reported that sonication for

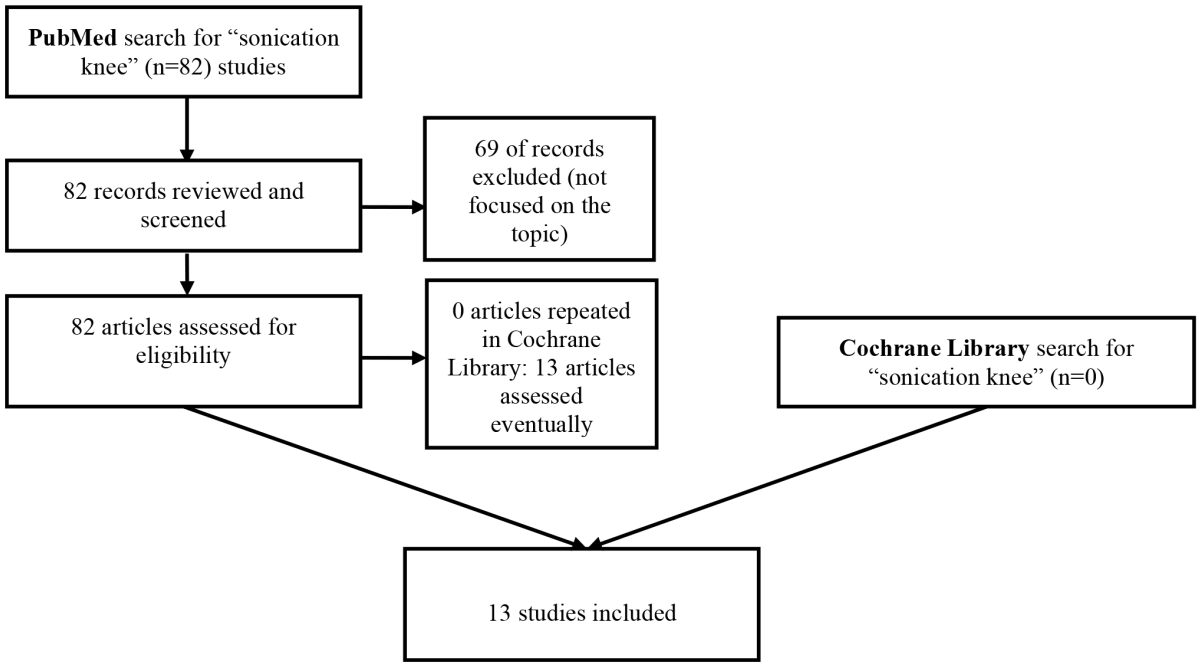

Figure 2. Flow chart of our search strategy concerning the value of sonication in the diagnosis of periprosthetic joint infection (PJI) after total knee arthroplasty (TKA).

identification of pathogens could be useful. However, this statement should be interpreted prudently due to the plausibility of contamination.[10]

What technique should we use?

Multiplex PCR of sonication fluid is an encouraging method for diagnosis of PJI, especially in subjects who beforehand underwent treatment with antibiotics. With modified primer sets, multiplex PCR has the potential for farther amelioration of the diagnosis of PJI.[11]

According to Portillo et al, multiplex PCR of sonication fluid showed big sensitivity (96%) and specificity (100%) for diagnosing PJI, giving good discriminative power towards aseptic failure, especially in subjects beforehand experiencing treatment with antibiotics.[3]

Should we sonicate all implants or just some?

Sonication of antibiotic spacers ameliorated the sensitivity of intraoperative cultures from 45% to 82%.[12] Sonication of antibiotic spacers seems to be valuable in foretelling failure explicable to recurrent infection following two-stage reimplantation.

