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ORIGINAL PAPER

Functional outcomes and complications of patients contaminated with *Cutibacterium acnes* during primary reverse shoulder arthroplasty: study at two- and five-years of follow-up

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Abstract

Purpose The objective of the study was to compare the functional outcomes and the complication rate of the patients with *C. acnes* contamination at the end of the primary reverse shoulder arthroplasty (RSA) surgery to those patients without *C. acnes* contamination.

Method A total of 162 patients were included. In all cases, skin and deep tissue cultures were obtained. A molecular typing characterization of the *C. acnes* strains was performed. Functional outcomes were assessed with the Constant score at the two and five year follow-up and all complications were also recorded.

Results A total of 1380 cultures were obtained from the 162 primary RSA surgeries. Of those, 96 turned out to be positive for *C. acnes*. There were 25 patients with positive cultures for *C. acnes*. The overall postoperative Constant score was not significantly different between those patients having *C. acnes*–positive cultures and those with negative cultures at the two and five year follow-up (59.2 *vs.* 59.6 at two years, *p* 0.870, and 59.5 *vs.* 62.4 at five years, *p* 0.360). Patients with positive cultures presented a higher complication rate (*p* 0.001) with two infections, one revision surgery, and one dislocation.

Conclusion Patients ending up with *C. acnes*–positive cultures after primary shoulder arthroplasty surgery do not have worse clinical outcomes when compared to patients having negative cultures, but a greater number of complications were found in those patients with *C. acnes*–positive cultures.

Keywords Reverse shoulder arthroplasty · *Cutibacterium acnes* · Periprosthetic infection · Contamination · Outcomes

Introduction

The presence of *Cutibacterium acnes* at the end of many primary shoulder surgeries has been extensively documented. Depending on the population studied, the surgery performed, and the number of cultures obtained, the *C. acnes*–positive culture rate can range from 9.3 to 41.8% [1–17]. Apparent aseptic revision shoulder arthroplasty cases constitute another source of positive cultures, mostly due to *C. acnes* detection [18–24]. The burden of the presence of *C. acnes* at the end of the primary surgery can be quite varied, with some patients having many positive cultures while others present with just one positive culture. Moreover, the positivity rate, the delay in detecting it, makes it even more difficult to interpret the meaning of these positive cultures [10, 12, 22, 25–27]. Indeed, there is still a gray zone and a debate when trying to exactly define the difference between *C. acnes* contamination and true infection relative to the different parameters suggested.

Consequently, the clinical meaning of these positive cultures at day seven, day ten or day 12 is still unclear. However, it remains a cause of concern since it has been recently reported that the *C. acnes* clinical strain present at the end of

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primary shoulder arthroplasties can be the cause of a future *C. acnes* periprosthetic joint infection a few months or a year later [28]. There is also evidence that the *C. acnes* subtypes most involved in periprosthetic shoulder joint infections are commonly found as contaminants in deep tissues at the end of the primary surgery [29]. Many times, commonly used lab tests to rule out infection like the C-reactive protein and erythrocyte sedimentation rate remain negative in torpid *C. acnes* infections. There can also be a lack of the common clinical signs of infection such as fever, erythema or swelling [1, 24]. Quite often, pain and stiffness are the only clinical signs present to suspect a *C. acnes* infection [30].

In this context, there is little information if the patients that end up with *C. acnes* contamination after the primary arthroplasty surgery have different functional outcomes or complication rates when compared to those without *C. acnes* contamination [31].

The objective of the present study was to compare the functional outcomes and the complication rates of the patients with *C. acnes* contamination at the end of the primary shoulder arthroplasty surgery to those without *C. acnes* contamination.

