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Cutibacterium acnes in Shoulder Surgery: Is It a Significant Risk Factor for Postoperative Infection?

Jong Pil Yoon, MD, Kang-San Lee, MD, Sung-Jin Park, PhD, Dong-Hyun Kim, MD, Junsung Kim, MD, Yoon Seong Choi, MS*, Hyun Joo Lee, MD, Seok Won Chung, MD†

Department of Orthopedic Surgery, Kyungpook National University Hospital, Daegu,
**Department of Carbon Hybrid Fiber Science, Kyungpook National University, Daegu,*
†Department of Orthopedic Surgery, Konkuk University Medical Center, Seoul, Korea

Cutibacterium acnes, a commensal, lipophilic, anaerobic Gram-positive bacterium, is well known for its potential to cause infections, particularly in the field of orthopedics, notably in the shoulder. However, its indolent strain nature presents challenges in the diagnosis of the bacterium using clinical, laboratory, and culture-based methods. There are controversies surrounding its actual threat as an infection-causing agent, leading to an incomplete consensus on treatment strategies after the infection. Furthermore, research is ongoing to explore preventive procedures before the onset of infection. This review aimed to comprehensively explore the diagnosis and treatment of *C. acnes* and determine whether it is a risk factor for shoulder joint infections.

Keywords: *Cutibacterium acnes, Shoulder joint, Surgical site infection*

Cutibacterium acnes, a bacterium with commensal, lipophilic, anaerobic, and Gram-positive properties, is critical in the regulation of skin homeostasis and prevents colonization from other harmful pathogens.[1] It can cause infection on its own; furthermore, it is widely recognized as an opportunistic pathogen and a causative agent of acne vulgaris.[2] In the field of orthopedics, *C. acnes*, with its commensal characteristics, has been reported to potentially cause infections intraoperatively, leading to conditions such as septic arthritis, osteomyelitis, and discitis.[3] In particular, it is associated with periprosthetic joint infection (PJI) in relation to shoulder surgery, and it has been reported that 76% of shoulder PJIs are caused by *C. acnes*.[4]

Despite these considerations, the diagnosis of *C. acnes* infections remains challenging, mainly due to the indolent nature of the bacterial strain.[5] In joint infections suspected to be caused by indolent microbiome, healthcare professionals often face difficulties in identifying infection signs or obtaining specific laboratory findings.[6] In addition, confirming the presence of *C. acnes* by culture is a time-consuming process, further contributing to delayed diagnosis.[7]

Even if the presence of *C. acnes* is confirmed by culture, it remains unclear whether the infections were indeed caused by this bacterium. Some studies have reported positive cultures of *C. acnes* without clear manifestations of active infection.[8] Furthermore, another study reported the use of postoperative antibiotic treatment in response to unexpected culture positivity for *C. acnes*.[9] This ambiguity regarding the potential risk for infection makes it difficult to establish a consensus on the appropriate course and aggressiveness of treatment.

While treatment strategies for *C. acnes* infections have not been firmly established, surgical intervention has been reported to be beneficial in cases of severe infection and difficult implant salvage.[10] In addition, the ability of *C. acnes* to form biofilms poses challenges to conventional antibiotic therapies.[11] Due to diagnostic and treatment difficulties, many surgeons have focused on preventive measures before surgery. The commensal nature of *C. acnes* on the skin suggests that various disinfection methods help

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Correspondence to: Kang-San Lee, MD
Department of Orthopedic Surgery, Kyungpook National University Hospital, 130 Dongdeok-ro, Jung-gu, Daegu 41944, Korea
Tel: +82-53-200-5628, Fax: +82-53-422-6605
E-mail: lksan202@gmail.com

reduce the risk of infection.[12]

This review aimed to comprehensively explore the diagnosis and treatment of *C. acnes* infections and determine whether it poses a genuine risk for shoulder joint infections.

DIAGNOSIS

Clinical Manifestation

Postoperative shoulder infections caused by *C. acnes* have a vague clinical presentation. The common symptoms include low-grade pain, discomfort, and persistent stiffness, particularly after arthroplasty.[13] General symptoms such as fever are relatively rare. These symptoms tend to develop gradually, contributing to the insidious nature of *C. acnes* infections.[14] Thus, distinguishing routine postoperative discomfort from *C. acnes* infections is challenging.

