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Diagnosis of Periprosthetic Joint infection: from Novel Synovial Fluid Biomarkers to Identification of the Etiological Agent

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Abstract

Periprosthetic Joint infection is probably the most devastating complication of joint replacement surgery. Its diagnosis remains a serious clinical challenge because of the low specificity of clinical signs and laboratorial tests. A single reference test for diagnosing this worrisome complication has been shifting investigators over the last years. Several synovial fluid biomarkers have already proven usefulness in diagnosing periprosthetic infection with high sensitivity and specificity. However, most are not available as point-of-care test kits and therefore are still far from routine use in daily clinical practice. Even when the gold-standard criteria defined by the Musculoskeletal Infection Society are fulfilled, the etiological agent of the infection needs to be identified in order to provide an effective treatment. In this review, we analyze the recent advances in diagnosing periprosthetic joint infection by using novel synovial fluid biomarkers and how to identify the causative agent of the infection

Introduction

Joint replacement surgery is a success story in orthopaedic surgery which brought clear clinical and economical benefits. As the prevalence of total joint arthroplasty continues to rise worldwide, the incidence of periprosthetic joint infection (PJI) is expected to increase [1]. Infection of the prosthesis is one of the most worrisome complications and has an overwhelming impact on patients and society. PJI is difficult to diagnose and treat as there remains no diagnostic 'gold-standard' method. A high index of suspicion is key due to the heterogeneous behaviour of the microorganisms involved and therefore the diverse clinical presentation [2]. Some of the patients submitted to an aseptic revision surgery might actually have PJI. Not every patient with a PJI meets the criteria of Musculoskeletal Infection Society (MSIS), which are the most used for diagnosing PJI and include 2 major and 5 minor criteria [3].

Suspicion of infection requires prompt assessment for serum inflammatory biomarkers and aspiration of the joint for laboratorial study of synovial fluid. According to the guidelines specified by the Infectious Diseases Society of America (IDSA), the erythrocyte sedimentation rate (ESR) and C-reactive protein (CRP) should be evaluated for all patients suspected as having PJI [4]. However, these tests lack specificity for infection as these biomarkers may indicate inflammation rather than infection and can be easily influenced by antibiotic therapy, trauma, and surgery [5]. Moreover, the ESR and CRP level may be normal in patients with PJI caused by slow-growing organisms such as Propionibacterium acnes [6,7]. In fact, the document introducing the MSIS criteria for PJI states that the levels of some of these markers may be normal in the presence of PJI caused by slow-growing organisms that do not elicit inflammatory reaction and cautions clinicians in interpreting the laboratorial results of serological markers in these specific situations [3]. According to recent studies, procalcitonin (PCT) is the most specific serum biomarker of PJI with a specificity of 0.92 [8].

Joint aspiration is conventionally performed in patients with suspected PJI. Numerous reports have claimed that the detection and measurement of synovial fluid markers represents a convenient reliable option for the diagnosis of PJI. The existing literature includes a broad consensus that these synovial fluid markers are superior to the more commonly performed serum tests [9]. The importance of joint synovial fluid analysis has evolved substantially over several decades. The most recent evidence has shown that synovial fluid biomarkers are more accurate in the diagnosis of peri-prosthetic joint infection than serum biomarkers. The search for a single standard reference test for determining PJI through analysis of synovial fluid has yielded numerous biomarkers as potential candidates.

The most commonly used synovial fluid tests have been the white cell count (WCC), the polymorphonuclear (PMN) leukocytes differential count, the CRP, the alpha-defensin, and

the leukocyte esterase [10]. Synovial fluid leukocyte count is considered to be the most sensitive preoperative test. There is a paucity of data regarding the threshold of synovial fluid WCC and PMN% percentage of the WBC count for the diagnosis of chronic PJI after total hip arthroplasty. Aspiration techniques and differences in laboratory analysis may affect the synovial fluid WCC. A bloody aspiration with increased synovial fluid red blood-cell count may lead to a higher measured value of the WCC, as there is a significant correlation between increased red blood-cell count and WCC count. Ghanem et al. hypothesized that systemic blood cells and neutrophils are introduced into the joint when syringe needle penetrates vascularized tissues [11].

