Incidence and predictors of positive intraoperative cultures in primary shoulder arthroplasty following prior ipsilateral shoulder surgery

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Background: To our knowledge, the rate of positive intraoperative cultures in patients undergoing primary shoulder arthroplasty with prior ipsilateral nonarthroplasty shoulder surgery is unknown. The aim of this study was to determine the incidence and predictors of positive cultures in these patients.

Methods: We performed a retrospective review of patients with prior ipsilateral shoulder surgery with intraoperative cultures taken at the time of primary shoulder arthroplasty. We evaluated culture results, demographics, and number of prior surgeries. Regression analysis was used to determine patient-related risk factors that predict positive cultures.

Results: A total of 682 patients underwent primary shoulder arthroplasty, 83 had at least 1 prior ipsilateral shoulder surgery: 65.1% male, mean age 64.2 ± 10.9 years. For the cohort of 83 patients, an average of 3.2 ± 1.2 tissue samples were obtained for each patient, with a mean of 0.84 ± 1.14 tissue cultures being positive (range 0-5). Thirty-seven of the 83 patients (44.5%) had at least 1 positive culture, with Cutibacterium acnes the most frequent organism (31/37; 83.4%). An average of 1.9 ± 0.96 tissue cultures resulted positive (range 1-5) for the 37 patients who had positive cultures, 40.5% (15/37) had only 1 positive tissue culture (12/15 C acnes, 2/15 Staphylococcus epidermidis, and 1/15 vancomycin-resistant enterococcus). Male sex and history of prior shoulder infection were predictive of culture positivity (odds ratios: 2.5 and 20.9, respectively). Age, race, medical comorbidities, number of prior shoulder surgeries, and time from index shoulder surgery were not predictive of culture positivity.

Conclusion: About 45% of patients with no clinical signs of infection and a history of prior ipsilateral shoulder surgery undergoing primary shoulder arthroplasty grew positive intraoperative cultures. The significance of these findings remains unclear with regard to risk of periprosthetic infection and how these patients should be managed.

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rate from the unprepared skin incision site preceding revision shoulder arthroplasty surgery.17

To date, previously published studies in the literature have reported intraoperative culture rates in otherwise presumed uninfected shoulders for primary shoulder arthroscopy,25,29 primary open shoulder surgery,12,21 primary shoulder arthroplasty,15,16 revision shoulder arthroscopy,8 and revision shoulder arthroplasty.5,7,11,13,19,23,26 To our knowledge, the rate of positive intraoperative cultures in patients undergoing primary shoulder arthroplasty who have had prior ipsilateral nonarthroplasty shoulder surgery has never been reported. The aim of this study was to determine the incidence and predictors (risk factors) of positive cultures in patients undergoing primary shoulder arthroplasty who have had prior nonarthroplasty shoulder surgery.

Methods

Participants

We performed a retrospective review of 682 consecutive patients undergoing shoulder arthroplasty surgery by a single surgeon at an academic university hospital over a 4-year period (January 1, 2015, to March 31, 2019). All arthroplasty surgeries were performed by the senior author, which included hemiarthroplasty, anatomic total shoulder arthroplasty, and reverse total shoulder arthroplasty. Patients undergoing revision shoulder arthroplasty (n = 88) or shoulder arthroplasty for fracture or malunion/nonunion (n = 105) were excluded. No patients had any documented clinical signs of ongoing shoulder or systemic infection. Of the remaining 489 patients undergoing primary shoulder arthroplasty, 83 had a history of prior ipsilateral shoulder surgery with intraoperative culture specimens taken at the time of primary shoulder arthroplasty (Fig. 1). Primary reverse total shoulder arthroplasty comprised the majority of procedures (n = 77), whereas the remaining included primary anatomic total shoulder arthroplasty (n = 5) and primary hemiarthroplasty (n = 2). Indications for surgical intervention included rotator cuff arthropathy (n = 66), glenohumeral arthritis (n = 13), and humeral head avascular necrosis (n = 4). The mean final follow-up for the cohort was 361.3 days (mean 12 months, range 1-43.5 months).