In 2019 Karbysheva et al analyzed 112 prosthetic components (58 knees, 54 hips) retrieved from 40 patients.[13] The bacterial load removed from the aforementioned components was assessed qualitatively and quantitatively in sonication-fluid cultures. Bigger bacterial counts were encountered on polyethylene than on titanium or cobalt-chromium alloy. Coagulase-negative Staphylococcus aureus and Streptococcus species were most usually isolated. Sonication of polyethylene liners, rather than the whole prosthesis, was enough for making the diagnosis of PJI.[13]

Discussion

According to Suster et al Staphylococcus spp. represents up to two thirds of all the microorganisms that cause PJI, being Staphylococcus aureus and Staphylococcus epidermidis the most frequent causative germs.[14]

According to Rodriguez-Merchan and Liddle, the microbiology of PJI of TKA is now well understood. The bacteria that cause PJI are commonly highly positive, mainly staphylococci and streptococci, although many bacteria can cause PJI, especially in patients with immunosuppression. PJI following TKA is difficult to manage because of the establishement of biofilms, which shield the bacteria causing the infection from the antibiotics.[15] Important factors for PJI are obesity and diabetes.[16]

Prophylactic antibiotics should protect at worst the most frequent microorganisms that cause infection in the postoperative period. They must get sufficiently high concentrations (at worst the minimum inhibitory concentration) in serum and osseous tissue, which must be maintained over time. Doses must be redone to maintain the adequate concentrations. For standard antibiotic prophylaxis, antibiotic administration must be performed within the first hour prior to the surgical incision. Cefazolin (1 to 3 grams depending on body weight every 2 to 5 hours) is the antibiotic most used for the prophylaxis of PJI in the United States and Europe. It is efficacious against gram-positive, aerobic gram-

Table 1. Musculoskeletal Infection Society (MSIS) definition of periprosthetic joint infection (PJI) (21,22): PJI exists when

1	There is a sinus tract communicating with the prosthesis; or
2	A pathogen is isolated by culture from 2 or more separate tissue or fluid samples obtained from the affected prosthetic joint; or
3	When 4 of the following 6 criteria exist: a. Elevated serum erythrocyte sedimentation rate (ESR) and serum C-reactive protein (CRP) concentration b. Elevated synovial white blood cell count c. Elevated synovial polymorphonuclear percentage (PMN%) d. Presence of purulence in the affected joint e. Isolation of a microorganism in one culture of periprosthetic tissue or fluid, or f. Greater than 5 neutrophils per high-power field in 5 high-power fields observed from histologic analysis of periprosthetic tissue at ×400 magnification

negative bacilli and anaerobes. However, cefazolin it is not efficacious against MRSA. Clindamycin (90 mg every 3 to 6 hours) and vancomycin (15 / kg every 6 to 12 hours) are suitable options when cefazolin is cannot be indicated (because of allergy).[17]

PJI after TKA is a very serious adverse event. The frequency of PJI after primary TKA is 1 to 3% and 8 to 10% after revision surgery. Management of a PJI following TKA costs between $ 25,000 and $ 100,000, and needs an enormous quantity of financial resources. By 2020, it is expected that the diagnosis and treatment of the PJI will cost the US health system $ 1.6 billion. It is therefore essential to diagnose a PJI in an appropriate way. The diagnosis is made taking into account the patient's history, the physical examination, the imaging tests, the serological and synovial fluid analysis, the microbiological tests, the histological assessment of the periprosthetic tissue, implant sonication and molecular testing (like polymerase chain reaction – PCR).[18]

The diagnosis of PJI is difficult, since there is no perfect test. The most commonly used method is a combination of serological, synovial, microbiological, histological and radiological tests. However, they are costly, invasive and imperfect for the diagnosis of PJI. Serum biomarkers are reliable diagnostic tools. However, it must be borne in mind that they are not exempt from limitations. Said biomarkers are the white blood cell (WBC) count, the ESR and the CRP. The combination of ESR and CRP is very efficacious in "discarding" the PJI. Other biomarkers have also demonstrated their usefulness in the diagnosis of PJI. They are IL-6, IL-4, TNF-alpha, procalcitonin and siCAM1.[4]

The diagnosis of PJI endures a challenge. Albeit a number of algorithms have been published, a combination of many examinations and clinical premonition remain the foundation of the diagnosis. Knee aspiration is a useful test and must be carried out routinely if inflammatory biomarkers (PCR, ESR) are elevated. Samples must be cultured for 2 weeks. The analysis of synovial fluid [white blood cells and the percentage of PMN (polymorphonuclear) cells] has achieved acceptance in recent years. Leukocyte esterase, alpha-defensine and techniques of genetic diagnosis could be important in the time to come.[19]

