The Journal of Arthroplasty Vol. 26 No. 8 2011

Brief Communication

New Definition for Periprosthetic Joint Infection

The Workgroup Convened by the Musculoskeletal Infection Society*

Abstract: Diagnosis of periprosthetic joint infection (PJI) remains a real challenge to the orthopedic community. Currently, there is no single standard definition for PJI. This communication presents the diagnostic criteria that have been proposed by a workgroup convened by the Musculoskeletal Infection Society. The diagnostic criteria were developed after the evaluation of available evidence. The role of every diagnostic test was examined, and the literature was reviewed in detail to determine the threshold for each test. It is hoped that the proposed definition for PJI will be adopted universally, bringing standardization into a field that has suffered extensive variability and heterogeneity. **Keywords:** diagnosis, periprosthetic, joint, infection.

Many believe that periprosthetic joint infection (PJI) is now the most challenging and frequent complication occurring after lower extremity total joint arthroplasty [1,2]. The challenges that the medical community faces with regard to this serious complication are on many fronts, one of which is the difficulty in reaching a timely diagnosis of PJI [3]. One factor that contributes to delay and inconsistent diagnosis of PJI is the lack of a standard definition for PJI. This lack of a standard definition has also made it difficult to compare the body of published evidence.

In view of these concerns, the Musculoskeletal Infection Society convened a workgroup to evaluate the available evidence and to propose a definition for PJI. The intention of the workgroup was to propose, to the best of our ability, a definition for PJI that can be universally adopted by physicians, surveillance authorities (including the Centers for Disease Control and Prevention), medical and surgical journals, the medicolegal community, and all involved in the management of PJI. It was hoped that this definition could be used as the "gold standard" against which new diagnostic tests for infection could be measured, although it is recognized that as new tests become available, this definition, too, may need to evolve.

A summary of the recommendations of those in attendance at a premeeting workshop of the 21st annual Musculoskeletal Infection Society held on August 4, 2011, pertaining to the definition of PJI was published in the November issue of *Clinical Orthopedics and Related Research* [4] and is also outlined below.

Definition of PJI

Based on the proposed criteria, a definite 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 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,

*Javad Parvizi, MD, FRCS, Benjamin Zmistowski, BS, Elie F. Berbari, MD, Thomas W. Bauer, MD, Bryan D. Springer, MD, Craig J. Della Valle, MD, Kevin L. Garvin, MD, Montri D. Wongworawat, MD, Charalampos G. Zalavras, MD, Thomas K. Fehring, MD, Douglas R. Osmon, MD, Michael A. Mont, MD, Robert L. Barrack, MD, Keith R. Berend, MD, John L. Esterhai, MD, Terence J. Gioe, MD, Steven M. Kurtz, PhD, Bassam A. Masri, MD, Arvind D. Nana, MD, Mark J. Spangehl, MD, and John Segreti, MD.
Submitted September 26, 2011; accepted September 27, 2011.
The Conflict of Interest statement associated with this article can be found at doi:10.1016/j.arth.2011.09.026.
Parts of this article have been reprinted from Clin Orthop Relat Res, vol 469, 2011, p. 2992, New definition for periprosthetic joint infection: from the workgroup of the Musculoskeletal Infection by Parvizi J, Zmistowski B, Berbar, EF, et al, © The Association of Bone and Joint Surgeons 2011, with kind permission of Springer Science and Business Media.
Reprint requests: Javad Parvizi, MD, FRCS, 925 Chestnut Street 5th Floors, Philadelphia, PA 19107.

0883-5403/2608-0002$36.00/0
doi:10.1016/j.arth.2011.09.026

(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.

Please note that a PJI may be present if less than 4 of these criteria are met.

The panel also acknowledged that in certain low-grade infections (eg, *Propionibacterium acnes*), several of these criteria may not be routinely met despite the presence of PJI.

Considerations

Microbiologic Testing

It is imperative that tissue for culture be obtained from representative periprosthetic tissue or fluid. To limit the risk of contamination, each sample should be taken with separate, sterile instruments. The definition of phenotypically identical organisms should be based on phenotypic similarities and in vitro antimicrobial susceptibility testing because confirmation of genetic identity is not routinely performed on clinical isolates. It is recommended that at least 3 and no more than 5 periprosthetic specimen culture samples be taken and incubated in an aerobic and anaerobic environment. Fungal and mycobacterial cultures should not be done routinely but, rather, reserved for higher risk scenarios. The time of culture incubation has not been standardized yet. Isolation of a single low-virulent pathogen such as coagulase-negative *Staphylococcus*, *P acnes*, or *Corynebacteria* in the absence of other criteria is not felt to necessarily represent a definite infection. Isolation of a single virulent organism such as *Staphylococcus aureus* may represent a PJI. Furthermore, recent evidence has identified that certain tests, such as Gram stain of periprosthetic tissue or fluid, are not sensitive for diagnosing PJI [5].

