The Journal of Arthroplasty 30 (2015) 1403–1406

Contents lists available at ScienceDirect

The Journal of Arthroplasty

journal homepage: www.arthroplastyjournal.org

Intraoperative Purulence Is Not Reliable for Diagnosing Periprosthetic Joint Infection

Pouya Alijanipour, MD [a], Bahar Adeli, BA [b], Erik N. Hansen, MD [c], Antonia F. Chen, MD/MBA [a], Javad Parvizi, MD/FRCS [a]

[a] Rothman Institute of Orthopaedics at Thomas Jefferson University Hospital, Philadelphia Pennsylvania
[b] St. George's University School of Medicine, Apt 1R, Philadelphia, Pennsylvania
[c] UCSF Department of Orthopaedic Surgery, Division of Adult Reconstructive Surgery, San Francisco, California

ARTICLE INFO

Article history:
Received 29 January 2015
Accepted 10 March 2015

Keywords:
purulence
periprosthetic joint infection
revision arthroplasty
synovial fluid
white blood cell count
culture

ABSTRACT

Purulence, defined as presence of pus, is based on subjective interpretation yet has been considered a definite sign of periprosthetic joint infection (PJI). 583 patients undergoing revision arthroplasty due to presumed PJI were retrospectively studied. PJI definition was independent of purulence, based on the definition of Musculoskeletal Infection Society recently modified by International Consensus Group on PJI. 498 patients fulfilled the criteria for definite PJI and 59 patients were deemed as aseptic. Purulence had sensitivity, specificity, positive and negative predictive values of 0.82, 0.32, 0.91, and 0.17, respectively. Purulence was not correlated with higher culture positivity yet was associated with higher synovial WBC counts (mean of 34.8 versus 5.2 $\times$ 10^3/μL in patients without purulence [$P < 0.001$]). In the absence of objective definition for purulence and in light of its inadequate test characteristics compared to a multi-criteria definition, purulence cannot serve as a single absolute diagnostic criterion for PJI. Level of Evidence: Level I, Diagnostic Studies.

The diagnosis of periprosthetic joint infection (PJI) remains a challenge. Currently, no single test is available with 100% accuracy for the diagnosis of PJI [1]. Therefore, multi-criteria definitions have been proposed to overcome the limitations of the individual diagnostic methods that comprise the standard PJI work-up [2,3].

Purulence, defined as the presence of pus, has conventionally been considered a definitive sign of PJI. Many studies have used intraoperative purulence as a single criterion to diagnose PJI [4–7]. While it might seem logical that purulence around an implant is consistent with an infection, the determination of purulence is based on a subjective interpretation. Although most surgeons would agree as to what frank pus is, they might have different thresholds for considering cloudy or turbid fluid as representative of infection. Turbid, yellowish-white fluid may represent the neutrophil-rich liquid that develops as part of an inflammatory reaction in response to an infection [8], but it may also be seen in non-infectious cases. In recent years the orthopedic community has become aware of the fact that purulence can exist in patients with failure of metal-on-metal bearing surface [9–11] and failure can also occur due to corrosion at the trunnion of the femoral stem [12] that does not represent a PJI. Moreover, concomitant infection and failed metal-on-metal arthroplasty have also been reported with indistinguishable appearance of the periprosthetic fluid or tissue from non-infected failed metal-on-metal implants [13,14]. Patients who are misdiagnosed with PJI may be subjected to unnecessary surgical procedures and long-term antibiotic treatment.

Therefore, in the absence of an objective definition, it is difficult to consider purulence as a simple dichotomous variable. Subjective opinion of the surgeon regarding periprosthetic fluid can vary based on their clinical impression or concerns regarding the consequences of misdiagnosing PJI. Moreover, PJI has a serious impact on patients' health and quality of life because patients may be subjected to additional surgical procedures and long-term antibiotic treatment. Therefore, surgeons should be cautious in applying subjective criteria for ruling in or ruling out PJI in suspected patients.