The overall threshold for absolute PMN count has already shown better operating characteristics than the thresholds for synovial fluid PMN% alone, with an accuracy of 91.8%. The absolute PMN count may be a better measure than the isolated synovial fluid WCC and PMN% but no clear-cut threshold for the diagnosis of PJI has been established [12]. The most frequently studied synovial fluid markers for the diagnosis of PJI are C-reactive protein, leukocyte esterase, interleukin-6, interleukin-1b, alpha-defensin and interleukin-17, all of which have high diagnostic utility [13].

Leukocyte esterase

Leukocyte esterase (LE) is an enzyme that is present in granulocytes and secreted by neutrophils when activated during a bacterial infection. By measuring LE in synovial fluid by lysis of neutrophils and quantifying esterase activity, an estimation of the synovial fluid WCC can be obtained. When LE is considered positive, the test yields a sensitivity of 80% and specificity of 100% [14-16] . The test is easy to perform and provides a final result within minutes, which may represent a valuable tool for the surgical team to decide the best procedure during an arthroplasty surgery [17].

All the studies illustrate the high sensitivity and specificity of LE for the diagnosis of PJI. Considering the low cost and accuracy of the LE test, it probably should combined with other minor criteria for diagnosing PJI, especially for exclusion of PJI in patients who do not meet any of the MSIS major criteria for PJI.

Alpha-defensin

Alpha-defensin is a biomarker that has been shown to have a very high accuracy to rule out periprosthetic joint infection. The alpha-defensin immunoassay has promising results, with sensitivity and specificity above 96% [18]. Alpha-defensin is an antimicrobial peptide released by neutrophils, macrophages, T-lymphocytes, and some epithelial cells in response to pathogens. It has been demonstrated that several pathogens trigger a consistent release of alpha-defensin into the synovial fluid [19-21]. An immunoassay of aspirated joint fluid for alpha-defensin molecules has high sensitivity and specificity for diagnosing periprosthetic infection [19,22]. The predictive negative value of the alpha-defensin assay for diagnosing periprosthetic infection is very high if the alpha-defensin test is negative, it's likely that the pain after total hip arthroplasty (THA) or total knee arthroplasty (TKA) is not caused by PJI [23].

If the test result is positive, then the likelihood of infection is high, but other reasons for positive test results (for example, metallosis), should be considered. The test is rarely associated with false-negative values, and most false-positives appear to be associated with metallosis [22]. When tested individually, the ESR, CRP and synovial fluid cell count do not perform as well as the alpha-defensin assay [24]. Modification of the test to a point-of-care kit that uses joint fluid aspirated during a revision arthroplasty transformed this test into a valuable tool in patients with equivocal pre-operative evaluations. This rapid lateral flow version of the alpha-defensin test was developed for daily clinical practice and was already introduced as a medical device in Europe to detect high levels of alpha-defensin in synovial fluid with ease. A recent study involving a case-series of 223 patients and the novel test kit of alpha-defensin showed an overall sensitivity of 92.1% and a specificity of 100%. No false-positive values have been observed, reflecting a positive predictive value of 100% [25]. This test provides better results compared with classic serum and synovial fluid analyses like the ESR and serum CRP, which have reported sensitivity and specificity ranging from 58% to 83%.

In a recently published meta-analysis, the pooled diagnostic sensitivity and specificity of alpha-defensin were largely better than those of the leukocyte esterase test [10]. Another meta-analysis compared the pooled accuracy of alpha-defensin and PCT; again, alpha-defensin also was superior in both sensitivity and specificity [26]. Until now, this method seems to be the most accurate test for the diagnosis of periprosthetic joint infection when compared with other previously used serum and synovial fluid analyses [23].