Serum Tests

Based on previous publications, an erythrocyte sedimentation rate of greater than 30 mm/h and a CRP greater than 10 mg/L would represent elevated levels [6,7]. However, it is important to note that there are variations in measuring these markers between laboratories. Furthermore, the level of these serum markers is affected by age, sex, and medical comorbidities of the patient. It has also been reported that these markers can be elevated for approximately 30 to 60 days in the immediate postoperative period [8,9].

Synovial Tests

Multiple studies have provided thresholds for synovial white blood cell count and percent PMN in the differential (PMN%). In the chronically infected knee arthroplasty, these values have been reported from 1100 to 4000 cells/μL and 64% to 69%, respectively [10-12]. In patients with acute periprosthetic knee infections (<3 months from index surgery or from the onset of symptoms), the level of synovial cell count and PMN% are much higher (approximately 20 000 cells/μL and 89%, respectively) [13]. The level of synovial fluid cell count and PMN% in the infected hip arthroplasty have not been well delineated. A sole study has provided a threshold of 3000 cells/μL for leukocytes and 80% for PMN% for the infected hip arthroplasty [7]. None of these studies have included patients with underlying inflammatory arthropathies and related diseases. Research is currently proceeding to provide more definitive thresholds for all patients.

Histology

Examination of periprosthetic tissues for evidence of neutrophils has been traditionally conducted by specially trained musculoskeletal pathologists. Histologic examination, consequently, may be operator dependent. It is, therefore, incumbent on the surgeon to ensure that their pathologist is in agreement with the diagnostic criteria for periprosthetic infection. When examining for the presence of neutrophils, the histopathologist should disregard neutrophils entrapped in superficial fibrin or adherent to the endothelium or small veins. Also, caution should be exercised in quantifying neutrophils in patients where elevated neutrophils might be expected, such as a recent periprosthetic fractures or an inflammatory arthropathy.

Future Developments

This proposed definition was based on evidence supporting the role of various tests in the diagnosis of PJI that are available in the literature. There are numerous other tests for the diagnosis of PJI under evaluation, which include the measurement of CRP from the synovial fluid [14], synovial leukocyte esterase [15], sonication of explanted prosthetics [16], and molecular techniques such as polymerase chain reaction [17] and other molecular markers including interleukin-6 [18-20].

Acknowledgments

We would like to thank Sandra Berrios-Torres, MD; Ryan Fagan, MD, MPH; and Teresa C. Horan from the Centers for Disease Control and Prevention for their valuable input and assistance in the process of reaching these criteria.

Appendix

The writing committee's affiliations are as follows: Department of Orthopaedics, The Rothman Institute at Thomas Jefferson University Hospital, Philadelphia, Pennsylvania *(J.P.)*; Department of Orthopaedics, The Rothman Institute at Thomas Jefferson University Hospital, Philadelphia, Pennsylvania *(B.Z.)*; Department of Infectious Diseases, Mayo Clinic, Rochester,

Minnesota *(E.F.B.)*; Department of Pathology Cleveland Clinic, Ohio *(T.W.B.)*; Ortho Carolina, Charlotte, North Carolina *(B.D.S.)*; Rush Presbyterian Hospital, Chicago, Illinois *(C.J.D.)*; Department of Orthopaedics, University of Nebraska, Lincoln, Nebraska *(K.L.G.)*; Department of Orthopaedics, Loma Linda University, Loma Linda, California *(M.D.W.)*; Department of Orthopaedics, University of Southern California, Los Angeles, California *(C.G.Z.)*; Ortho Carolina, Charlotte, North Carolina *(T.K.F.)*; Department of Infectious Disease, Mayo Clinic, Rochester, Minnesota *(D.R.O.)*; Rubin Institute, Baltimore, Maryland *(M.A.M.)*; Department of Orthopaedics, Washington University, St Luis, Missouri *(R.L.B.)*; Joint Implant Surgeons, New Albany, Ohio *(K.R.B.)*; Department of Orthopaedics, University of Pennsylvania, Philadelphia, Pennsylvania *(J.L.E.)*; Department of Orthopaedics, Minneapolis VAMC, Minneapolis, Minnesota *(T.J.G.)*; Exponent, University of Drexel, Philadelphia, Pennsylvania *(S.M.K.)*; Department of Orthopaedics, University of Vancouver, Vancouver, Canada *(B.A.M.)*; Health Sciences Center, Fort Worth, Texas *(A.D.N.)*; Department of Orthopaedics, Mayo Clinic, Scottsdale, Arizona *(M.J.S.)*; and Infectious Disease, Rush University Medical Center, Chicago, Illinois *(J.S.)*.

