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Cutibacterium acnes in primary reverse shoulder arthroplasty: from skin to deep layers

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Background: The aim of this study was to determine the presence of *Cutibacterium acnes* (formerly *Propionibacterium acnes*) on the skin and in deep tissue in a real clinical scenario of primary reverse shoulder arthroplasty.

Methods: This prospective study included 90 primary reverse shoulder arthroplasties, and 12 cultures were obtained from each patient. Each sample was homogenized and used to inoculate PolyVitex (bioMérieux, Marcy-l'Etoile, France) agar and Schaedler (bioMérieux) agar plates. The same procedure was also followed with a thioglycolate broth. Culture was considered positive for *C acnes* when 2 or more colonies were observed. Total DNA from *C acnes* isolates was extracted using the InstaGene Matrix (Bio-Rad Laboratories, Hercules, CA, USA) method. The phylotype was determined, and single-locus sequence typing was done on all isolates.

Results: We obtained 1080 tissue cultures from the 90 patients included, and 62 of those tissue cultures (5.7%) were positive for *C acnes*. There were 22 *C acnes*–positive tissue cultures before prosthesis implantation and 40 after implantation. *C acnes* was isolated in 17 patients (18.8%). We sent 38 positive samples for blinded phylotyping, single-locus sequence typing, and multi-locus sequence typing type determination. Many of the clusters isolated belonged to phylotype IB and clonal complex (CC) 36 or phylotype II and CC53.

Discussion: In the real scenario of patients undergoing primary reverse shoulder arthroplasty using antibiotic prophylaxis and standard preoperative skin preparation with chlorhexidine, *C acnes* was isolated in the deep layers of 18.8% of the patients. The *C acnes* K1 and K2 subtypes (belonging to phylotype II and CC53), reported to be commonly involved in prosthetic joint infection, were usually isolated.

Level of evidence: Level III; Cross Sectional Design; Epidemiology Study

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Keywords: Reverse shoulder arthroplasty; *Cutibacterium acnes*; *Propionibacterium acnes*; primary surgery; infection; complications

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During the last decade, the number of total shoulder arthroplasties (TSA) has increased exponentially, especially since the introduction of the reverse shoulder arthroplasty (RSA).[20] Although the infection rate in primary shoulder arthroplasty has been reported to be less than 2% (1.6% in TSA and 2.2% in RSA), prosthetic infection remains one of the most dreaded complications due to increased morbidity and the substantial costs associated with it.[13,43]

In shoulder arthroplasty, unlike what happens in hip and knee arthroplasty, *Cutibacterium acnes* (formerly *Propionibacterium acnes*) is one of the most commonly isolated organisms in chronic infections.[24,40,41] *C acnes* is well known as a skin commensal but has also been associated with the chronic skin disease acne vulgaris.[19] However, this microorganism is often an opportunistic pathogen and is responsible for infections involving devices, especially joint implant–associated infection.[1,36]

Recent studies have indicated that the presence of *C acnes* on the shoulder skin area and around the acromion is higher than in other body regions such as the knee or the hip.[33] The incidence of *C acnes* on the shoulder skin surface before presurgical skin preparation has been reported to be as high as 18.6%.[37] After presurgical skin preparation with different solutions, a persistence of *C acnes* is observed regardless of the solution applied.[15,37]

Some controversy still exists about the origin of the *C. acnes* isolated in deep cultures of the shoulder. Although some authors advocate for transectional inoculation,[34] others suggest that *C acnes* may be an inhabitant of the deep layer tissue.[17,23]

The presence of *C acnes* on and in the skin dermis around the shoulder, even after standard skin preparation and prophylactic antibiotic, and in the deep tissue in primary shoulder replacement is yet to be clearly defined. Indeed, the data reported are confusing because of the inclusion of treatments other than primary shoulder replacement, such as arthroscopy, as well as sex and age bias.[17,30,37]

The aim of this study was to determine the presence of *C acnes* in a real clinical scenario of primary RSA, in and on the skin and in deep tissue.