IL-6

IL-6 is a 212-amino acid interleukin encoded by a single gene mapped to chromosome 7 in humans [27]. IL-6 is produced by lymphoid and non-lymphoid cells, and participates in the inflammatory response. Serum IL-6 levels increase in diverse clinical conditions as trauma, infection and surgery. In patients with aseptic prosthetic loosening, IL-6 levels decrease to the normal level within 48h after arthroplasty. However, following infection, IL-6 activates the release of CRP.

In a recent study, the pooled sensitivity and specificity for PJI diagnosis using synovial fuid IL-6 were 0.91 (95% CI: 0.82–0.96) and 0.90 (95% CI: 0.84–0.95), respectively [28]. The positive likelihood ratio (PLR) and negative likelihood ratio (NLR) of synovial fluid IL-6 for PJI diagnosis were 9.5 (95% CI: 5.3–17.2) and 0.09 (95% CI: 0.04–0.21), respectively. This study also showed that the diagnostic accuracy of synovial fluid IL-6 was not affected by the presence of inflammatory diseases, making this test very specific for detection of PJI in daily practice.

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Other biomarkers

There are other synovial fluid tests that demonstrate good diagnostic performance and can also be used in combination for the diagnosis of PJI such as: IL-8, IL-10, vascular endothelial growth factor (VEGF) and granulocyte-colony stimulating factor (G-CSF). Recently, several studies have shown a role of the long pentraxin-related protein PTX3 as a biomarker in patients undergoing revision surgery for painful THA or TKA. IL-17, IL-1b, and IL-6 are measured by means of bead-based multiplex immunoassays, which require less time than standard ELISA takes but are not point-of-care options yet. Synovial IL-17 combined with synovial alpha-dephensin showed to be a powerful tool for diagnosing PJI [13].

Agent identification

Despite the potential to increase the diagnostic accuracy of PJI with these novel synovial biomarkers, traditional culture techniques to identify the etiological micro-organism and to determine antimicrobial sensitivities are still required to guide appropriate treatment. Periprosthetic tissue culture, which has a positive detection rate of 0.70 – 0.90, is still regarded by many as the gold standard test for PJI diagnosis [4]. Synovial fluid culture has a sensitivity and specificity of 0.72 and 0.95, respectively [29]. However, In up to 50% of PJI cases, cultures fail to isolate the infecting organism [30]. Negative cultures have been associated with a 4.5 times increased risk of reinfection in comparison with culture-positive cases [31,32]. Multiplex polymerase chain reaction (mPCR) revealed that the molecular techniques for isolation of the infecting organism was thought to be useful. However, this technique demonstrated a false-positive rate of 88% it didn't outperform culture, with a sensitivity of 81% [33].

Next-generation Sequencing

Next-generation sequencing (NGS) can performed the sequencing of all DNA present in a given sample, making this tool a useful adjunct in identificating the causative organism(s) in culture-negative periprosthetic joint infection [34]. Moreover, some cases of monomicrobial PJI may have additional organisms that escape detection when culture is used. NGS was found to be capable of identifying an organism in almost 90% of patients with PJI (as determined by the MSIS criteria) compared with culture with a sensitivity of 60.7%. More importantly, NGS was able to detect a pathogen in 81.8% of culture-negative cases [35]. Many infections associated with implants are known to exist as a biofilm [36], which sometimes difficults the isolation of the infecting organism using traditional culture methods. Interestingly, NGS also detected an organism in many revision surgeries considered to be aseptic [35].

Earlier studies have shown bacteria to be present in presumed aseptic revisions in up to 77% of cases. Some of these may be subclinical infections [37]. In many of these cases, P. acnes is the predominant organism. Propionibacterium is known to cause PJI, particularly in the shoulder, and typically follows an indolent clinical course. Several molecular diagnostics methods have been suggested to overcome the difficulties associated with diagnosing biofilm-associated infections. The main issue with these methods relates to the uncertainties of whether identified organisms are resident in the joint, contaminants, or true pathogens.