To address this diagnostic difficulty, the 2018 International Consensus Meeting on Orthopedic Infections introduced a new scoring system specifically for diagnosing PJI in the shoulder.[15] This system encompasses various criteria including clinical signs, laboratory results, and microbiological findings. It assigns points to different parameters such as elevated serum markers, positive histology, presence of a sinus tract, and positive cultures. The incorporation of this system into clinical practice aids in the more accurate and timely diagnosis of PJIs, particularly those caused by organisms like *C. acnes* that have subtle presentations.

Laboratory Findings

Unlike typical suppurative infections caused by bacteria, key laboratory markers, such as white blood cell (WBC), C-reactive protein (CRP), and erythrocyte sedimentation rate (ESR), do not significantly increase in *C. acnes* infections.[16] Villacis et al.[17] reported that even in patients with confirmed postoperative *C. acnes* infections, when cutoff values were used for these laboratory markers (CRP > 10 mg/L, ESR > 30 mm/hr, and WBC > 11.0 $\times 10^9$), ESR exhibited sensitivity and specificity of 21% and 65%; CRP, 0% and 95%; and WBC count, 7% and 95%, respectively.

Recent research has investigated various alternative laboratory markers, particularly interleukin (IL), leukocyte esterase, and synovial fluid alpha-defensin. However, Grosso et al.[18] reported that serum IL-6 exhibited a low sensitivity of 12%, making it an ineffective diagnostic tool. Furthermore, Frangiamore et al.[19] have suggested that synovial fluid IL-6 is a more valuable marker than serum IL-6 in shoulder arthroplasty patients. On the other hand, leukocyte esterase and alpha defensin have shown promise in diagnosing periprosthetic shoulder infections. Unter Ecker et al.[20] reported that leukocyte esterase exhibited sensitivity and specificity of 50% and 87%, respectively, whereas alpha defensin exhibited 75% and 96%, respectively.

Culture

Culture of *C. acnes* presents unique challenges contributing to diagnostic complexity. The slow growth rate of the bacterium indicates that culture can take an extended period of time, typically ranging from 5 to 10 days. Namdari et al.[21] retrospectively evaluated a cohort of 90 patients who underwent shoulder arthroscopy, of whom 18 were confirmed to have at least 1 positive culture sample. The mean time required to isolate *C. acnes* through culture was 6.5 days (range, 5–8 days). In another study conducted by Frangiamore et al.,[22] 46 patients who developed infection following shoulder arthroplasty were assessed. The mean time for culture confirmation was 13.1 days (range, 8–26 days). Similarly, in the study by Dilisio et al.,[23] the mean time was 10.1 days (range, 5–18 days). Dodson et al.[24] reported a mean time of 9 days (range, 8–10 days), whereas Kelly et al.[25] reported 7 days (range, 4–10 days). These results are summarized in Table 1.[21-25] Kim et al.[26] performed two-stage revision arthroplasty in 11 cases of shoulder infection, and they did not find any cases of *C. acnes* in the cultures. The authors explained that this might be due to the incubation period for organisms was routinely only 3

Table 1. Summary of Culture Confirmation Times in Shoulder Infection

Study	Number of patients	Type of procedure	Mean time for culture growth (day)	Range (day)
Namdari et al. (2020)[21]	18	Arthroscopy/primary arthroplasty	6.5	5–8
Frangiamore et al. (2015)[22]	46	Revision arthroplasty	13.1	8–26
Dilisio et al. (2014)[23]	90	Primary/revision arthroplasty	10.1	5–18
Dodson et al. (2010)[24]	11	Primary arthroplasty	9	8–10
Kelly et al. (2009)[25]	27	Revision arthroplasty	7	4–10

days in their institute, which they believed was insufficient time to identify *C. acnes*. This suggests that the extended confirmation time raises the possibility that standard culture may not be an appropriate diagnostic method.