Materials and methods

It is a retrospective study, with the data obtained prospectively, including primary reverse shoulder arthroplasties (RSA) performed by a single shoulder surgeon in a tertiary center. In all cases, a Delta Xtend (DePuy, Warsaw, IN) was implanted. This is a series of consecutive cases of patients that had undergone primary surgery with an RSA from September 2013 to December 2016 because of a rotator cuff–deficient shoulder, an acute fracture or a fracture sequela. The exclusion criteria included an active infection, an invasive shoulder treatment in the six months prior to surgery, an Arthro-SCAN or Arthro-MRI in the last 6 months before surgery, previous shoulder surgeries, and revision cases. One hundred sixty-seven patients met the inclusion criteria. Five patients were excluded because of incomplete sample collection, leaving 162 patients. In the first 67 cases, five cultures were obtained. In the remaining 95 cases, 11 cultures were obtained because of the design of a study that was published elsewhere reporting the number of positive cultures. The cultures were marked to identify their origin in the following manner. When 11 cultures were obtained, numbers one and two belonged to skin, number three belonged to subcutaneous tissue, numbers four and five to the bursa over the greater tuberosity, numbers six through nine to the area around the long head of the biceps insertion, and numbers ten and 11 again to the bursa over the greater tuberosity. When five cultures were obtained, the first two belonged to skin, and the last three to deep tissues. Skin cultures were obtained just after skin incision and included dermal and subdermal tissue. In all the cases, every culture was obtained after opening a set of sterile instruments. All the cultures were obtained after skin preparation with the "Bactiseptic®" solution (Vesismin Chemicals, Barcelona, Spain) composed of 2% chlorhexidine gluconate and 70% isopropylic alcohol. It was also after standard antibiotic prophylaxis, consisting in cefazolin 2 g endovenous (ev) 30 to 60 min before incision, when it was administrated. Patients were functionally assessed at the two and five year follow-up. The functional outcomes of the patients included were obtained with the aid of the Constant score by an independent examiner blinded to the results of the cultures at the two and five year follow-up [32]. Any complication at any point in the follow-up was also prospectively recorded (dislocation, infection, loosening of the components). Periprosthetic joint infections were also recorded following the International Consensus on Musculoskeletal Infection (ICM) with the break down into definite, probable, possible, and unlikely [33].

Age, gender, diagnosis, laterality, BMI, ASA, approach, glenosphere size, cementation of the implant, comorbidities, and the medications taken by the patients were also recorded.

Microbiology culture

Each tissue sample was individually homogenized with a mortar and pestle and was inoculated on a PolyVitex agar plate (bioMérieux, Marcy-l'Etoile, France), a Schaedler agar plate (bioMérieux), and in thioglycolate broth (BBL™ Becton Dickinson, Le Pont de Claix, France). These cultures were incubated at 37 °C aerobically (with 5% CO_2) for seven days and anaerobically for 14 days. A culture was considered positive for *C. acnes* when two or more colonies were observed. Bacterial identification was performed by Matrix-Assisted Laser Desorption/Ionization-Time of Flight (MALDI-TOF) spectrometry (Brucker, Germany).

Molecular typing characterization of the *C. acnes* strains was performed following the protocol previously described [16, 28].

Statistics

For descriptive statistics, quantitative variables were described as mean and standard deviations. Qualitative variables were described with frequency tables (number and percentage).

Between group comparisons were performed for negative *vs*. positive cultures and from those positives. The statistical tests used for these comparisons were the chi-square or Fisher exact, as appropriate, for categorical variables and the Mann–Whitney *U* for continuous variables. The choice of this non-parametric option was because the violation of

normality assumption in a significant number of continuous variables.

Statistical analyses were performed using STATA 15.1. Results were considered statistically significant at p value < 0.05.

All the included patients signed informed consent to participate in this study. The study was approved by the ethical committee with number 2014/5996/I (CEIC-Parc de Salut Mar).

Results

This study included 136 females (84%) and 26 males (16%) with a mean age of 74 years (55–89). The indication for surgery was a rotator cuff–deficient shoulder in 123 cases (75.9%), an acute fracture in 22 cases (13.6%), and a fracture sequela in 17 cases (10.5%).