Moving forward in the development of a standardized definition of what constitutes a true PJI, it is important to determine the utility of the subjective identification of intraarticular purulence as a diagnostic criterion. Therefore, based on a multi-criteria definition proposed by the Musculoskeletal Infection Society (MSIS) and recently modified by the International Consensus Group on PJI [3], we conducted this study to evaluate the following: 1) the reliability of intraoperative purulence as a single diagnostic criterion for the diagnosis of PJI, 2) the correlation between the presence of intraoperative purulence and individual PJI

One or more of the authors of this paper have disclosed potential or pertinent conflicts of interest, which may include receipt of payment, either direct or indirect, institutional support, or association with an entity in the biomedical field which may be perceived to have potential conflict of interest with this work. For full disclosure statements refer to http://dx.doi.org/10.1016/j.arth.2015.03.005.

Disclosures: Each author certifies that our institution has approved the human protocol for this investigation and that all investigations were conducted in conformity with ethical principles of research. Each author has contributed substantially to the research, preparation and production of the paper and approves of its submission to the Journal.

Reprint requests: Javad Parvizi, MD, FRCS, Rothman Institute of Orthopaedics at Thomas Jefferson University Hospital, 925 Chestnut Street, Philadelphia PA 19107.

http://dx.doi.org/10.1016/j.arth.2015.03.005
0883-5403/

criteria, and 3) the correlation between the presence of purulence and the pathogens responsible for PJI. Our hypothesis was that purulence is not sufficiently reliable for the diagnosis of PJI as a single diagnostic criterion; and secondly, we hypothesized that purulence may correlate with parameters of local inflammatory response, including white blood cell (WBC) count and polymorphonuclear cell (PMN) percentage. Finally, we hypothesized that infecting organisms differ in how they provoke purulent local inflammation in periprosthetic tissues.

Methods

Following institutional review board approval, we accessed our institutional database on PJI to identify all patients who underwent revision total knee and hip arthroplasty for presumed PJI between 2000 and 2012. Patients were excluded if they had an inadequate workup for PJI or no clear description of periprosthetic fluid at the time of surgery, and those who had previously been treated for PJI before receiving treatment at our hospital. We identified 583 patients, of which 333 underwent revision total knee (57%) and 250 underwent revision hip arthroplasty (43%). The mean age was 66 years (range 24–94 years), mean body mass index (BMI) was 32 kg/m^2 (range 17–63), and gender distribution was almost equal (301 females, 52%).

Based on the PJI definition proposed by MSIS and recently modified by the International Consensus Group on PJI, 498 cases were classified as definite PJI (85%) including 286 knee revision and 212 hip revisions. Briefly, this definition consists of two major and six minor criteria. Major criteria, each being diagnostic of PJI, include the presence of a draining sinus and isolation of an infecting organism from two separate tissue or fluid cultures. Alternatively, the presence of three out of six minor criteria was also proposed as being diagnostic of PJI. The six minor criteria were elevated erythrocyte sedimentation rate (ESR) and C-reactive protein (CRP), elevated synovial WBC count, increased synovial fluid PMN percentage, isolation of a pathogen from only one culture, positivity of leukocyte esterase, and histopathologic evidence of acute inflammation in periprosthetic tissue samples [3]. Laboratory values obtained within one month prior to revision surgery were considered. In contrast to the criteria proposed by MSIS [2], the definition of the International Consensus Group does not consider the presence of intraoperative purulence as a minor diagnostic criterion. We classified patients as early-postoperative PJI if it occurred within 4 weeks of the index arthroplasty (161 patients). This definition is arbitrary yet practical in terms of making decisions, since prognosis of prosthesis salvage in the early postoperative period is favorable for early PJI cases [15]. The rest of the cases were classified as chronic PJI (298 patients), except for infections that happened later than one month after the index surgery and a concomitant remote infection (with the same pathogenic organisms as PJI) preceded the occurrence of PJI (39 patients). Purulence was defined as the dictating surgeon's subjective interpretation of periprosthetic fluid/tissue during the surgery or aspiration of joint in the clinic (11 attending surgeons). In our institution, we utilize the semi-automated method for measuring ESR (Streck ESR autoplus, Omaha NE, USA), turbidimetric method for CRP (Beckman Coulter, Brea, CA, USA) and automated analyzers for synovial WBC count/differential (Sysmex XE5000; Sysmex, Mundelein, IL, USA). The presence of leukocyte esterase in the synovial fluid was determined using a standard chemical strip (Chemstrip 7 urine test strip; Roche Diagnostics, Indianapolis, IN).

