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Editorial

Microbiologial diagnosis of prosthetic joint infection: Is there a need for standardization?

Diagnóstico microbiológico de la infección de prótesis osteoarticulares: ¿Es necesaria una estandarización?

The number of joint prostheses that were implanted during 2019 in Spain was higher than 100,000, according to some non-official statistics. These prostheses have improved the quality of life of a similar number of patients and undoubtedly represent one of the most important procedures that have been performed in biomedicine during the last decades. However, this procedure is not exempt from complications, and infection is probably one of the most devastating ones. Between 1 and 3% of all the prostheses became infected (according to the commonly published data in the literature),[1] and the implications of these infections in morbidity, mortality and health-associated costs are enormous, because the increasingly high number of affected patients.

The diagnosis of prosthetic joint infection (PJI) is a complex issue that includes clinical, radiological, microbiological and analytical data. All these data are usually included in the consensus definitions of different scientific societies, including the most recent ones.[2–4] In all these definitions, the role of Clinical Microbiology is an essential one, being considered as a major criterion for such diagnosis in all cases.

Microbiological diagnosis is still based in the culture of different samples from the patients, using previously described criteria that allow us to differentiate between contaminations and true infections.[5] This diagnosis usually starts in the preoperative scenario, where the only available sample is usually the synovial fluid. Despite it is difficult to obtain in some cases (especially in hip joints), if available, it can give a lot of information that can be used for the diagnosis of PJI. From the microbiological point of view, this sample usually shows low sensibility and high specificity. Sensibility is usually lower in chronic infections, where microorganisms are usually attached to the implant and surrounding tissues inside the biofilm, and they cannot be detected in synovial fluid. In acute infections, where planktonic forms are more frequent, sensibility increases, being a useful tool for a preoperative diagnosis. Sensibility of synovial fluid culture can be improved by inoculating blood culture bottles from automated systems,[6] but in this case, careful interpretation of some isolates (like Coagulase-Negative *Staphylococcus* or *Cutibacterium acnes*) is mandatory, because these organisms can be a potential contamination, and they are also among the commonly found causes of chronic PJI.

The gold standard methodology for culture-based diagnosis is still the culture of several samples (usually 3–6) of periprosthetic tissue biopsies. Using different methods for homogenization of the samples, the use of Atkins criteria for interpretation of the results of these cultures is essential for the diagnosis of PJI,[7] and it appears as a major criterion in most of the currently available guidelines.[3–5] The original methodology that uses agar plates has been combined with inoculation in blood culture bottles[8,9] and with a prolonged incubation[10,11] aiming for an improvement in sensibility without losing specificity. With all these improvements, the usefulness of this methodology made it to be the key for the diagnosis of PJI.

Probably the last advance in culture-based diagnosis of PJI is the introduction of sonication of the removed prosthesis. The original article of Trampuz et al.,[12] was followed by many others that have shown the usefulness of this methodology, with sensibility values similar to that of other methods, maintaining good specificity.[1,13–15] This methodology has been used with many other implants, and it is not described as a substitute of currently available methods, but to complement them. Despite sonication showed no great increases in sensibility compared to the gold standard, its addition to the previously available cultures (synovial fluid, biopsies) increases the performance of clinical microbiology laboratories in the routine diagnosis of PJI.[16]

However, despite all these advances and available samples, there are still several infected patients without a positive culture. For these patients, molecular biology has been used as a complement of culture-based methods for the diagnosis. First studies used homemade PCR-based techniques, mainly using 16S rDNA sequencing. These studies showed good sensibility and specificity with different samples (especially synovial fluid and periprosthetic tissue samples),[14] but standardization has been a problem for the implementation of this approach, and only those laboratories with specific molecular biology facilities have used it.

The introduction of commercial syndromic tests (first designed for blood cultures) opened a potential approach that can be used with other samples. The first studies showed good performance of these modified commercial kits,[13] and a specific commercial kit

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was then developed. This test showed low sensibility, but high specificity in different validation studies,[17] and a recently published study also shown the clinical usefulness of this technique integrated in a full diagnostic system that includes both culture-based and molecular-based methods.[18]

In any case, despite the potential existence of many different methodologies that can be integrated in the clinical microbiology laboratory, the use of the different techniques is not homogeneous, and the differences between centers can be of importance. In this number, Falces-Romero and Rico-Nieto[19] report the results of a nationwide survey designed to know the methodology used for the diagnosis of PJI in Spain. According to this study, most laboratories receive several samples (at least 5 of them), mainly synovial fluid and periprosthetic tissue biopsies. Interestingly, sonication is only used by half of the laboratories, and the Gram stain remains as the preferred method for a rapid diagnosis (wile the study do not show the samples where it is used). Almost all laboratories used liquid and solid media, and most centers used an incubation period of around a week (a period that have shown good results in some studies[20]), with the possibility of prolonging this period in some cases with high suspicion of infection. Molecular diagnosis, the last available tool, is used in 40% of the centers (almost as high as sonication), using mainly homemade PCR-based techniques.

This study showed that most laboratories involved in the diagnosis of PJI use a combination of techniques and samples that can lead to good results in this process. However, there is still some heterogeneity in the use of the most recent methods (sonication, molecular methods), but probably in the future there will be a more homogeneous methodology. For this setting, the role of study groups like GEIO will be very important, because it depends on the clinical microbiologists, in a close relationship with the clinicians, to develop a common protocol for the diagnosis, and implementing the teaching of these methodologies to all laboratories in order to have the best possible diagnosis of these complex patients.