A total of 1380 cultures were obtained from the 162 primary RSA surgeries, and 96 of them turned to be positive for *C. acnes* (7.0%) for the deep tissues. Out of the 162, there were 25 patients with positive cultures. Thirteen of them were male and 12 were female. Males had an overall rate of positivity rate of 50% while it was 8.8% in the females ($p < 0.001$). Among the patients with positive cultures for *C. acnes*, eight belonged to subtype IA (33.3%), four to IB (16.7%), three to II (12.5%), four to IA and IB (16.7%), and two to II and IB (8.3%). Unfortunately, subtyping of the *C. acnes* isolated was not done in four patients.

The age was significantly higher in the non-positive group (75.4 vs. 71.7, $p = 0.008$). The ASA score was significantly higher in the positive group ($p = 0.007$). Overall, patients with positive cultures had a marginally significantly higher number of comorbidities. Antidepressant medication intake was more commonly detected in patients with negative *C. acnes* cultures, but that was because of the prevalence of this intake in females (Table 1).

The overall preoperative Constant score was not significantly different between those patients having *C. acnes*–positive cultures and those with negative cultures. However, there was a significant non-clinically relevant difference in pain. At the two year follow-up, the Constant score was not significantly different between those patients having *C. acnes*–positive cultures and those with negative cultures. Again, there was a significant non-clinically relevant difference in internal rotation. At the five year follow-up, the Constant score was not significantly different between those patients having *C. acnes*–positive cultures and those with negative cultures. Here, there was a significant non-clinically relevant difference in lateral rotation (Table 2).

No significant difference was noted at final follow-up relative to scapular notch development between the two groups. However, there were two *C. acnes* infections in the positive culture group. Both belonged to subtype II, clonal complex 53 and the K and SLST-type. According to the ICM criteria, in the *C. acnes* culture–positive group, there were 2 definite infections (8%), zero probable infection (0%), 11 possible infections (44%), and 12 unlikely infections (48%). According to the ICM criteria, in the *C. acnes* culture–negative group, there were zero definite infection (0%), zero probable infection (0%), zero possible infection (0%), and 137 unlikely infections (100%). None of the 11 possible infections in the *C. acnes* culture–positive group turned to definite infection during the five year follow-up period. Definite infection was determined following ICM criteria in two patients of the *C. acnes* culture–positive group, because of the presence of more than two *C. acnes*–positive cultures with phenotypically identical *C. acnes* at the revision surgery in both. In one of them also because of the presence of a sinus track, both patients presented pain and stiffness as well. [33] They required a two-stage exchange of the components. In the *C. acnes* culture–positive group, a third patient needed revision surgery because of unexplained pain, and

Table 1 Description of patients without *C. acnes* and patients with *C. acnes*. Values in mean and standard deviations

	C. acnes negative	*C. acnes* positive	*p* value
Age	75.44 (6.18)	71.72 (7.13)	0.008
BMI	28.72 (4.38)	27.45 (4.64)	0.206
ASA	2.18 (0.50)	2.48 (0.59)	0.007
Gender			0.001
Male	13 (9.5%)	13 (52.0%)	
Female	124 (90.5%)	12 (48.0%)	
Diagnosis			0.547
Cuff-arthropathy	106 (77.4%)	17 (68.0%)	
Acute fracture	17 (12.4%)	5 (20.0%)	
Fracture sequelae	14 (10.2%)	3 (12.0%)	
Laterality			0.056
Right	93 (67.9%)	12 (48.0%)	
Left	44 (32.1%)	13 (52.0%)	
Glenosphere size			0.319
38 ECC	96 (70.1%)	15 (60.0%)	
42	41 (29.9%)	10 (40.0%)	
Approach			0.222
Deltopectoral	64 (46.7%)	15 (60.0%)	
Antero superior	73 (53.3%)	10 (40.0%)	
Stem cemented			0.188
No	85 (62.0%)	12 (48.0%)	
Yes	52 (38.0%)	13 (52.0%)	
Comorbidities			0.035
No	111 (86.7%)	17 (68.0%)	
Yes	17 (13.3%)	8 (32.0%)	
Antidepressants treatment			0.028
No	66 (51.6%)	19 (76.0%)	
Yes	62 (48.4%)	6 (24.0%)	