Sonication of Arthroplasty Implants

Implant sonicate culture enhances the diagnostic assessment for PJI by identifying pathogens that are inaccessible to traditional intraoperative tissue and synovial fluid cultures. By amplifying the sampling of microbiologic cellular material, sonication improves the sensitivity of cultures such as alternative methods such as mPCR or other molecular-based diagnostic methods while also providing antibiotic sensitivity testing [38]. The sensitivity of implant sonication was shown to be greater than tissue culture and synovial fluid culture, whereas there was no difference in specificity. In fact, in that study, 15% of aseptic revisions had positive implant sonicate cultures.

In PJI where bacteria form protective biofilms, they become more resistant to antibiotics and difficult to detect with conventional tissue cultures [39]. Implant sonication may be useful in patients with presumed aseptic revisions where there is a low pretest suspicion for the presence of a microorganism. Sonication with subsequent mPCR of the cultured fluid has been shown to have improved accuracy in identifying microorganisms of presumed aseptic loosening with negative tissue culture [39]. In 2013, the International Consensus Meeting on Periprosthetic Joint Infection advocated against the routine sonication of explanted prosthesis. The group concluded that it should be used in cases of suspected or proven PJI in which preoperative aspirates have failed to reveal any pathogens and in cases where antibiotics have been administered within 2 weeks from revision surgery [40].

Conclusion

Perhaps the most challenging aspect of managing periprosthetic joint infection is reaching a definitive diagnosis with identification of the causative agent. PJI is difficult to diagnose before revision surgery in the absence of uniform and well standardized criteria. Currently, an absolute test for the diagnosis of PJI does not exist, compelling clinicians to rely on a combination of synovial fluid tests and serological markers. No clear consensus has been reached on which synovial fluid markers are of greatest diagnostic utility in patients with suspected PJI. All markers cited have shown to be statistically equivalent and can be used alternatively to aid in the diagnosis of PJI. LE and alpha-defensin are considered the most promising synovial fluid biomarkers for diagnosing PJI. Both reportedly had high diagnostic accuracy and alpha-defensin has greater specificity for diagnosing PJI. Particularly, the alpha-defensin assay in combination with synovial fluid CRP level is a good test to diagnose or rule out a PJI. Leukocyte esterase and alpha-defensin are currently available as a point-of-care test and have diagnostic utility in daily practice.

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Any given test is intended to be used as an adjunct to diagnostic criteria currently recommended by the MSIS, and its results should be interpreted in context with the global clinical picture of each patient. Infection must always be ruled out in revision arthroplasthy surgery because of the unexpectedly high rate of positive cultures in the absence of MSIS consensus criteria to diagnose PJI. Further investigation is required to determine the clinical implications of isolated organisms in samples from patients who undergo aseptic arthroplasty revision surgery. Future research will probably also focus on seeking a preoperative test that does not require aspirated joint fluid.

