RESEARCH ARTICLE

Significance of Perioperative Tests to Diagnose the Infection in Revision Total Shoulder Arthroplasty

Shahryar Ahmadi, MD; Thomas M. Lawrence, MD; Shawn Sahota, MD; Cathy D. Schleck, BS; William S. Harmsen, MS; Robert H. Cofield, MD; John W. Sperling, MD

Research performed at Mayo Clinic, Rochester, USA

Received: 09 August 2017 *Accepted: 21 October 2017*

Abstract

Background: The purpose of this study was to evaluate the value of perioperative tests for the diagnosis of infection in revision shoulder arthroplasty.

Methods: A retrospective analysis was performed on 537 shoulder arthroplasties (429 patients) that underwent revision shoulder arthroplasty at our institution. Periprosthetic tissue cultures were positive in 169/537 surgeries.

Results: White-blood cell count (WBC) was elevated in 3.8% revision arthroplasties. Erythrocyte sedimentation rate (ESR) was elevated in 23.1% revision arthroplasties. The C-reactive protein (CRP) was elevated in 20.8% revision arthroplasties. Bone scans (technetium, indium) were performed on 9.9% patients and it was positive for osteomyelitis in just one revision arthroplasty. Intra-operative pathology was read as consistent with acute inflammation in 11.9% revision arthroplasties. The positive and negative predictive values for intra-operative pathology were 56.7% and 71.6% respectively.

Conclusion: All of the perioperative tests had a high specificity and negative predictive value, but low sensitivity and positive predictive value.

Level of evidence: III

Keywords: Infection in Revisions Shoulder Arthroplasty, Perioperative Tests, Shoulder, Shoulder Arthroplasty

Introduction

Infection after total shoulder arthroplasty (TSA) is a devastating complication. The reported prevalence of deep periprosthetic infection involving shoulder arthroplasty ranges from 0 to 15.4% and infection remains a common reason for failure, especially in the revision setting (1-3). In one study Kelly et al reported 29% unexpected positive culture after revision shoulder arthroplasty (4).

Although the number of the papers on the rates of subclinical infection in shoulder arthroplasty especially by Propionibacterium Acnes are increasing, there is not much information on the value of perioperative laboratory tests to diagnose the infected shoulder arthroplasty (1, 3-6). The preoperative diagnosis of infection in failed shoulder arthroplasty still remains a challenge and the clinical scenario of discovering an unexpected positive culture after revision arthroplasty in a joint with no other symptoms or signs of infection represents a management dilemma. Complex reconstruction with revision implants and allograft augmentation are sometimes required in revision shoulder arthroplasty. Traditionally, positive cultures in samples obtained at the time of surgery are considered the "gold standard" for the diagnosis of a periprosthetic

Corresponding Author: John W. Sperling, The Department of Orthopedic Surgery, Rochester, USA
Email: sperling.john@mayo.edu

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infection, but the surgeon has already committed to these complex surgeries by the time they receive the result of the intra operative cultures (7). The purpose of this study was to determine the value of prioperative laboratory studies in predicting infected shoulder arthroplasty.

Materials and Methods

After review and approval of this study by our Institutional Review Board, our joint registry database was utilized to identify all patients who underwent revision shoulder arthroplasty at our institution between January 1, 1994 and December 31, 2008. During this period 465 patients underwent 592 revision shoulder arthroplasty at the Mayo Clinic. We performed a review of the medical records of all of these patients. All patients underwent revision arthroplasty by 6 experienced shoulder surgeons.

We excluded any surgeries without intra-operative culture and included any revision shoulder arthroplasties with intra-operative culture. Fifty five surgeries (11.8%) did not have any intra operative culture and were excluded from the study. A retrospective analysis was performed on 537 surgeries (429 patients) that had at least one intra-operative culture (from swabs, tissue or removed implants) after revision shoulder arthroplasty. Each patient's history and physical examination findings before revision were also reviewed. Recorded data included fever. Preoperative investigations in patients suspected to have infection included a white-blood-cell (WBC) count, percentage of polymorphonuclear cells, erythrocyte sedimentation rate (ESR), C-reactive protein (CRP), joint aspiration and Technetium/Indium bone scan. Intra-operative investigations included culture of periprosthetic tissue and histologic evaluation of frozen sections from intra-operative samples of periprosthetic tissue.