BMI body mass index, *ASA* American Society of Anesthesiologists

Table 2 Preoperative, 2-, and 5-year follow-up functional outcomes measured with the constant score. Values in mean and standard deviations

	C. acnes negative	*C. acnes* positive	*p* value
CS preoperative	28.4 (14.55)	32.6 (16.12)	0.243
Pain	4.9 (2.44)	6.2 (2.59)	0.038
DLA	8.3 (3.48)	9.4 (3.53)	0.206
FE	3.6 (2.90)	4.3 (3.63)	0.386
ABD	3.2 (2.59)	3.6 (3.15)	0.610
LR	2.7 (2.99)	3.8 (3.04)	0.163
IR	3.8 (2.60)	2.9 (2.29)	0.148
Strength	1.7 (2.44)	2.4 (3.46)	0.271
FE°	77 (42.48)	84 (52.15)	0.550
CS 2-years	59.6 (10.84)	59.2 (10.74)	0.870
Pain	12.2 (2.55)	13.0 (2.35)	0.211
DLA	16.3 (2.80)	16.3 (3.09)	0.926
FE	7.3 (1.76)	7.2 (1.70)	0.902
ABD	6.7 (1.64)	6.3 (1.71)	0.324
LR	5.5 (1.70)	5.5 (1.84)	0.941
IR	4.8 (2.09)	3.1 (2.67)	0.001
Strength	6.6 (3.30)	7.7 (4.44)	0.160
FE°	129 (23.40)	127 (22.39)	0.642
CS 5-years	62.4 (9.28)	59.59 (15.39)	0.360
Pain	12.7 (1.97)	13.4 (2.03)	0.213
DLA	12.7 (1.97)	13.4 (2.03)	0.213
FE	7.4 (1.56)	6.8 (2.37)	0.197
ABD	6.7 (1.52)	6.1 (1.92)	0.191
LR	6.0 (0.90)	5.0 (2.71)	0.019
IR	4.9 (1.97)	4.1 (2.67)	0.179
Strength	7.3 (3.66)	8.5 (5.81)	0.326
FE°	131 (20.30)	118 (33.93)	0.049

CS Constant score, *DLA* daily living activities, *FE* forward elevation, *ABD* abduction, *LR* lateral rotation, *IR* internal rotation

the fourth one needed revision because of dislocation. One patient in the non-positive *C. acnes* group presented with aseptic loosening. Revision surgery was proposed but the patient chose not to proceed with further surgery. Any infection was recorded in the non-positive *C. acnes* group, not by *C. acnes* and any other different bacteria such as coagulase negative or others. The overall complication rate was significantly higher for the *C. acnes*–positive culture group (Table 3).

There were 12 patients with one positive culture for *C. acnes*, two with two positive cultures, three with three positive cultures, four with four positive cultures, two with five positive cultures, one with six positive cultures, and one with eight positive cultures. No correlation could be found between the number of positive cultures and the outcomes as measured with the Constant score or with the complication rate (Table 4).