Procedures and measures

Tissue samples were taken in a standardized fashion with new clean instruments used for each tissue specimen. Tissue specimens for culture were taken at the same location in every case including subdeltoid space, tissue from the greater tuberosity at the site where sutures/suture anchors remained, and deep capsular layer adjacent to the anterior inferior glenoid rim. An average of 3.2 ± 1.2 (range 1-8) tissue specimens were taken from each shoulder joint at the time of surgery and sent to the microbiology laboratory. All patients received routine perioperative intravenous antibiotics 30 minutes before skin incision, which were continued for 24 hours postoperatively. Each sample was grown in 4 aerobic mediums (blood agar, chocolate agar, MacConkey agar, thioglycolate broth) and 3 anaerobic mediums (blood agar Centers for Disease Control formulation, biplate of bacteroides isolation agar with laked blood with kanamycin and vancomycin, anaerobic phenylethyl alcohol agar) using the standard protocol at this institution’s microbiology lab. Cultures were held through the time of positive growth, or for a mean of 3.1 days for aerobic cultures and 12.2 days for anaerobic cultures that were negative for growth.

Outcome variables

The primary outcome variable was the presence of positive cultures during primary shoulder arthroplasty in the setting of patients with a history of prior ipsilateral shoulder surgery. Thus, positive culture growth was operationalized as a binary outcome, where those with at least 1 documented positive culture were

![Figure 1 Flow diagram for patient inclusion.](image-url)
considered positive. We modeled the probability of a positive culture. The total number of positive intraoperative cultures as a count variable was a secondary outcome measure.

Potential predictor variables

An initial pool of 10 characteristic variables was selected for analysis as potential predictors of presence of positive intraoperative culture. These variables were selected based on the results of previously published findings and other factors that have been associated with patients who had prior ipsilateral shoulder surgery. Covariates were selected a priori. The pool of potential predictors included age (years), sex (male vs. female), body mass index, type of prior shoulder surgery (open vs. arthroscopic), total number of concurrent medical problems, number of previous ipsilateral shoulder surgeries, and duration (years) between first shoulder surgery and first shoulder arthroplasty. Current smoking status, type 2 diabetes mellitus, and history of ipsilateral shoulder infection were binary indicators (yes vs. no) and also included in the pool of potential predictors.

Statistical analysis

Demographic and clinical characteristics of patients with and without positive cultures during shoulder arthroplasty

Table I

![Table with data](image)

M. sample mean; SD, standard deviation; BMI, body mass index; CRP, C-reactive protein; ESR, erythrocyte sedimentation rate; WBC, white blood cell.

Positive culture was operationalized as the presence of at least 1 positive culture. The P value (2-tailed) is associated with the test of Group differences (positive cultures vs. no presence of positive cultures) on each characteristic; t test was used for continuous variables and Fisher exact test was used for categorical variables. Duration between surgeries = time (years) between first shoulder surgery and first shoulder arthroplasty.

* False discovery rate = 0.27.
number of ipsilateral shoulder surgeries was $1.4 \pm 0.87$ (range, 1–7), with an average of $9.7 \pm 10.1$ years between first shoulder surgery and primary shoulder arthroplasty. About 80% of patients had arthroscopic-only procedures compared with about 20% having at least 1 open procedure. Approximately 6% had a history of ipsilateral shoulder infection, all of whom grew at least 1 positive culture. History of prior ipsilateral shoulder postoperative infection was defined based on patient history detailing treatment with a course of either oral or intravenous antibiotics.

An average of $3.4 \pm 1.2$ tissue samples were sent for culture for each patient. Cultures were positive in at least 1 tissue sample in 44.5% (37/83) of patients. An average of $1.9 \pm 0.96$ tissue samples were positive (range 1–5) from the average $3.4 \pm 1.5$ samples taken in these 37 patients, accounting for 47 total positive cultures of the 88 total samples drawn (53.4%). C acnes was the most frequent organism, present in 83.4% (31/37) of the patients who grew at least 1 positive culture. The remaining pathogens included Staphylococcus epidermidis, diphtheroid bacilli, Staphylococcus saccharolyticus, Enterococcus faecalis, Enterococcus ammigenus, vancomycin-resistant enterococcus, and Cladosporium fungal species. The average time to final positive growth and speciation among the aerobic and anaerobic organisms was 2.3 and 7.4 days, respectively. Fifteen of 37 patients (40.5%) grew only 1 positive tissue culture (12 C acnes, 2 S epidermidis, and 1/15 vancomycin-resistant enterococcus), whereas the remainder grew 2 or more positive tissue samples.