A positive result (suggestive of infection) or a negative result (not suggestive of infection) was defined for each frozen section. With use of the criteria of Mirra a result of the frozen section was considered positive when any single high-power field contained at least 5 stromal neutrophils (8). For this study, only 1 culture had to be positive for the shoulder to be considered culture positive. The white-blood-cell count was considered to be elevated when it was more than 11.0 × 10^{10}/L. The number of polymorphonuclear cells was considered increased (a so-called left shift) when more than 80% of the total white-blood-cell count consisted of granulocytes. For the purposes of this analysis, an erythrocyte sedimentation rate of more than 22 mm/h and a C-reactive of more than 1 mg/dl deemed a positive result. We also adjusted the ESR for age but not for patients with active inflammation. We used the following formula to adjust the ESR for age. Men= age/2 and Women= (age+10)/2 (9).

A preoperative aspiration was obtained in those surgeries suspected of having a chronic occult infection. These aspirations were considered positive (suggestive of infection) if any culture was positive.

Infected shoulder arthroplasties were treated with appropriate antibiotic after surgery.

Statistical Methods

Descriptive statistics are reported as either mean (range) or frequency (percentage). The performance of pathology, elevated WBC, elevated Neutrophils, elevated CRP, and abnormal ESR were compared with the result by culture for the identification of any organism. Results reported are sensitivity, specificity, positive predictive value (PPV), and negative predictive value (NPV), along with 95% exact binomial confidence intervals. Pair-wise comparisons among tests (pathology, elevated WBC, elevated Neutrophils, elevated CRP, and abnormal ESR) for sensitivity, as well as specificity, were made using a Mc Nemar test. The significance tests reported are not/are adjusted for multiple comparisons, a Bonferroni adjustment would require a $P<0.005$ to be statistically significant.

The alpha-level was set at 0.05 for statistical significance.

Results

This retrospective assessment included 537 surgeries (429 patients) that had at least one intra-operative culture after revision shoulder arthroplasty. The mean age of the patients at the time of revision shoulder arthroplasty was 64 years (range 23-89 years). There were 220 (51%) men and 209 women (49%). Seventy one patients underwent 2 revision shoulder arthroplasties, eight underwent 3 and seven underwent 4 revision shoulder arthroplasties. Three hundred and eighteen (59%) revision shoulder arthroplasties were done on right and 219 (41%) on left shoulders. The mean follow-up time for all surgeries (537) was 3.7 years (range, 0-15.4 years) [Table 1].

The mean follow-up time for 368 culture negative revision shoulder arthroplasties was 3.6 years (range, 1 day-15.4 years) [Table 1].

Cultures were positive in 169 of the 537 surgeries (31.5%). Among those 169 infected revision shoulder arthroplasties, 63.9% were solely positive for Propionibacterium Acnes (P-Acnes) and 36.1% were positive for other bacteria [Table 2]. An average of 3.0 cultures was taken per operation. The mean number of positive cultures in infected revision shoulder arthroplasties was 3.5. An average of 3.2 cultures was

Table 1. Patients demographic data

Variables	
Number of Surgeries	537
Number of Patients	429
Age at surgery, mean (range)	64 years (23-89)
Gender, n (%)	
Male	220 (51%)
Female	209 (49%)
Follow up, mean (range)	3.7 years (0-15.4)

Table 2. Among Positive cultures, the proportions of the organisms identified

Positive cultures based on the organisms	N (%)
Propionibacterium Acnes	108 (63.9%)
Coagulase Negative Staphylococcus	39 (23.1%)
Staphylococcus Aureus	7 (4.1%)
Propionibacterium Acnes and Staphylococcus Coagulase Negative	8 (4.7%)
Propionibacterium Acnes and Staphylococcus Aureus	2 (1.2%)
others	5 (3.0%)
Total number of positive cultures	169

There are 9 infections in patients without a pathology result.
That is why the table now reads as 169 total rather than the 160.

Table 3. Results assessing infection as No Infection, Propionibacterium Only, Other bacterium

	None N (%)	Non-P. Acnes infection N (%)	P. Acnes infection N (%)
Elevated WBC (>11× 10^{1}º/L)	12 (3.5%)	3 (4.9%)	4 (4.0%)
Elevated Neutrophils >80%	10 (3.2%)	1 (2.7%)	2 (2.1%)
Elevated CRP >1 mg/dl	45 (20.6%)	17 (33.3%)	10 (13.0%)
Abnormal ESR >22 mm/h	14 (5.8%)	11 (21.1%)	4 (4.8%)

taken for the 108 revision shoulder arthroplasties cultured positive with only P-Acnes, and an average of 4.1 cultures was taken for the 61 revision shoulder arthroplasties cultured positive for all others. In the 368 revision shoulder arthroplasties with no infection an average of 2.8 cultures were taken.