Materials and methods

Study design

This prospective study included all primary RSAs performed from January 2015 to December 2016 by a single shoulder surgeon in a tertiary center. In all the cases, a Delta X-tend (DePuy, Warsaw, IN, USA) was implanted. The inclusion criteria were any indication for primary reverse arthroplasty such as cuff tear arthropathy, an acute fracture, or fracture sequelae in patients aged older than 18 years who agreed to participate in the study. The exclusion criteria included an active infection, an invasive shoulder treatment in the last 6 months, an Arthro-scan or a magnetic resonance imaging arthrogram in the last 6 months, previous shoulder operations, and revision cases.[7] The inclusion of different etiologies may have had an
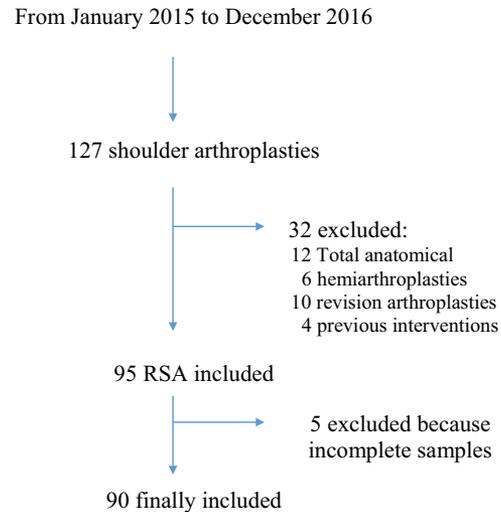

Figure 1 Flowchart of patient inclusion.

influence on the heterogeneity of the population but may also reflect the common indications for RSA.

Patient characteristics

During the study period, 127 shoulder prostheses operations were performed, and 32 were excluded because they did not meet the criteria. Twelve were anatomic TSAs, 6 were hemiarthroplasties, 10 were revision arthroplasties, and 4 had undergone previous shoulder interventions.

Consequently, 95 patients met the inclusion criteria. Five patients were subsequently excluded because all of the cultures were not obtained (Fig. 1) The 90 patients (74 women, 16 men) finally included were a mean age of 74.6 (standard deviation [SD] 6.2) years. The indications for RSA were cuff-tear arthropathy in 58 patients, an acute fracture in 20, and fracture sequelae in 12.

An anterosuperior skin incision was used in 49 patients, and a deltopectoral approach was used in 41. Even though 2 different incisions were used, the area from which the samples were collected was approximately the same. The anterosuperior incision samples were collected at the inferior edge of incision near the coracoid process. The deltopectoral incision samples were collected at the superior part of the incision also near the coracoid process.

All patients received preoperative antibiotic prophylaxis with intravenous cefazolin (2 g) 30 to 60 minutes before the incision. Intravenous vancomycin (1 g) 60 minutes before incision was used in 5 patients with penicillin allergy. The skin was prepared twice with the Bactiseptic solution (Vesismin Chemicals, Barcelona Spain), which is composed of 2% chlorhexidine gluconate and 70% isopropyl alcohol.

Tissue samples recovering

Twelve cultures were obtained from each patient following the Oxford protocol (opening a new sterile set of instruments for each biopsy).[3]

Once the skin was prepared and before the skin incision was performed, 2 biopsies (samples 1 and 2) for culture were obtained with a Kai Medical (Kai Industries Co. Ltd., Seki City, Japan) 3-mm skin punch. The samples included all the dermis and subcutaneous tissue.

These skin samples were taken from the anterior edge of the incision if the superolateral approach was performed and from upper edge of the incision if the deltopectoral approach was used. Both biopsy samples were taken 5 mm from each other. Immediately after the skin incision was done, a sterile instrument was used to obtain another subcutaneous tissue biopsy (sample 3) culture.

Upon reaching the humerus, 2 more samples (samples 4 and 5) were taken from the bursa over the greater tuberosity. Upon reaching the glenoid, 2 more samples (samples 6 and 7) were taken around the long head of the biceps insertion. After the components of the arthroplasty were in place, 2 samples (samples 8 and 9) were obtained from the glenoid, 2 (samples 10 and 11) from the humeral side, and 1 (sample 12) from the subcutaneous tissue.