Table 3 Complications in patients with positive cultures vs. patients without positive cultures for *C. acnes*

	C. acnes negative	*C. acnes* positive	*p* value
No complications	98.4%	83.3%	0.001
Infection	0 (0.0%)	2 (8.3%)	
Revision surgery	0 (0.0%)	1 (4.3%)	
Dislocation	0 (0.0%)	1 (4.3%)	
Aseptic loosening	1 (0.8%)	0 (0.0%)	
Scapular notch			0.287
Grade 0	84 (70.0%)	11 (50.0%)	
Grade 1	22 (18.3%)	6 (27.3%)	
Grade 2	10 (8.3%)	4 (18.2%)	
Grade 3	4 (3.3%)	1 (4.5%)	

Discussion

Patients that end up having *C. acnes*–positive cultures after primary reverse shoulder arthroplasty surgery do not differ in terms of clinical outcomes when compared to those patients that do not have positive cultures after the surgery. However, an increased number of complications were encountered in those patients when C. *acnes* contamination was found at the end of their primary surgery (16% *vs.* 0.8%).

The clinical meaning of *C. acnes*–positive cultures found at the end of primary shoulder prosthetic surgeries remains unclear. The prevalence of these positive cultures differs depending on many factors like the gender ratio (having males higher prevalence ratio), the age of the patients, the number of cultures obtained, the method of obtaining the cultures, and the number of colonies needed to declare a *C. acnes*–positive culture [4–6, 10, 17, 22, 26, 30, 34]. Currently, it is not completely clear what should be called *C.*

Table 4 Correlation of outcomes and complications according to the number of positive cultures for *C. acnes*

	Mean number of positive cultures (STD)	*p* value
Complications	3.5 (3.1)	0.406
No complications	2.3 (1.6)	
Infection	4.5 (4.9)	0.881
Revision surgery	2.0 (–)	
Dislocation	3.0 (–)	
	Correlation with Constant score	*p* value
	rho	
Constant score preoperative	0.245	0.299
Constant score at 2 years	0.337	0.135
Constant score at 5 years	0.372	0.190

STD standard deviation

acnes contamination and what should be called infection. Indeed, some authors feel that too much attention has been paid to the presence of *C. acnes* while others feel that *C. acnes* detection at the end of the primary surgery is a source of concern. Nevertheless, there is a recent publication showing that the *C. acnes* clinical strain detected at the end of primary surgeries can be responsible for periprosthetic joint infections [28].

The commonly used antibiotic prophylaxis (intravenous Cefazolin 2 g) and the standard skin preparation (2% chlorhexidine gluconate and 70% isopropyl alcohol) fail to completely eradicate *C. acnes* from skin surfaces and most likely from deep tissues, and different *C. acnes* phylotypes living in the sebaceous glands can be present at the end of primary shoulder surgery at different rates depending on the type of surgery, the gender and age of the patients included, the number of the cultures taken, and the definition of culture positivity [1, 6, 14, 16]. In the present study, the rate of colonization of primary reverse shoulder arthroplasty has been found to be of 15.4%. This rate may reflect the characteristics of the sample, mostly composed of elderly females.

Patients suffering a shoulder prosthetic infection caused by *C. acnes* usually do not show skin reactions such as swelling, erythema or sinus tract. Blood tests such as C-reactive protein (CRP), or the erythrocyte sedimentation rate (ESR), and other biomarkers available can also be normal [1, 24]. Pain and stiffness can be the only symptoms present in chronic *C. acnes* infections [30]. In the present study, patients having contamination with *C. acnes* found at the end of primary surgery with a reverse shoulder prosthesis do not have more pain at midterm follow-up when compared with patients having negative cultures. Patients with positive cultures have a significant but non-clinically relevant pain difference before surgery (6.2 vs. 4.9 in a 15-point scale). Nevertheless, both groups significantly improve pain without significant differences between them at the two and five year follow-up (13 *vs*. 12.7 points at the 2-year follow-up and 13.4 and 12.7 at the five year follow-up).

Patients with positive cultures for *C. acnes* do not have worst outcomes when compared to patients with negative cultures in forward elevation or in abduction. At the two year follow-up, a significant but clinically non-relevant difference could be found with reference to internal rotation (3.1 vs. 4.8 in a 10-point scale). At the five year follow-up, a significant but clinically non-relevant difference could be found regarding external rotation (5.0 vs. 6.0 on a 10-point scale). Patients having positive cultures for *C. acnes* do not seem to present with any more stiffness at the midterm follow-up when compared to those having negative cultures. However, and because of the small number of patients having positive *C. acnes*, the study is not powerful enough to give a strong conclusion on that.