No patients presented with fever. The mean preoperative leukocyte count was 7.1 (range 3.4 – 14.0) in culture negative revision shoulder arthroplasties and 7.0 (range 3.0 – 12.7) in culture positive revision shoulder arthroplasties.

Table 3 shows the mean preoperative leukocyte count, mean polymorphonuclear, mean CRP and mean ESR in P-Acnes culture positive revision arthroplasty versus non P-Acnes culture positive revision shoulder arthroplasty [Table 3].

Table 4 shows the sensitivity, specificity, PPV and NPV of WBC, PMN, ESR and CRP [Table 5].

Culture of aspiration was done before 34 (6.3%) revision shoulder arthroplasties. It was negative in 26 revision shoulder arthroplasties and positive in 8 revision shoulder arthroplasties. Five aspirations grew P-Acnes and 3 CNS. There were 9 false negative and 1 false positive aspirations. The false positive aspiration grew P-Acnes. Four false negative aspirated shoulders grew CNS from intra-operative cultures, 3 P-Acnes and 2 of them, both CNS and P-Acnes [Table 4].

Bone scans (technetium, indium) were performed on 53 (9.9%) patients. It was positive for osteomyelitis in just one patient. Intra-operative culture grew CNS in 8 of the revision shoulder arthroplasties and P-Acnes in 12 of the revision shoulder arthroplasties. Table 4 shows the sensitivity, specificity, PPV and NPV of aspiration and bone scan [Table 4].

Pathologic evaluation was performed at the time of the revision in 503 (93.7%) revision shoulder arthroplasties. An average of 1.4 pathologies was sent per revision shoulder arthroplasty. Sixty (11.9%) pathologies were originally read as being positive for acute inflammation. Pathology was true positive in 34 (6.8%) revision shoulder arthroplasties, true negative in 317 (63.0%) revision shoulder arthroplasties, false positive in 26 (5.2%) revision shoulder arthroplasties and false negative in 126 (25.0%) revision shoulder arthroplasties. Table 4 shows the sensitivity, specificity, PPV and NPV of the pathology [Table 4].

Pathology was true positive in 14 (2.8%) and false negative in 89 (17.7%) P-Acnes positive surgeries, a sensitivity of 13.6%. Pathology was true positive in 20 (4.0%) and false negative in 37 (7.4%) of non P-Acnes culture positive revision shoulder arthroplasties, a sensitivity of 35.1%. Table 5 shows the sensitivity, specificity, positive and negative predictive value of intra operative pathology for revision shoulder arthroplasties

Table 4. Performance of Testing Methods in Identification of Infection (Yes vs. No) Relative to the Culture Identification

Method	Number patients, N(%)	Sensitivity	Specificity	Positive Predictive Value (PPV)	Negative Predictive Value (NPV)
Culture	537				
Pathology	503 (93.7%)	34/160 (21.2%)	317/343 (92.4%)	34/60 (56.7%)	317/443 (71.6%)
ESR	376 (70.0%)	29/135 (21.5%)	183/241 (75.9%)	29/87 (33.3%)	183/289 (63.3%)
CRP	346 (64.4%)	27/128 (21.1%)	173/218 (79.4%)	27/72 (37.5%)	173/274 (63.1%)
WBC	501 (93.3%)	7/161 (4.4%)	328/340 (96.5%)	7/19 (36.8%)	328/482 (68.0%)
PMN	479 (89.2%)	3/155 (1.9%)	314/324 (96.9%)	3/13 (23.1%)	314/466 (67.4%)
Aspiration	34 (6.3%)	7/16 (43.8%)	17/18 (94.4%)	7/8 (87.5%)	17/26 (65.4%)
Bone scan	53 (9.9%)	1/20 (5%)	33/33 (100%)	1/1 (100%)	33/52 (63.5%)

Table 5. Result of the intra operative pathology for shoulders with positive culture for "P. Acnes only" versus any other findings (i.e. any other positive cultures and negative culture results) compared with the result by Culture

Pathology	n/N (%)	95% Confidence Interval
Sensitivity	14/103 (13.6%)	7.6-21.8
Specificity	354/400 (88.5%)	85.0-91.5
Positive Predictive Value	14/60 (23.3%)	13.4-36.0
Negative Predictive Value	354/443 (79.9%)	75.9-83.5

with positive culture for P-Acnes only versus any other findings (i.e. any other positive cultures and negative culture results) [Table 5].