Histology is another test accessible to the orthopedic surgeon in the diagnosis of PJI at the time of the surgical procedure, especially when preoperative tests have not been able to appropriately exclude PJI. It is a fairly economical and simple test. The literature supports that the presence of a high number of PMN per high power field (HPF) in the periprosthetic tissue collected during the surgical procedure suggests a high probability of PJI. However, its accuracy is not totally reliable.[20]

PJI can be arduous to precisely diagnose because there are many factors that potentially can affect the outcome. Observation of instructions, such as those from the Musculoskeletal Infection Society, and ameliorating sampling and analysis can enhance diagnostic precision. Nonetheless, taking into account that there is a grade of diagnostic doubt, results must be interpreted on the basis of clinical findings [Table 1].[21,22]

Culturing of the sonication fluid of extracted implants has demonstrated to be more sensitive than conventional periprosthetic tissue culture for the microbiological diagnosis of PJI.[23] According to Rak et al the precise diagnosis of PJI can be arduous because bacteria form a biofilm on the surface of the implant.[24] The sensitivity of culture from sonication fluid is better than that from periprosthetic tissue, but no comparison studies using molecular methods have been carried put.

Sonication of explanted prostheses represents a dependable technique for the diagnosis of PJI after TKA with a higher sensitivity and specificity than the conventional periprosthetic tissue cultures. In a recent report it was shown that sonication of polyethylene liners rather than of the complete prosthesis was sufficient for bacteria discovery in PJIs.