Microbiology culture

Each tissue sample was individually homogenized with a mortar and pestle and used to inoculate a PolyVitex agar plate (bioMérieux, Marcy-l'Etoile, France) and a Schaedler agar plate (bioMérieux). The same procedure was followed in a thioglycolate broth (BBL; Becton Dickinson, Le pont de Claix, France). These cultures were incubated for 7 days at 37°C aerobically (with 5% CO_2) and anaerobically for 14 days. A culture was considered positive for *C acnes* when 2 or more colonies were observed. Bacterial identification was performed by matrix-assisted laser desorption/ionization-time of flight spectrometry (Bruker, Hamburg, Germany).

Molecular typing characterization of *C acnes* strains

DNA extraction
Total DNA from *C acnes* isolates was extracted using the InstaGene Matrix method (Bio-Rad Laboratories, Hercules, CA, USA) in accordance with the manufacturer's instructions. After centrifugation, the supernatant was used as the DNA template for polymerase chain reaction analysis.[42]

Phylotype determination
The phylotype was determined based on the method recently developed by Barnard et al.[6]

Single-locus sequence typing type determination
The single-locus sequence typing (SLST) was performed on all isolates as described by Scholz et al.[39] This simple scheme is based on partial sequencing of a DNA sequence of 484 base pairs that can resolve all the recently described phylogenetic clades. Reference sequences for alignment and trimming are found in the web-interface typing tool at http://medbac.dk/slst/pacnes.

Multilocus sequence typing type determination
Multilocus sequence typing (MLST) was performed on all isolates as described by Kilian et al.[18] This scheme is based on partial sequences of 9 housekeeping genes comprising 4287 nucleotides and is available at http://pacnes.mlst.net/.

Statistics

Categorical variables are described with frequencies and percentages, and continuous variables are expressed as the mean and SD.

The Fisher exact test was used to compare qualitative variables. *P* values of <.05 were considered statistically significant. All statistical analyses were conducted with SPSS 17 software (IBM, Armonk, NY, USA).

Results

A total of 1080 tissue cultures were obtained from the 90 patients included, and 62 (5.7%) were positive for *C acnes*. There were 22 tissue cultures positive for *C acnes* before prosthesis implantation and 40 after prosthesis implantation. There were 19 skin-positive cultures and 43 deep layer-positive cultures (12 before the arthroplasty was implanted and 31 after the arthroplasty was implanted). *C acnes* was isolated in 17 (18.8%) of the 90 included patients, and 7 (7.7%) presented skin-positive cultures. A *C acnes* culture positive for surface skin and deep layers was obtained in 7 (7.7%) of those patients, whereas a *C acne* culture positive only in deep layers was seen in 10 patients (11.1%). For the entire sample, there was a significant male predominance ($P < .0001$). Of the 7 patients with positive cultures on the skin and in deep layers, 5 were men and 2 were women. Among the 10 patients with positive cultures only in deep layers, 4 were men and 6 were women. However, that did not reach significance ($P = .335$). The results for patients with cultures positive for *C acnes* are summarized in Table I.

There were no significant differences in the presence of *C acnes* with regard to etiology ($P = .644$), deltopectoral vs. anterosuperior approach ($P = .175$), or time of surgery ($P = .403$; Table II). None of the patients who were administered vancomycin presented a positive culture for *C acnes*.

Blinded phylotyping, SLST, and MLST type determination were performed in 38 positive samples that belonged to 12 different patients. Many of the clusters isolated belonged to phylotype IB and clonal complex (CC) 36 or phylotype II and CC53. Detailed data on phylotype, SLST type, and MLST type determination are presented in Table III.

Patient 8, a 72-year-old man who received an RSA due to cuff arthropathy, presented a positive culture for *C acnes* that belonged to the K1 SLST type (phylotype II and CC53). An infection developed 6 months after the operation that required a 2-stage operation. Cultures obtained during the revision operation were all positive for *C acnes* that belonged to the same phylotype II, CC53 and SLST type K1. No other infection was registered at a minimum follow-up of 1 year.