The sensitivity of pathology, CRP, and ESR was significantly higher than either WBC or PMN ($P<0.05$). Also, pathology and CRP have a significantly higher sensitivity than ESR ($P<0.05$). CRP has a significantly lower specificity than any of the other four tests. Additionally pathology has a significantly lower specificity than either WBC or PMN ($P<0.05$) [Table 4].

Discussion

We reviewed the results of 537 revision shoulder arthroplasty that was done in our institution between January 1, 1994 and December 30, 2008. Cultures were positive in 169 (31.5%) surgeries. P-Acnes was the most common cause of infection (63.9%) and, CNS was the second (23.1%) most common cause in our study. Similar results have been reported in other published series in the literature (4, 5, 10, 11).

Propionibacterium acnes is a gram-positive, non-spore-forming, anaerobic bacillus that is usually found in skin sites with high numbers of sebum excreting sebaceous follicles (1, 12). Men are reported to more commonly have an infection caused by P-Acnes than women (1, 12-14). P-Acnes is difficult to culture. It can reside intracellularly and remain in a dormant state for weeks. False-negative results are common when samples are cultured for only 5 days and, prolonged incubation (up to 14 days) are required to isolate it (12). This organism usually inoculates the periprosthetic tissue at the time of implant placement and remains in a relatively quiescent biofilm state (1, 12). It is usually associated with low grade infections and typically present with subtle sings (unexplained pain and/or stiffness) and often presents late (usually within 24 months of implantation) (10, 11, 15-17).

Unexpected positive intra operative culture has been reported in many studies before and the most common organism has been P-Acnes. There is no consensus for the diagnosis of a true subclinical infection and defining an indolent infections after total shoulder arthroplasty is still a challenge (4, 5).

In our study an average of 3 cultures was taken per operation. Some of our patients had just one intra-operative culture. Atkins et al. noted that there is a tendency to submit fewer specimens for culture when the intra-operative findings suggest a non-infective scenario (18). Some authors have considered a single periprosthetic tissue culture positive to indicate infection (5, 19-21). There is no consensus in the literature on the ideal number of cultures that should be taken during revision shoulder arthroplasty surgery.

Although the sensitivity and specificity of intra-operative pathology for P-Acnes positive surgeries compared to all culture positive surgeries combined were lower but the difference was not significant. The PPV and NPV of intra-operative pathology for P-Acnes positive surgeries compared to all culture positive surgeries combined were significantly lower in current study.

Overall, none of the preoperative tests (WBC, PMN, ESR, CRP, aspiration and bone scan) in our study were sensitive enough [Table 4] to diagnose the infected shoulder arthroplasty and this has been reported by several other studies before (5, 11, 16, 22, 23).

For example, Kelly et al reported elevated WBC and PMN in 4% (1/28), elevated CRP in 42% (5/12) and ESR in 25% (4/16) of culture positive revision shoulder arthroplasty (15). Topolski et al reported 9.6% (7/73) positive intra-operative pathology in culture positive revision shoulder arthroplasties (5).

In our study, all of the perioperative tests had a high specificity and negative predictive value, but low sensitivity and positive predictive value. The high Specificity and NPV of the tests in our study is the result of big sample size of culture negative shoulder arthroplasty. A negative test result is useful in the exclusion of deep infection, but the presence of a positive test is not sensitive or predictive enough to be of value and this has been similar to other studies (11,20). So the result of these tests (especially when positive) should be reviewed in conjunction of the overall clinical picture.

Our study has a few limitations. First, it was a retrospective study that can have significant patient and treatment selection biases. Secondly, the number of cultures was not consistent in all of the patients in our study; there was not a standardized protocol for perioperative tests and cultures including timing of preoperative blood tests. Nevertheless, to our knowledge, our study is the biggest in the literature to determine the value of perioperative laboratory studies in predicting infected shoulder arthroplasty.

In conclusion, the data from this study suggest that there are no good single preoperative or intra-operative investigations to detect who will have a positive intra-operative culture at the time of revision shoulder arthroplasty and the whole clinical and para-clinical picture should be considered. We think that a standardized protocol to work up the patients before revision shoulder arthroplasty to detect the infection should be established. Also there is a need for further prospective studies.

Shahryar Ahmadi MD
Thomas M. Lawrence MD
Shawn Sahota MD
Cathy D. Schleck BS
William S. Harmsen MS
Robert H. Cofield MD
John W. Sperling MD
The Department of Orthopedic Surgery, Rochester, USA

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