Of the 85 patients who did not meet the criteria for PJI, 26 had at least one positive microbiological culture consisting of methicillin-sensitive coagulase negative *Staphylococci* (8 patients), multiple bacteria (5 patients), methicillin-resistant coagulase negative *Staphylococci* (4 patients), *Streptococci* (3 patients), *Corynebacteria* (2 patients), and *Enterobacter Cloacae*, methicillin-sensitive *Staphylococcus aureus*, methicillin-resistant *Staphylococcus aureus* and *Candidia parapsilosis* (one patient each). Although these patients were treated for PJI, they did not meet the International Consensus Group or the MSIS criteria for PJI. We excluded these patients for statistical analysis when comparing PJI versus non-PJI groups. However, we used the data of these patients for correlation of purulence with the individual criteria of PJI.

Three to five samples (either from preoperative joint aspirate or from intraoperative samples of fluid or periarticular tissue) were available for microbiologic culture, which were routinely cultured for one week. Samples from draining sinus were not included [16]. Isolates were considered significant if they grew on solid agar, or when an indistinguishable strain grew on enrichment media more than once. An average of 4.1 microbiologic cultures were taken, which resulted in identification of the pathogens and their antibiotic resistance profile in 452 patients (91%). Culture-negative PJI constituted 9% (46/498) of the cohort. All patients were treated as PJI except 9 patients in whom the revision surgery was indicated for corrosion failure. Another patient was revised for a symptomatic metal-on-metal (MOM) hip failure. In all of these ten patients with either corrosion failure (9 cases) or MOM hip failure (1 case), the appearance of periprosthetic fluid was reported as purulent. However, the patient with metal-on-metal arthroplasty was the only one among these ten patients who met the criteria for PJI with the responsible pathogen being *S. aureus*. The possibility that the corrosion cases might have been culture-negative PJI is low based on lab results and the postoperative course.

Based on the most common infecting organisms, we limited grouping of PJI cases into the following groups: *Staphylococcus aureus*, coagulase-negative *Staphylococci*, *Streptococci*, gram-negative bacteria, culture-negative PJI and others (including commensal anaerobes and yeasts).

Statistical comparisons for categorical variables were made using Fisher's exact test. Logistic regression was performed for continuous variables. Wilcoxon test was done for variables with nonparametric distribution (synovial WBC count and PMN percentage). Statistical tests were performed using R software (version 3.11, R Foundation for Statistical Computing, Vienna, Austria), with statistical significance at $P < 0.05$. Optimal thresholds were calculated using receiver operating characteristics analysis.

Results

Purulence was noted in the operative report of 467 patients (80%), of which 408 fulfilled the criteria for PJI. Table 1 lists the characteristics of the PJI patients with and without purulence. No difference was observed between the two groups in terms of age, gender, BMI, and Charlson comorbidity index. The diagnostic characteristics of purulence for PJI, as defined by the International Consensus Group, were sensitivity of 0.82, specificity of 0.32, positive predictive value of 0.91, negative predictive value of 0.17, and accuracy of 0.77. Purulence was more commonly observed in PJI cases (82%) compared to non-PJI group (68%) ($P = 0.01$). Purulence was noted in 92% (36/39) of patients with acute hematogenous PJI and 89% (265/298) of patients with chronic PJI. However, surgeons reported purulence in only 66% (106/161) of patients with early postoperative PJI, and the difference was statistically significant ($P < 0.001$). In patients with early PJI and no purulence, the periprosthetic fluid was described as bloody in 65% (36/55) of patients.

Table 1
Demographic Data of Periprosthetic Joint Infection Patients (n = 498) With and Without Purulence.

	Purulence	No Purulence	*P* Value
Age [a] (years)	67 (32–94)	65 (24–87)	0.08
Female Gender[b]	50 (203/408)	53 (48/90)	0.16
Body Mass Index[a] (kg/m^2)	31 (22–52)	31 (18–55)	0.74
Charlson Comorbidity Index[b] = 0	<1 (1/393)	1 (1/84)	0.10
= 1	4 (14/393)	8 (7/84)	
= 2	13 (51/393)	15 (63/84)	
≥3	78 (306/393)	75 (63/84)	

[a] Values represent average with range in parentheses.
[b] Values represent percentage with raw proportion in parentheses. For CCI, there were 15 and 6 missing values in the purulence and no-purulence groups, respectively.