Patients that have *C. acnes*–positive cultures found at the end of primary reverse shoulder arthroplasty do not have more pain or stiffness than patients having negative cultures. However, they do have a significantly higher rate of complications. In the present study, two patients with positive *C. acnes* cultures developed an infection that required a two-stage exchange of the components. Another patient with positive cultures required revision surgery because of unexplained pain, and a fourth patient presented a dislocation of the reverse shoulder arthroplasty that required an open reduction and an exchange of the components. In the culture negative group, only one patient developed aseptic loosening of the glenoid component and went on to refuse a component exchange. Interestingly, the number of positive cultures for *C. acnes* does not correlate with the outcomes or with the complications rate, meaning that patients having many positive cultures do not do worse than those having only one positive culture. Zmistowski et al., in a recent publication, also failed to find significant differences in clinical outcomes when comparing patients with positive cultures *vs.* those without positive cultures. Moreover, they also did not find significant differences in the complication rate between the two cohorts [31].

Comorbidities seem to correlate with *C. acnes* contamination. Consequently, patients with positive cultures have significantly higher ASA score values. However, the BMI, diagnosis, laterality, glenosphere size, approach, and use of cement to fix the humeral component do not seem to correlate with *C. acnes* contamination.

Although the clinical meaning of the presence of *C. acnes* contamination at the end of primary shoulder arthroplasty surgery is not clear, it represents a cause of concern since the number of complications at the midterm follow-up of the patients having positive cultures seems to be higher than in patients with negative cultures. The fact that skin preparation and antibiotic prophylaxis are suboptimal in eradicating *C. acnes* from skin might push us to search for better alternatives [1, 6, 11, 14]. Recent studies have shown the efficacy of the topical application of benzoyl peroxide in reducing the burden of the *C. acnes* in skin. However, we still do not know whether this reduction will result in a reduction in the number of infections or complications [8, 35–37].

Among the strengths of the study is the uniformity of the methods of obtaining the cultures, the homogeneity of the patients included (primary reverse shoulder prostheses), and the length of the follow-up. As for the weaknesses, there is the retrospective nature of the study and the fact that only 25 patients turned out to be positive for *C. acnes* even though 162 patients were included. The purpose of the study was to know the influence of *C. acnes* in primary reverse shoulder arthroplasty, and that is the reason why females are much more predominant in the population included. The higher number of complications found in the *C. acnes*–positive group could

be influenced by the fact that males were more predominant in the *C. acnes*–positive group, being gender a confounder; however, and because of the small number of complications, a multivariate analysis could not be done. Although the follow-up was 5 years, some complications, including infection, can show up after a longer follow-up period.

In conclusion, patients ending primary shoulder arthroplasty surgery with positive cultures for *C. acnes* do not have worse clinical outcomes when compared to patients with negative cultures. However, a greater number of complications were found in those patients having *C. acnes*–positive cultures.

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Author contribution All authors contributed to the study conception and design. Material preparation, data collection, and analysis were performed by Carlos Torrens, Raquel Marí, Lluís Puig-Verdier, Fernando Santana, Albert Alier, Eva García-Jarabo, Alba Gómez-Sánchez, and Stèphane Corvec. The first draft of the manuscript was written by Carlos Torrens and all authors commented on previous versions of the manuscript. All authors read and approved the final manuscript.

Declarations

Ethics approval The study was approved by the ethical committee with number 2014/5996/I (CEIC-Parc de Salut Mar).

Consent to participate Informed consent was obtained from all individual participants included in the study.

Consent to publish The authors affirm that human research participants provided informed consent for publication.

Competing interests The authors declare no competing interests.

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