Discussion

Controversy remains around different aspects of *C acnes*, including the amount of *C acnes* persistent on and in the skin. The question remains unanswered whether *C acnes* deep layer infection is caused by skin transection during surgery or whether *C acnes* can be considered a commensal of deep layers. The significance of unexpected *C acnes*–positive

Table I Characteristics of the patients with *Cutibacterium acnes* positive cultures

Patient	Age (yr)	Sex	Diagnosis	Approach	Length of surgery (min)	Positive samples, No.					
						Skin	HBP	GBP	HAP	GAP	SubAP
1	78	F	AF	DP	117	0	1	0	0	0	0
2	76	F	CA	AS	90	0	1	0	0	0	0
3	67	F	AF	DP	96	0	0	0	1	0	0
4	59	M	FS	AS	103	1	1	0	2	2	0
5	78	M	CA	AS	104	0	1	0	1	0	0
6	76	M	CA	AS	63	0	0	0	2	2	1
7	79	M	AF	AS	68	1	2	1	2	2	1
8	72	M	CA	DP	90	1	1	2	2	2	0
9	82	F	CA	DP	90	2	0	0	1	2	1
10	66	F	AF	AS	75	0	0	0	0	0	1
11	73	M	AF	DP	83	0	0	0	1	1	0
12	69	M	CA	AS	67	1	1	0	1	2	1
13	82	F	AF	DP	86	0	0	1	0	0	0
14	58	F	CA	DP	60	0	0	0	0	0	1
15	76	F	CA	DP	91	3	0	0	0	1	1
16	71	M	CA	DP	89	0	0	0	1	0	1
17	79	M	AF	DP	89	1	0	0	2	1	1
Percentages		M, 52	CA, 53	DP 59		41	41	18	65	53	53
		F, 47	AF, 41	AS 41							
			FS, 6								

HBP, humerus before prostheses; *GBP*, glenoid before prostheses; *HAP*, humerus after prostheses; *GAP*, glenoid after prostheses; *SubAP*, subcutaneous after prostheses; *F*, female; *AF*, acute fracture; *DP*, deltopectoral; *CA*, cuff arthropathy; *AS*, anterosuperior; *M*, male; *FS*, fracture sequelae.

Table II Characteristics of the patients with and without *Cutibacterium acnes*–positive cultures

Variables	With + cultures (n = 17)	Without + cultures (n = 73)	*P* value
Age, mean (SD), yr	73.1 (7.63)	75.0 (6.06)	.429
Diagnosis, %			
Cuff arthropathy	47.0	68.4	
Acute fracture	41.1	17.8	
Fracture sequelae	11.7	13.6	.370
Approach, %			
Anterosuperior	41.2	57.5	
Deltopectoral	58.8	42.5	.796
BMI, mean (SD) kg/m^2	30.7 (4.81)	29.1 (4.27)	.812
Length of surgery, mean (SD), min	85.9 (15.3)	73.2 (17.5)	.403

SD, standard deviation; *BMI*, body mass index.

cultures that grow after the standard culturing period may have its root in the same unresolved issue.[8,11]

The present study found that *C acnes* was present in deep layers at the end of the operation in 18.8% of the patients undergoing primary RSA. Moreover, subtypes K1 and K2 belonging to phylotype II and CC53, which have been reported to be frequently involved in prosthetic joint infection (PJI), were commonly isolated among these patients.[4]

The implication of *C acnes* in the shoulder has recently been the topic of many publications, but the reported data are confusing.[2,10,12,14,16,17,21,25,27-30,32,33] Patel et al[33] described a higher incidence of *C acnes* on shoulder skin compared with that

obtained on hip or knee skin using surface swabs. They also stated that men had a higher bacterial burden than women. This result might be explained by the predominance of hairs and perspiration on men's shoulders.[33] *C acnes* is more commonly found on the shoulder because it is a common ecological niche with sebaceous glands with hair follicles.[5]

Some studies suggest that those host factors (such as sex and shoulder location) may predispose to infection.[1,17,27,28,35] Men significantly present more positive cultures for *C acnes* than women after surgical skin preparation and antibiotic prophylaxis, corroborating preexisting data.[33] However, this difference is not present if only patients with positive *C acnes*