To enhance diagnostic accuracy, recent studies have explored the use of arthroscopic tissue culture in evaluating shoulder PJI. Dilisio et al.[23] reported that arthroscopic biopsy prior to revision surgery for suspected shoulder PJI demonstrated 100% sensitivity, specificity, and positive and negative predictive values. This contrasts with fluoroscopically guided glenohumeral aspiration, which showed lower sensitivity and negative predictive value. Akgun et al.[27] performed a retrospective analysis of 23 cases, obtaining tissue samples from at least 3 sites during diagnostic arthroscopy for painful PSA. They found that when at least 2 positive samples yielded the same organism, the sensitivity and specificity were 80% and 94%, respectively, with a positive predictive value of 80%. These findings suggest that arthroscopic tissue culture, especially when multiple positive samples are obtained, can be a more effective diagnostic tool for shoulder PJI, offering higher sensitivity and specificity compared to traditional methods.

New Techniques

As it stands, *C. acnes* infections can present with ambiguous symptoms, and traditional culture methods are time-consuming, highlighting the need for alternative diagnostic approaches in clinical practice. Next-generation sequencing (NGS) is a novel DNA sequencing technique that offers high speed and throughput, enabling sequencing of extensive genomic data. While NGS is applied in various biotechnological fields, its clinical utility is particularly notable in several domains of diagnostic virology.[28]

Rao et al.[29] compared NGS with skin and deep tissue culture in patients undergoing primary shoulder arthroplasty. Among the 25 samples analyzed, standard culture yielded positive results in 10 skin samples and 3 deep tissue samples, whereas NGS detected bacteria in 17 and 7, respectively. This finding indicates that NGS identified bacteria at higher rates in both samples than standard culture.

Namdari et al.[30] compared standard cultures and NGS in 44 patients who underwent revision arthroplasty. The results indicated that culture data from these patients often consisted of monomicrobial findings, whereas NGS data commonly consisted of polymicrobial findings. The authors concluded that there was a reasonable level of agreement between the results of traditional culture methods and NGS.

However, in another study by Namdari et al.[21] conducted in 2020, they assessed 90 patients who underwent shoulder arthroscopy or primary arthroplasty. Among these patients, *C. acnes* was positive in 18 and 14 in the culture method and NGS, respectively, and only 4 tested positive in both methods. Based on these findings, the authors concluded that there was limited agreement between culture and NSG for *C. acnes* identification.

In summary, NGS demonstrates promising potential in diagnosing *C. acnes* infections compared with traditional methods. Several studies have shown positive results. However, further research is warranted to validate the results.

ACTUAL RISK

Risk of Infection

C. acnes is reportedly the most commonly isolated bacterium when infections occur following shoulder surgery.[31] Athwal et al.[32] reported that between 1975 and 2003, 38 of 39 patients who underwent rotator cuff repair developed deep infection, with *C. acnes* being the most frequently isolated organism, infecting 20 out of 39 patients (51%). Even after shoulder arthroplasty, *C. acnes* infections have been observed in roughly 0.9% to 1.9% of patients, but this may be underestimated due to the difficulty in detection.[33] Egglestone et al.[34] conducted a review of 88 articles about shoulder arthroplasty infections; in 33 articles, *C. acnes* was identified as the most common pathogen, surpassing coagulase-negative staphylococci and *Staphylococcus aureus*.

This phenomenon is believed to stem from the inherent nature of commensal bacteria, which makes contamination prevention during surgery challenging. When making surgical incisions, the surgical site may be contaminated, leading to a higher risk of infection. Notably, male patients had 66 times higher odds (95% CI, 6–680) of having a positive culture indicating subdermal colonization than female patients ($p < 0.001$).[12] Other studies have reported similar findings of higher infection rates in male patients, further supporting the possibility of *C. acnes* colonization in the glands.[35]

Overrated Threat

Despite the time-consuming and challenging nature of culturing, positive cultures for *C. acnes* do not always correlate with symptomatic infections. Furthermore, the possibility of contamination of sample specimens cannot be excluded. Falconer et al.[12] compared the studies by Levy et al.[36] and Maccioni et al.,[37] demonstrating the possibility of specimen contamination. Levy et al.[36] identified *C. acnes* in synovial fluid from shoulder arthroplasty patients

at a rate of 41.5%, indicating the potential of this microorganism to be a causative agent in shoulder osteoarthritis. Contrarily, Maccioni et al.[37] conducted a similar study but employed the Oxford technique for specimen collection, confirming culture positivity in capsule tissue at a rate of only 3.1%.[38] The comparison of these 2 studies revealed differences in culture results depending on the method used for specimen collection, highlighting the possibility of contamination during the collection process.