Using a binary outcome of positive vs. negative cultures, bootstrapped results from the logistic regression model revealed that the predicted or expected log odds of number of positive cultures during shoulder arthroplasty was significantly greater for males than for females (geometric mean $= 2.43$ positive cultures, 95% bootstrap CI $= 1.25, 5.61$), while controlling for a history of shoulder infection. And those with a history of shoulder infection had significantly greater predicted or expected log odds of number of positive cultures during shoulder arthroplasty than those without a history of shoulder infection (mean OR $= 20.95$, 95% bootstrap CI: $5.54, 67.22$), while controlling for sex. The bootstrapped area under the curve (AUC) for this logistic regression model was 0.64 (Table II).

Similar findings emerged for the count variable of number of positive cultures. The bootstrapped results from the negative binomial regression model revealed that the predicted or expected log odds of number of positive cultures during shoulder arthroplasty was significantly greater for males than for females (geometric mean $= 3.49$ positive cultures, 95% bootstrap CI $= 2.08, 7.29$), while controlling for sex. The bootstrapped results for the negative binomial regression model for number of positive cultures are shown in Table III.

At the time of final follow-up at 361.3 days (mean 12 months, range 1–43.5 months), no complications were reported related to infection, implant loosening/failure, or return to surgery. One patient did sustain a periprosthetic fracture during the postoperative course after a fall during an altercation, which was fixed with open reduction internal fixation and revision arthroplasty.

### Discussion

The results of this investigation demonstrate a high rate of positive cultures in this patient population, with 44.5% of patients having at least 1 positive intraoperative culture at the time of their primary shoulder arthroplasty procedure. Postoperative shoulder infection may present as indolent shoulder pain, stiffness, or implant loosening, and poses a major challenge to patient outcomes and health care costs following shoulder arthroplasty.

| Table II | Multiple logistic regression model for predictors of positive culture |
| --- | --- |
| **Model outcome and predictor variables** | **Bootstrapped parameter estimates** |
| Positive culture (positive vs. negative) | Mean estimate | SD | 95% CI for mean estimate | Mean OR | 95% CI for OR | Standardized estimate | Mean AUC |
| Intercept | $-0.9999$ | $0.4565$ | $-1.9938$, $-0.1910$ | $2.5191$ | $0.9637$, $7.5791$ | $0.0$ | $0.6468$ |
| Sex (male vs. female) | $0.9239$ | $0.5324$ | $-0.0369$, $2.0254$ | $2.5191$ | $0.9637$, $7.5791$ | $0.2098$ | $-$ |
| History of ipsilateral shoulder infection (yes vs. no) | $3.0423$ | $0.6175$ | $1.7135$, $4.2081$ | $20.9533$ | $5.5483$, $67.2287$ | $0.4233$ | $-$ |

SD, standard deviation; OR, odds ratio; AUC, area under the curve.

The parameter estimates were based on 10,000 bootstrap samples of the logistic regression model, with penalized maximum likelihood estimation along with Firth’s bias correction. The mean and variance were estimated on the logarithmic scale and represent log odds; 95% CI for the mean parameter estimate. For the 95% CI for estimate that does not contain zero (0), the respective mean parameter estimate is statistically significant at alpha $= 0.05$. Observed sample, $N = 83$.