Table III Molecular typing characterization of *Cutibacterium acnes* strains

Patient	Age (yr)	Sex	Diagnosis	Approach	Sample location	Phylotype	MLST	SLST
1	78	F	AF	DP	HBP 1	IB	CC36	H1
2	76	F	CA	AS	HBP 2	II	CC53	K2
4	59	M	FS	AS	Skin 3	IB	CC36	H8
					HBP 1	IA1	CC28	D1
					HAP 1	IB	CC36	H8
					HAP 2	IB	CC36	H8
					GAP 1	IA1	CC28	D1
					GAP 2	IB	CC36	H8
8	72	M	CA	DP	Skin 3	II	CC53	K1
8*	72	M	CA	DP	Débridement	II	CC53	Neg
					Débridement	II	CC53	K1
					Débridement	II	CC53	K1
					Débridement	II	CC53	K1
					Débridement	II	CC53	K1
					Débridement	II	CC53	K1
					Débridement	II	CC53	K1
9	82	F	CA	DP	Skin 4	IA1	CC28	D1
11	66	F	AF	AS	Skin 4	IB	CC36	D1
12	73	M	AF	DP	GAP 1	IA1	CC18	A1
13	69	M	CA	AS	Skin 1	IA1	CC28	D1
					Skin 3	IA1	CC18	A1
					HBP 2	IB	CC36	H1
					HAP 1	IB	CC36	H1
					HAP 2	IB	CC36	H1
					GAP 1	IB	CC36	H1
					Skin 4	IB	CC36	H1
14	58	F	CA	DP	Skin 4	IA1	CC18	A1
15	76	F	FS	DP	Skin 1	II	CC53	K1
					Skin 2	II	CC53	K2
					HAP 2	II	CC53	K1
					Skin 4	II	CC53	K1
16	71	M	CA	DP	GAP 2	IA1	CC18	A1
					Skin 4	IB	CC36	H1
17	79	M	CA	DP	Skin 1	II	CC53	K1
					HAP 2	II	CC53	K1
					GAP 1	IB	CC36	H1
					GAP 2	II	CC53	K1
					Skin 4	II	CC53	K1

MLST, multi-locus sequence typing; *SLST*, single-locus sequence typing; *F*, female; *AF*, acute fracture; *DP*, deltopectoral; *Neg*, negative; *HBP*, humerus before prostheses; *CC,* clonal complex; *CA*, cuff arthropathy; *AS*, anterosuperior; *M*, male; *FS*, fracture sequelae; *HAP*, humerus after prostheses; *GAP*, glenoid after prostheses.

*Patient 8 presented *C acnes* CC53 K1 in the skin during the index surgery and revision was required because of infection. Samples obtained during the revision (débridement) showed the presence of *C acnes* CC53 K1.

in deep layer samples are included. Moreover, there seemed to be a tendency to female predominance but that did not reach significance. Surprisingly, no significant difference was observed in the approach used (deltopectoral vs. anterosuperior) compared with the Hudek et al[17] results. This difference can be explained due to the different populations included. Although there was a male predominance in the Hudek et al[17] study, there was a female predominance in the present study.

Confusing data on the presence of *C acnes* in the skin have been reported because some studies mixed different populations (patients undergoing arthroscopy, instability repairs, proximal humeral fractures, and shoulder arthroplasty), and other studies included younger patients or were predominantly male.[22,30,33,35,37] A further source of controversy is related to whether the microorganisms isolated from chronic infections are deep tissue colonizers or are transported from the skin during surgery.[17,23,35]

Levy et al[22] were the first to suggest that *C acnes* might play a role in the development of primary osteoarthritis after isolating *C acnes* in 41.8% of the patients undergoing primary

shoulder joint replacement. Later on, Hudek et al[17] also found *C acnes* in more than one-third of patients undergoing first-time shoulder surgery. The present study did not include primary; therefore, no conclusion can be drawn about the role *C acnes* plays in the development of osteoarthritis. However, we failed to find a significant difference among the different etiologies included and the presence of *C acnes*.