E. Carlos Rodriguez-Merchan MD PhD[1]
1 Department of Orthopedic Surgery, La Paz University Hospital, Madrid, Spain

References

1. Rodríguez-Merchán EC, Liddle AD, eds. The Infected Total Knee Arthroplasty, Epidemiology of the infected total knee arthroplasty: incidence, causes, and the burden of disease. 1st ed. Springer International Publishing AG; 2018. DOI: 10.1007/978-3-319-66730-0_1.
2. Trampuz A, Piper KE, Jacobson MJ, et al. Sonication of removed hip and knee prostheses for diagnosis of infection. N Engl J Med 2007; 357:654-663. DOI: 10.1056/NEJMoa061588
3. Portillo ME, Salvadó M, Sorli L, et al. Multiplex PCR of sonication fluid accurately differentiates between prosthetic joint infection and aseptic failure. J Infect 2012; 65(6):541-8. doi: 10.1016/j.jinf.2012.08.018
4. Rondon AJ, Tan TL, Parvizi J, eds. The Infected Total Knee Arthroplasty, Serological markers of infection in the infected total knee arthroplasty. 1st ed. Springer International Publishing AG; 2018. DOI: 10.1007/978-3-319-66730-0_9
5. Gómez-Barrena E, García-Rey E, eds. The Infected Total Knee Arthroplasty, Sonication of removed implants in the infected total knee arthroplasty. 1st ed. Springer International Publishing AG; 2018. DOI: 10.1007/978-3-319-66730-0_14.
6. Trampuz A, Piper KE, Hanssen AD, et al. Sonication of explanted prosthetic components in bags for diagnosis of prosthetic joint infection is associated with risk of contamination. Journal of clinical microbiology. J Clin Microbiol 2006; 44(2):628-31. doi: 10.1128/JCM.44.2.628-631.2006..
7. Holinka J, Bauer L, Hirschl AM, Graninger W, Windhager R, Presterl E. Sonication cultures of explanted components as an add-on test to routinely conducted microbiological diagnostics improve pathogen detection. J Orthop Res 2011; 29(4):617-22. doi: 10.1002/jor.21286. Epub 2010 Dec 7.
8. Van Diek FM, Albers CG, Van Hooff ML, Meis JF, Goosen JH. Low sensitivity of implant sonication when screening for infection in revision surgery. Acta Orthop 2017; 88(3):294-299. doi: 10.1080/17453674.2017.1300021.
9. Tani S, Lepetsos P, Stylianakis A, Vlamis J, Birbas K, Kaklamanos I. Superiority of the sonication method against conventional periprosthetic tissue cultures for diagnosis of prosthetic joint infections. Eur J Orthop Surg Traumatol 2018; 28(1):51-57. doi: 10.1007/s00590-017-2012-y.
10. Park HJ, Kim HJ, Kim S, et al. Safety of temporary use of recycled autoclaved femoral components in infected total knee arthroplasty: confirming sterility using a sonication method. Clin Orthop Surg 2018; 10(4):427-432. doi: 10.4055/cios.2018.10.4.427.
11. Achermann Y, Vogt M, Leunig M, Wüst J, Trampuz A. Improved diagnosis of periprosthetic joint infection by multiplex PCR of sonication fluid from removed implants. J Clin Microbiol 2010; 48(4):1208-14. doi: 10.1128/JCM.00006-10.
12. Nelson CL, Jones RB, Wingert NC, Foltzer M, Bowen TR. Sonication of antibiotic spacers predicts failure during two-stage revision for prosthetic knee and hip infections. Clin Orthop Relat Res 2014; 472(7):2208-14. DOI: 10.1007/s11999-014-3571-4.
13. Karbysheva S, Grigoricheva L, Golnik V, Popov S, Renz N, Trampuz A. Influence of retrieved hip-and knee-prosthesis biomaterials on microbial detection by sonication. Eur Cell Mater 2019; 37:16-22. doi: 10.22203/eCM.v037a02.
14. Šuster K, Podgornik A, Cör A. Quick bacteriophage-mediated bioluminescence assay for detecting Staphylococcus spp. in sonicate fluid of orthopaedic artificial joints. New Microbiol 2017; 40(3):190-196.
15. Rodríguez-Merchán EC, Liddle AD, eds. The Infected Total Knee Arthroplasty, Microbiological concepts of the infected total knee arthroplasty. 1st ed. Springer International Publishing AG; 2018. DOI: 10.1007/978-3-319-66730-0_2
16. Putnis SE, Oussedik S, eds. The Infected Total Knee Arthroplasty, Preoperative Optimization to Prevent an Infected Total Knee Arthroplasty: Host Factors. 1st ed. Springer International Publishing AG; 2018. DOI: 10.1007/978-3-319-66730-0_3
17. Vaquero-Picado A, Rodríguez-Merchán EC, eds. The Infected Total Knee Arthroplasty, Antibiotic pophylaxis to prevent infection in total knee arthroplasty. Springer International Publishing AG, Cham, Switzerland, 2018, pp 36-46. DOI: 10.1007/978-3-319-66730-0_5.
18. Petis SM, Abdel MP, eds. The Infected Total Knee Arthroplasty, Clinical Diagnosis of the Infected Total Knee Arthroplasty. 1st ed. Springer International Publishing AG; 2018. DOI: 10.1007/978-3-319-66730-0_7
19. Ruiz-Pérez JS, Agüera-Gavaldá M, Rodríguez-Merchán EC, eds. The Infected Total Knee Arthroplasty, The Role of Knee Aspiration in the Infected Total Knee Arthroplasty. 1st ed. Springer International Publishing AG; 2018. DOI: 10.1007/978-3-319-66730-0_10
20. Subramanian P, Patel R, eds. The Infected Total Knee Arthroplasty, Histological Diagnosis in the Infected Total Knee Arthroplasty. 1st ed. Springer International Publishing AG; 2018. DOI: 10.1007/978-3-319-66730-0_12
21. Raymond AC, Oussedik S, eds. The Infected Total Knee Arthroplasty, Intraoperative Cultures for the Suspected Total Knee Arthroplasty Infection. 1st ed. Springer International Publishing AG; 2018. DOI: 10.1007/978-3-319-66730-0_13
22. Parvizi J, Gehrke T, Chen AF. Proceedings of the international consensus on periprosthetic joint infection. Bone Joint J 2013; 95-B(11):1450-2. doi: 10.1302/0301-620X.95B11.33135.
23. Mariconda M, Ascione T, Balato G, et al. Sonication of antibiotic-loaded cement spacers in a two-stage

revision protocol for infected joint arthroplasty. BMC Musculoskelet Disord 2013; 14:193. DOI: 10.1186/1471-2474-14-193.

24. Rak M, KavčIč M, Trebše R, CőR A. Detection of bacteria with molecular methods in prosthetic joint infection: sonication fluid better than periprosthetic tissue. Acta Orthop 2016; 87(4):339-45. doi: 10.3109/17453674.2016.1165558.