* Predictor variables for the model were selected from a pool of 10 potential predictor variables via SAS’s PROC HPREDUCE to perform supervised variable selection and then implemented in the context of a penalized logistic regression model that was based on 10,000 bootstrap samples.

| Table III | Multiple negative binomial regression model for predictors of number of positive cultures |
| --- | --- |
| **Model outcome and predictor variables** | **Bootstrapped parameter estimates** |
| Number of positive cultures | Mean estimate | SD | 95% CI for mean estimate | GM | 95% CI for GM |
| Intercept | $-0.9585$ | $0.3852$ | $-1.7492$, $-0.3629$ | $0.3834$ | $0.1739$, $0.6956$ |
| Sex (male vs. female) | $0.8912$ | $0.4089$ | $0.2239$, $1.7248$ | $2.4381$ | $1.2509$, $5.6114$ |
| History of ipsilateral shoulder infection (yes vs. no) | $1.2515$ | $0.3451$ | $0.7339$, $1.9871$ | $3.4955$ | $2.0832$, $7.2943$ |

SD, standard deviation; CI, confidence interval; GM, geometric mean (natural antilogarithm of the ln mean estimate).

The parameter estimates were based on 10,000 bootstrap samples of the negative binomial model. The mean and variance were estimated on the logarithmic scale. For the 95% CI that does not contain zero, the respective mean parameter estimate is statistically significant at alpha $= 0.05$. Observed sample, $N = 83$.

* Predictor variables for the model were selected from a pool of 10 potential predictor variables via SAS’s PROC HPREDUCE to perform supervised variable selection and then implemented in the context of a penalized logistic regression model that was based on 10,000 bootstrap samples.
surgery. Therefore, a focus on prevention and recognition is paramount. The goal of this study was to identify the incidence and risk factors of UPCs in the setting of primary shoulder arthroplasty in a cohort of patients with a history of prior ipsilateral shoulder surgery. To our knowledge, this is the first study examining the incidence of positive cultures found at the time of primary shoulder arthroplasty in patients who have undergone prior ipsilateral shoulder surgery. These findings are comparable to the rates of UPCs found at the time of revision shoulder arthroplasty.\textsuperscript{5,7–9, 11–13,18,19,21,23,26} The ramification of these findings as well as how and if these cultures should be treated with antibiotics to prevent future perioperative infection is unknown.

UPC rates in revision shoulder arthroplasty have been well documented. Foruria et al\textsuperscript{5} found a 15% rate of UPCs in a cohort of 107 consecutive patients undergoing revision shoulder arthroplasty without any other cause for suspicion of infection. In other studies, the reported rates have been even higher, ranging from 23.9%–56.0% UPCs during revision shoulder arthroplasty.\textsuperscript{13,23,26} Although Foruria et al\textsuperscript{5} postulated that at least one-quarter of their positive cultures had no true clinical relevance, persistent infection was found in as many as 10% (11 of 107), from which the organisms matched the index intraoperative findings. They further discovered that the number of previous surgeries statistically correlated with the likelihood of true infection vs. contamination, a risk factor that did not reach statistical significance in predicting culture positivity in our study.\textsuperscript{5}

In similarly conducted studies, Mook et al\textsuperscript{21} reported a 20.5% rate of UPCs in primary open shoulder surgery and Sethi et al\textsuperscript{29} reported a 56% rate of UPCs in primary shoulder arthroscopy. Levy et al\textsuperscript{15} reported a 41.8% rate (23/55 patients) of unexpected positive \textit{C. acnes} cultures in primary shoulder arthroplasty, although patients with previous ipsilateral shoulder surgery were excluded.

We found that 44.5% (37/83) of the patients in our cohort had at least 1 positive culture. Within this cohort of 37 patients with a UPC, 53.4% (47/88) of the intraoperative tissue samples drawn were positive. \textit{C. acnes} was by far the most frequent organism, present in 83.4% (31/37) of the patients who grew at least 1 positive culture. Fifteen of the 37 patients (40.5%) grew only 1 positive tissue culture. It is uncertain if there is any significance to these cultures given there is a 20% false positive culture rate for \textit{C. acnes}.\textsuperscript{20,22} Additionally, the incidence of positive \textit{C. acnes} cultures in native shoulders with no history of prior shoulder surgery is 9%–41% at the time of primary shoulder arthroplasty.\textsuperscript{2,15,18,22} Therefore, it is unknown if the percentage of patients who grew \textit{C. acnes} (80%) in this series is consistent with what has been shown previously as a result of pre-existing \textit{C. acnes} in the subdermal skin layer or as a result of the previous surgery.