References

1. Kurtz SM, Lau E, Watson H, Schmier JK, Parvizi J (2012) Economic burden of periprosthetic joint infection in the United States. J Arthroplasty 27(8 suppl): 61-65.
2. Parvizi J, Fassihi SC, Enayatollahi MA (2016) Diagnosis of periprosthetic joint infection following hip and knee arthroplasty. Orthop Clin North Am 47(3): 505-515.
3. Parvizi J, Zmistowski B, Berbari EF, Bauer TW, Springer BD, et al. (2011) New definition for periprosthetic joint infection: from the Workgroup of the Musculoskeletal Infection Society. Clin Orthop Relat Res 469(11): 2992-2994.
4. Osmon DR, Berbari EF, Berendt AR, Lew D, Zimmerli W, et al. (2013) Diagnosis and management of prosthetic joint infection: clinical practice guidelines by the Infectious Diseases Society of America. Clin Infect Dis 56(1): 25.
5. Hausfater P (2014) Biomarkers and infection in the emergency unit. Med Mal Infect 44(4): 139-145.
6. Piper KE, Fernandez Sampedro M, Steckelberg KE, Mandrekar JN, Karau MJ, et al. (2010) C-reactive protein, erythrocyte sedimentation rate and orthopedic implant infection. PLoS One 5(2): 9358.
7. Kanafani ZA, Sexton DJ, Pien BC, Varkey J, Basmania C, et al. (2009) Postoperative joint infections due to Propionibacterium species: a case-control study. Clin Infect Dis 49(7):1083-1085.
8. Xie K, Qu X, Yan M (2016) Procalcitonin and alpha-Defensin for Diagnosis of Periprosthetic Joint Infections. J Arthroplasty 32(4): 1387-1394.
9. Konigsberg BS, Hartman CW, Hewlett AL, Garvin KL (2014) Current and future trends in the diagnosis of periprosthetic hip infection. Orthop Clin North Am 45(3): 287-293.
10. Wyatt MC, Beswick AD, Kunutsor SK, Wilson MJ, Whitehouse MR, et al. (2016) The Alpha-Defensin Immunoassay and Leukocyte Esterase Colorimetric Strip Test for the Diagnosis of Periprosthetic Infection: A Systematic Review and Meta-Analysis. J Bone Joint Surg Am 98(12): 992-1000.
11. Ghanem E, Houssock C, Pulido L, Han S, Jaberi FM, et al. (2008) Determining true leukocytosis in bloody joint aspiration. J Arthroplasty 23(2): 182-187.
12. Higuera CA, Zmistowski B, Malcom T, Barsoum WK, Sporer SM, et al. (2017) Synovial Fluid Cell Count for Diagnosis of Chronic Periprosthetic Hip Infection. J Bone Joint Surg Am 99(9): 753-759.
13. Saleh A, Ramanathan D, Siqueira MBP, Klika AK, Barsoum WK, et al. (2017) The Diagnostic Utility of Synovial Fluid Markers in Periprosthetic Joint Infection: A Systematic Review and Meta-analysis. J Am Acad Orthop Surg 25(11): 763-772.
14. Parvizi J, Jacovides C, Antoci V, Ghanem E (2011) Diagnosis of periprosthetic joint infection: The utility of a simple yet unappreciated enzyme. J Bone Joint Surg Am 93(24): 2242-2248.
15. Matsen Ko L, Parvizi J (2016) Diagnosis of periprosthetic infection: Novel developments. Orthop Clin North Am 47(1): 1-9.
16. Parvizi J, Alijanipour P, Barberi EF, Hickok NJ, Phillips KS, et al. (2015) Novel developments in the prevention, diagnosis, and treatment of periprosthetic joint infections. J Am Acad Orthop Surg 23(suppl): S32-S43.
17. Wang C, Li R, Wang Q, Wang C (2017) Synovial Fluid Leukocyte Esterase in the Diagnosis of Peri-Prosthetic Joint Infection: A Systematic Review and Meta-Analysis. Surg Infect (Larchmt).
18. Deirmengian C, Kardos K, Kilmartin P, Cameron A, Schiller K, et al. (2015) The alpha-defensin test for periprosthetic joint infection outperforms the leukocyte esterase test strip. Clin Orthop Relat Res 473(1): 198-203.
19. Deirmengian C, Kardos K, Kilmartin P, Gulati S, Citrano P, et al. (2015) The alpha-defensin test for periprosthetic joint infection responds to a wide spectrum of organisms. Clin Orthop Relat Res 473(7): 2229-2235.
20. Ganz T, Selsted ME, Szklarek D, Harwig SS, Daher K, et al. (1985) Defensins: natural peptide antibiotics of human neutrophils. J Clin Invest 76(4): 1427-1435.
21. Chalifour A, Jeannin P, Gauchat JF, Blaecke A, Malissard M, et al. (2004) Direct bacterial protein PAMP recognition by human NK cells involves TLRs and triggers alpha-defensin production. Blood 104(6): 1778-1783.
22. Deirmengian C, Kardos K, Kilmartin P, Cameron A, Schiller K, et al. (2014) Combined measurement of synovial fluid alpha-Defensin and C-reactive protein levels: Highly accurate for diagnosing periprosthetic joint infection. J Bone Joint Surg Am 96(17): 1439-1445.
23. Bonanzinga T, Zahar A, Dütsch M, Lausmann C, Kendoff D, et al. (2017) How Reliable Is the Alpha-defensin Immunoassay Test for Diagnosing Periprosthetic Joint Infection? A Prospective Study. Clin Orthop Relat Res 475(2): 408-415.
24. Berbari E, Mabry T, Tsaras G, Spangehl M, Erwin PJ, et al. (2010) Inflammatory blood laboratory levels as markers of prosthetic joint infection: A systematic review and meta-analysis. J Bone Joint Surg Am 92(11): 2102-2109.
25. Gehrke T, Lausmann C, Citak M, Bonanzinga T, Frommelt L, et al. (2018) The Accuracy of the Alpha Defensin Lateral Flow Device for Diagnosis of Periprosthetic Joint Infection. J Bone Joint Surg Am 100(1): 42-48.
26. Xie K, Qu X, Yan M (2017) Procalciton in and a-defensin for diagnosis of peri-prosthetic joint infections. J Arthroplasty 32(4): 1387-1394.
27. Ferguson Smith AC, Chen YF, Newman MS, May LT, Sehgal PB, et al. (1988) Regional localization of the interferon-beta 2/B-cell stimulatory factor 2/hepatocyte stimulating factor gene to human chromosome. Genomics 2(3): 203-208.
28. Kai Xie, Kerong Dai, Xinhua Qu, Mengning Yan (2017) Serum and Synovial Fluid Interleukin-6 for the Diagnosis of Periprosthetic Joint Infection. Sci Rep 7(1): 1496.
29. Qu X, Zhai Z, Wu C, Jin F, Li H, et al. (2013) Preoperative aspiration culture for preoperative diagnosis of infection in total hip or knee arthroplasty. J Clin Microbiol 51(11): 3830-3834.
30. Shanmugasundaram S, Ricciardi BF, Briggs TWR, Sussmann PS, Bostrom MP. (2014) Evaluation and management of periprosthetic joint infection: an international, multicenter study. HSS J 10(1): 36-44.
31. Parvizi J, Erkocak OF, Della Valle CJ. (2014) Culture-negative periprosthetic joint infection. J Bone Joint Surg Am 96(5): 430-436.