References

1. Bozic KJ, Kurtz SM, Lau E, et al. The epidemiology of revision total knee arthroplasty in the United States. Clin Orthop Relat Res 2010;468:45.
2. Kurtz SM, Ong KL, Lau E, et al. Prosthetic joint infection risk after TKA in the Medicare population. Clin Orthop Relat Res 2010;468:52.
3. Bauer TW, Parvizi J, Kobayashi N, et al. Diagnosis of periprosthetic infection. J Bone Joint Surg Am 2006;88: 869.
4. Parvizi J, Zmistowski B, Berbar EF, et al. New definition for periprosthetic joint infection: from the workgroup of the Musculoskeletal Infection Society. Clin Orthop Relat Res 2011;469:2992.
5. Ghanem E, Ketonis C, Restrepo C, et al. Periprosthetic infection: where do we stand with regard to gram stain? Acta Orthop 2009;80:37.
6. Parvizi J, Ghanem E, Menashe S, et al. Periprosthetic infection: what are the diagnostic challenges? J Bone Joint Surg Am 2006;88(Suppl 4):138.
7. Schinsky MF, Della Valle CJ, Sporer SM, et al. Perioperative testing for joint infection in patients undergoing revision total hip arthroplasty. J Bone Joint Surg Am 2008; 90:1869.
8. Bilgen O, Atici T, Durak K, et al. C-reactive protein values and erythrocyte sedimentation rates after total hip and total knee arthroplasty. J Int Med Res 2001;29:7.
9. Larsson S, Thelander U, Friberg S. C-reactive protein (CRP) levels after elective orthopedic surgery. Clin Orthop Relat Res 1992;237.
10. Ghanem E, Parvizi J, Burnett RSJ, et al. Cell count and differential of aspirated fluid in the diagnosis of infection at the site of total knee arthroplasty. J Bone Joint Surg Am 2008;90:1637.
11. Trampuz A, Hanssen AD, Osmon DR, et al. Synovial fluid leukocyte count and differential for the diagnosis of prosthetic knee infection. Am J Med 2004;117:556.
12. Della Valle CJ, Sporer SM, Jacobs JJ, et al. Preoperative testing for sepsis before revision total knee arthroplasty. J Arthroplasty 2007;22(6 Suppl 2):90.
13. Bedair H, Ting N, Jacovides C, et al. The Mark Coventry Award: diagnosis of early postoperative TKA infection using synovial fluid analysis. Clin Orthop Relat Res 2011; 469:34.
14. Parvizi J, Jacovides C, Adeli B, et al. Coventry Award: synovial C-reactive protein: a prospective evaluation of a molecular marker for periprosthetic knee joint infection. Clin Orthop Relat Res 2011. Available at: http://www.ncbi.nlm.nih.gov/pubmed/21786056.
15. Parvizi J, Jacovides C, Antoci V, Jr., et al. Diagnosis of periprosthetic joint infection: the role of a simple, yet unrecognized enzyme. J Bone Joint Surg Am 2011;90.
16. 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.
17. Mariani BD, Martin DS, Levine MJ, et al. The Coventry Award. Polymerase chain reaction detection of bacterial infection in total knee arthroplasty. Clin Orthop Relat Res 1996;11.
18. Berbari E, Mabry T, Tsaras G, et al. Inflammatory blood laboratory levels as markers of prosthetic joint infection: a systematic review and meta-analysis. J Bone Joint Surg Am 2010;92:2102.
19. Di Cesare PE, Chang E, Preston CF, et al. Serum interleukin-6 as a marker of periprosthetic infection following total hip and knee arthroplasty. J Bone Joint Surg Am 2005;87:1921.
20. Deirmengian C, Hallab N, Tarabishy A, et al. Synovial fluid biomarkers for periprosthetic infection. Clin Orthop Relat Res 2010;468:2017.