In addition, several other studies have addressed the disparities between culture results and the actual onset of infection. When cases with positive cultures were analyzed, the infection rate ranged from 3.6% to 25%, and there were instances where positive cultures reappeared after the initial positive culture or upon the onset of clinical symptoms classified as genuine infections.[9,25] Consistent with these findings, Falstie-Jensen et al.[39] retrospectively evaluated 124 patients who underwent revision shoulder arthroplasty, comparing 97 culture-negative patients with 27 patients who had unexpectedly positive cultures. They did not observe any differences in outcomes after a presumed aseptic revision, irrespective of the presence of unexpectedly positive cultures. Considering these aspects, as discussed in the review paper by Patel et al.,[40] while *C. acnes* is clearly a significant contributor to shoulder PJI, it is difficult to definitively classify it as the most common cause of shoulder PJI. A more appropriate description may be that *C. acnes* is frequently cultured in cases of primary and revision shoulder arthroplasty.

As indicated above, commencing invasive treatment solely based on culture testing is excessive. Surgeons should first exercise caution to prevent specimen contamination during collection. Even in cases where positive cultures are obtained, it is imperative to correlate them with clinical symptoms and laboratory findings. Subsequently, it becomes crucial to develop a plan utilizing modern, rapid, and accurate tests like NGS for informed decision-making.

TREATMENT

Surgical Treatment

As *C. acnes* is a well-known strain that typically forms biofilms, implant removal is warranted when infection is suspected.[33] In cases where soft-tissue procedures have been performed and in arthroplasty cases, removal of fixed anchors and revision surgery are considered, respectively.[41] For surgical irrigation and debridement, open surgery is recommended over arthroscopic surgery.[42,43] Simple abscess drainage is deemed insufficient, whereas circumferential, complete synovectomy across all joint compartments, wherever possible, is necessary.[13]

In arthroplasty cases, implant revision is mainly considered due to the aforementioned significant biofilm formation.[44] For thorough eradication of infection, removal of all components is necessary.[45] Generally, the removal of all components suspected of infection, including cement, is the principle in revision arthroplasty. However, some studies suggest that in certain scenarios, retaining the cement might be advantageous, as complete removal can pose technical challenges and increase the risk of complications.[46] As for the choice of revision techniques, whether to opt for the 1- or 2-step technique remains controversial and often depends on the surgeon's preference. However, the single-stage approach is increasingly preferred. Mercurio et al.[47] conducted a systematic review including 34 studies and reported that 1-stage revision yielded superior clinical outcomes and fewer postoperative complications compared with 2-stage surgery. The eradication rate of infection was notably higher in 1-stage (96%) than in 2-stage (86%) revisions. However, as the authors have noted, due to the nature of a systematic review, it is impossible to eliminate the selection bias inherent in individual studies. In cases of more severe and chronic infections, or when the bacterium is unidentified, a 2-stage operation should be considered preferentially.

During 2-stage arthroplasty revisions, especially for infection management, the use of antibiotic-impregnated cement spacers plays a critical role.[48] The choice of antibiotics incorporated into the cement depends on several factors, including the type of bacteria identified in the infection, the patient's antibiotic sensitivities, and the preference of surgeons. Commonly used antibiotics in these cements include vancomycin, tobramycin, and gentamicin, chosen for their broad-spectrum coverage and efficacy against a range of bacteria commonly involved in orthopedic infections.

Before re-implantation in a 2-stage revision, several key factors are assessed over a specific period, typically ranging from 6 weeks to several months.[49] These include the resolution of clinical symptoms of infection, normalization of inflammatory markers such as CRP and ESR, and negative results on repeat joint aspiration cultures. The decision for re-implantation is made only after these criteria are met, ensuring that the infection has been adequately controlled or eradicated. This process is vital to minimize the risk of recurrent infection and to ensure the success of the second-stage surgery.[50]