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32. Mortazavi SMJ, Vegari D, Ho A, Zmistowski B, Parvizi J (2011) Two-stage exchange arthroplasty for infected total knee arthroplasty: predictors of failure. Clin Orthop Relat Res 469(11): 3049-54.

33. Melendez DP, Uhl JR, Greenwood-Quaintance KE, Hanssen AD, Sampath R, et al. (2014) Detection of prosthetic joint infection by use of PCR-electrospray ionization mass spectrometry applied to synovial fluid. J Clin Microbiol 52(6): 2202-2205.

34. Whitley R (2008) The new age of molecular diagnostics for microbial agents. N Engl J Med 358(10): 988-999.

35. Tarabichi M, Shohat N, Goswami K, Alvand A, Silibovsky R, et al. (2018) Diagnosis of Periprosthetic Joint Infection: The Potential of Next-Generation Sequencing. J Bone Joint Surg Am 100(2): 147-154.

36. Costerton JW (2005) Biofilm theory can guide the treatment of device-related orthopaedic infections. Clin Orthop Relat Res 437: 7-11.

37. Nelson CL, McLaren AC, McLaren SG, Johnson JW, Smeltzer MS. (2005) Is aseptic loosening truly aseptic? Clin Orthop Relat Res 437: 25-30.

38. Rothenberg AC, Wilson AE, Hayes JP, O'Malley MJ, Klatt BA (2017) Sonication of Arthroplasty Implants Improves Accuracy of Periprosthetic Joint Infection Cultures. Clin Orthop Relat Res 475(7): 1827-1836.

39. Tani S, Lepetsos P, Stylianakis A, Vlamis J, Birbas K, et al. (2018) Superiority of the sonication method against conventional periprosthetic tissue cultures for diagnosis of prosthetic joint infections. Eur J Orthop Surg Traumatol 28(1): 51-57.

40. Parvizi J, Gehrke T, Chen AF (2013) Proceedings of the International Consensus on Periprosthetic Joint Infection. Bone Joint J 95(B-11): 1450-1452.

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