Ethical disclosures

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References

1. Tande AJ, Patel R. Prosthetic joint infection. Clin Microbiol Rev. 2014;27:302–45.
2. McNally M, Sousa R, Wouthuyzen-Bakker M, Chen AF, Soriano A, Vogely HC, et al. The EBJIS definition of periprosthetic joint infection. Bone Joint J. 2021;103-B:18–25.
3. Parvizi J, Tan TL, Goswami K, Higuera C, Della Valle C, Chen AF, et al. The 2018 definition of periprosthetic hip and knee infection: an evidence-based and validated criteria. J Arthroplasty. 2018;33:1309–14.e2.
4. Ariza J, Cobo J, Baraia-Etxaburu J, Benito N, Bori G, Cabo J, et al. Executive summary of management of prosthetic joint infections. Clinical practice guidelines by the Spanish Society of Infectious Diseases and Clinical Microbiology (SEIMC). Enferm Infecc Microbiol Clin. 2017;35:189–95.
5. Marin M, Esteban J, Meseguer MA, Sanchez-Somolinos M. Microbiological diagnosis of bone-joint infections. Enferm Infecc Microbiol Clin. 2010;28:534–40.
6. Font-Vizcarra L, García S, Martínez-Pastor JC, Sierra JM, Soriano A. Blood culture flasks for culturing synovial fluid in prosthetic joint infections. Clin Orthop Relat Res. 2010;468:2238–43.
7. Atkins BL, Athanasou N, Deeks JJ, Crook DW, Simpson H, Peto TE, et al. Prospective evaluation of criteria for microbiological diagnosis of prosthetic-joint infection at revision arthroplasty. The OSIRIS Collaborative Study Group. J Clin Microbiol. 1998;36:2932–9.
8. Peel TN, Dylla BL, Hughes JG, Lynch DT, Greenwood-Quaintance KE, Cheng AC, et al. Improved diagnosis of prosthetic joint infection by culturing periprosthetic tissue specimens in blood culture bottles. mBio. 2016;7:e01715–76.
9. Li C, Ojeda-Thies C, Trampuz A. Culture of periprosthetic tissue in blood culture bottles for diagnosing periprosthetic joint infection. BMC Musculoskelet Disord. 2019;20:299.
10. Schäfer P, Fink B, Sandow D, Margull A, Berger I, Frommelt L. Prolonged bacterial culture to identify late periprosthetic joint infection: a promising strategy. Clin Infect Dis. 2008;47:1403–9.
11. Drago L, De Vecchi E, Cappelletti L, Vassena C, Toscano M, Bortolin M, et al. Prolonging culture to 15 days improves bacterial detection in bone and joint infections. Eur J Clin Microbiol Infect Dis. 2015;34:1809–13.
12. Trampuz A, Piper KE, Jacobson MJ, Hanssen AD, Unni KK, Osmon DR, et al. Sonication of removed hip and knee prostheses for diagnosis of infection. N Engl J Med. 2007;357:654–63.
13. Zhai Z, Li H, Qin A, Liu G, Liu X, Wu C, et al. Meta-analysis of sonication fluid samples from prosthetic components for diagnosis of infection after total joint arthroplasty. J Clin Microbiol. 2014;52:1730–6.
14. Esteban J, Sorli L, Alentorn-Geli E, Puig L, Horcajada JP. Conventional and molecular diagnostic strategies for prosthetic joint infections. Expert Rev Mol Diagn. 2014;14:83–96.
15. Bellova P, Knop-Hammad V, Königshausen M, Mempel E, Frieler S, Gessmann J, et al. Sonication of retrieved implants improves sensitivity in the diagnosis of periprosthetic joint infection. BMC Musculoskelet Disord. 2019;20:623.
16. Prieto-Borja L, Aunon A, Blanco A, Fernandez-Roblas R, Gadea I, Garcia-Canete J, et al. Evaluation of the use of sonication of retrieved implants for the diagnosis of prosthetic joint infection in a routine setting. Eur J Clin Microbiol Infect Dis. 2018;37:715–22.
17. Esteban J, Gomez-Barrena E. An update about molecular biology techniques to detect orthopaedic implant-related infections. EFORT Open Rev. 2021;6:93–100.
18. Auñon Á, Coifman I, Blanco A, Garcia-Canete J, Parron-Cambero R, Esteban J. Usefulness of a multiplex PCR assay for the diagnosis of prosthetic joint infections in the routine setting – PubMed [Internet]. Available from: https://pubmed.ncbi.nlm.nih.gov/34978153/ [cited 4.1.22].
19. Falces-Romero I, Rico-Nieto A. Processing of osteoarticular samples for microbiological diagnosis: results of a national multi-center survey. Enferm Infecc Microbiol Clin (Engl Ed). 2022;40:317–21.
20. Esteban J, Alvarez-Alvarez B, Blanco A, Fernandez-Roblas R, Gadea I, Garcia-Canete J, et al. Prolonged incubation time does not increase sensitivity for the diagnosis of implant-related infection using samples prepared by sonication of the implants. Bone Joint J. 2013;95-B:1001–6.

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