Maccioni et al[25] obtained a low rate of *C acnes* from the glenohumeral joint in primary total shoulder replacement using a strict specimen collection technique in 32 patients (18 women, 14 men) with an average age of 75 years. Only 3.1% of the specimens were positive for *C acnes*, without evidence of infection.[25] The results of that study are in concordance with the results of the present study (5.5% samples) in similar populations even though the samples were obtained from different anatomic regions.

Koh et al[21] found a higher rate of *C acnes* (73%) in primary shoulder arthroplasty among 30 patients. Patient characteristics were slightly different from that of the present study, however, because 20 of those patients had primary osteoarthritis and 15 of the 30 had undergone previous steroid injections.[21] Wong et al[44] recently found a similar rate of *C. acnes* in patients undergoing primary shoulder arthroplasty. At least 1 positive culture was found in 38% of the patients in that cohort, with *C acnes* involved in 67% of the positive cultures.[44]

Morrison et al[31] proposed that using the surgical skin preparation twice before skin incision in knee and hip arthroplasties resulted in a significant reduction in the rate of periprosthetic joint infection in patients undergoing elective surgery. The present study is the only one that did surgical skin preparation twice before skin biopsy samples were taken. That fact may have had an influence on the low rate of *C acnes* isolated from skin. However, further studies are called for to confirm this because there was no control group with a once-only skin disinfection protocol.

The presence of *C acnes* in deep layer samples in nearly 20% of the patients after primary RSA surgery is of great concern, especially because the *C acnes* isolated belongs to clusters commonly involved in PJI in many cases.[4] However, skin contamination is suspect when only 1 or 2 samples taken during the operation are positive. Indeed, the molecular characterization revealed specific *C acnes* clusters, in particular *C acnes* belonging to phylotype IA1, CC18, and SLST type A1, or phylotype IB, CC36, and SLST type H8, that are quite often detected on skin surface in during acne. On the contrary, when several samples are positive, skin contamination via surgery can be suspect.[9,34]

Regarding the patient in whom an infection was diagnosed 6 months after the surgery, the *C acnes* isolated in both the primary surgery and during the revision surgery belonged to the same K1 cluster (phylotype II, CC53). Although no conclusion can be drawn from a single case, it was a concern that the same cluster isolated in primary surgery was also isolated in the revision surgery.

To the best of our knowledge, this study represents the first with an accurate molecular characterization of the strains. Further studies will be needed to find out whether infection will develop over time in these patients with *C acnes* present in deep layers. Hopefully, newly developed diagnostic tests will be able to detect the presence of *C acnes* more quickly after shoulder surgery.[26,38]

The present study has some limitations. The inclusion of 2 different approaches and the site where the biopsy samples were taken was arbitrarily decided. Because 2 different approaches (anterosuperior and deltopectoral) were used to implant primary reverse arthroplasties, biopsy samples were taken in the area where the 2 incisions met. Nevertheless, no significant difference in positive cultures was noted relative to etiology. The use of different approaches and the inclusion of different etiologies may both have influenced the results.

Even though samples were obtained in approximately the same zone, the length of the incision may have an effect on contamination during surgery in the same way that the inclusion of different etiologies may have an effect on the results because of known or unknown circumstances. Then again, this study was not powered to detect this possibility.

No significant differences were noted between the groups; however, we cannot guarantee that increasing the sample size would make for notable differences.

Not all of the positive cultures could be characterized by strain molecular typing because the analysis was done after all of the samples were collected and some of them were lost in the microbiology laboratory.

Among the strengths, there is the size of the sample, all the patients included underwent primary RSA, the use of the dermal punch instead of skin swabs to collect the samples, and the use of the Oxford protocol to collect the cultures.

Conclusions

In the real scenario of patients undergoing primary RSA using antibiotic prophylaxis and standard preoperative skin preparation with chlorhexidine, *C acnes* can be isolated in the deep layer tissue in 18.8% of the patients. Subtypes K1 and K2 (belonging to phylotype II and CC53) of *C acnes*, which have been reported to be frequently involved in PJI, are commonly isolated among these patients.

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Disclaimer

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