We also found that male sex and those with a history of prior shoulder infection were predictive of culture positivity within this cohort and have greater predicted number of positive cultures. As demonstrated in several previous studies, we also found greater risk of positive cultures in male shoulders.\textsuperscript{4,9,13,14,19,21,23,28}

The remainder of the potential risk factors had no statistically relevant prediction to the likelihood of having positive intraoperative cultures. These included patient age, race, smoking status, body mass index, number or type of comorbidities, total number of prior ipsilateral shoulder surgeries, and the proportion of open (vs. arthroscopic) procedures. The presence of elevated preoperative inflammatory markers (white blood cell count, erythrocyte sedimentation rate, C-reactive protein) was also not predictive of positive intraoperative cultures, which is similar to the previously reported notion that indolent \textit{C. acnes} infection or colonization can present with quite variable or even normal indices.\textsuperscript{3,30}

At the time of final follow-up, no patients had any clinical evidence of infection, infection-related complications, or infection-related return to surgery. With a mean follow-up of 12 months, it is not possible to draw any definite conclusions from these findings, although that was not the primary purpose of the investigation. To substantiate long-term infection risks from this patient cohort, extended follow-up is necessary.

The retrospective nature of this study presents several limitations. First, it potentiates a selection bias. It has been standard practice of the senior surgeon to obtain tissue samples in this type of patient population who could be considered higher risk, although the lack of a well-defined prospective protocol obviated what could have made for a higher sample size in this investigation. A second limitation is the relatively small sample size, which does not allow for subgroup analysis of the patient-related factors, which could explain why only approximately half of the subjects had positive cultures. Patzer et al\textsuperscript{15} found a higher prevalence of \textit{C. acnes} in the glenohumeral space compared with the subacromial space in patients undergoing primary shoulder arthroscopy, whereas Maccioni et al\textsuperscript{16} highlighted the importance of strict tissue collection techniques to decrease contamination and positive cultures. Prospectively defining a protocol for reliable tissue collection sites and methods could mitigate any inconsistency.

Given surgeries within this patient cohort were performed at a single institution by a single surgeon, extrapolating data to other institutions could be limited by differences in specific lab protocols and contamination rates, a factor not specifically addressed by this study. Time to final growth and speciation of \textit{C. acnes} was 8.4 days in our study, comparable to the average duration in similar studies.\textsuperscript{2,6} Frangiameo et al\textsuperscript{19} found that the time to \textit{C. acnes} growth was significantly shorter in a probably-true positive culture group (5 days) compared with a probable contaminant group (9 days). The duration of time that samples were held for our study, therefore, was likely adequate, as the samples that never resulted in positive growth were kept for a mean of 3.1 and 12.2 days for aerobic and anaerobic cultures, respectively.

The results of this study help to better understand the likelihood of obtaining a positive culture result in the setting of primary shoulder arthroplasty in patients with a history of previous ipsilateral shoulder surgery. We found that 83.4% of these patients will have a positive culture for \textit{C. acnes}. Although further investigation is needed to determine its significance in regard to long-term clinical outcomes and implant survivorship, it does reinforce the importance of cautious awareness of sterile technique as well as the increased risk of \textit{C. acnes} bacterial biofilm in a patient population that is otherwise categorized as undergoing “primary” arthroplasty surgery. Additionally, what is unknown is if these cultures are a result of contamination from prior surgical procedures or identification of the already existing bacteria that is found in the subdermal layers.

**Conclusions**

About 45% of patients with no clinical signs of infection and a history of prior ipsilateral shoulder surgery undergoing primary shoulder arthroplasty grew positive intraoperative cultures for \textit{C. acnes}. Male sex and a history of prior shoulder infection were predictive of culture positivity within this cohort. Similar to UPCs found during revision shoulder arthroplasty, the significance of these findings remain unclear in regard to risk of progression to clinically meaningful infection and how these patients should be managed.
Disclaimer

Michael Khazzam is a consultant for Tornier/Wright Medical, but the consulting work is unrelated to the subject of this work. The other authors, their immediate families, and any research foundations with which they are affiliated have not received any financial payments or other benefits from any commercial entity related to the subject of this article.

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