Antibiotic Therapy

In the initial stages where infection is suspected, it is cru-

cial to obtain intraoperative samples, and the use of broad-spectrum antibiotics immediately after sample collection is allowed.[13] Careful sample collection is paramount for confirming the infection. Subsequently, culture results can be obtained at around 2 weeks. Based on the results, a treatment decision can be made through a multidisciplinary team meeting. To date, no consensus on the optimal antibiotic regimen for *C. acnes* PJI treatment has been reached. The Infectious Diseases Society of America guidelines recommend first-line monotherapy with penicillin G or ceftriaxone, with clindamycin or vancomycin as alternative options.[51]

Once the infection is confirmed, antibiotic therapy is continued. Typically, the duration of antibiotic therapy for PJIs ranges from 6 to 12 weeks. Kusejko et al.[52] reported that antibiotic treatment lasting for at least 6 weeks has yielded favorable outcomes. In cases of unexpectedly positive cultures following surgery, some studies reported that antibiotic therapy may be unnecessary. Grosso et al.[53] reported that among 17 patients with unexpectedly positive cultures, only 1 experienced infection recurrence despite not receiving antibiotic treatment.

There is ongoing debate regarding the efficacy of oral rifampin. *In vitro* studies have demonstrated that rifampin is highly effective against *C. acnes* biofilms and is superior to other antibiotics.[54] However, clinical studies have not consistently demonstrated significant differences. A retrospective study by Vilchez et al.[55] suggested that rifampin-based combinations do not seem to improve prognosis. Furthermore, Saltiel et al.[56] concluded that rifampin has no clear benefit compared with monotherapy without rifampin.

PREVENTION

Due to the challenging nature of the diagnosis and treatment of *C. acnes* infections, infection prevention has gained considerable amount of interest.[57] This bacterium is predominantly found in the sebaceous glands and hair follicles, commonly located on the shoulders, back, and head.[58] Its prevalence in male patients is likely associated with higher testosterone levels, leading to increased sebum production. During shoulder surgery, the superficial skin colonization rate of *C. acnes* ranges from 42% to 73%. It is known to cause infections through dermal rather than epidermal incisions, making eradication with conventional skin preparation challenging.[59]

Saltzman et al.[60] reported that chlorhexidine is more effective than povidone-iodine in reducing bacterial burden during shoulder surgery. In addition, topical benzoyl peroxide (BPO) has been successfully used against *C. acnes* vulgaris and exhibits toxicity to *C. acnes* without producing resistant strains.[61] Many studies have aimed to reduce *C. acnes* colonization using prophylactic agents, which are presented in Table 2.[59,62-65]

Chuang et al.[59] reported a reduction from 72.5% to 19.6% in positive cultures when using 4% chlorhexidine scrub followed by 70% isopropyl alcohol along with IV cephazolin pre- and postoperatively. However, the randomized controlled trial by Murray et al.[62] did not show a significant decrease in colonization, suggesting that the efficacy of chlorhexidine is insufficient. Scheer et al.[63] reported that a 2-day topical treatment with BPO before conventional preparation reduced colonization from 95% to 35% compared with the reduction of 5% with BPO alone. The same authors conducted a randomized controlled trial in 2021 and reported that BPO gel significantly reduced *C.*

Table 2. Summary of Efficacy of Various Prophylactic Methods

Study	Number of patients	Prophylactic method	Type of procedure	Pre-application colonization rate (%)	Post-application colonization rate (%)	Culture duration (day)
Murray et al. (2011)[62]	100	2% Chlorhexidine cloth	Arthroscopy/open surgery	58	46	7
Chuang et al. (2015)[59]	51	4% Chlorhexidine scrub and 2% chlorhexidine gluconate/70% isopropyl alcohol paint	Arthroscopy	72.5	19.6	21
Dizay et al. (2017)[65]	65	1.2% Clindamycin phosphate + 5% Benzoyl peroxide gel	Arthroscopy	47.7	12.3	21
Scheer et al. (2018)[63]	40	5% Benzoyl peroxide gel	Nonoperative	95	35	5
		4% Chlorhexidine soap			5	
Scheer et al. (2021)[64]	100	5% Benzoyl peroxide gel	Primary arthroplasty	97	4.7	10

acnes skin load when compared with regular soap alone.[64]

In a randomized controlled trial by Dizay et al.,[65] combined use of topical BPO and clindamycin effectively reduced *C. acnes* colonization in arthroscopic surgery. Furthermore, Meyer et al.[66] conducted a systematic review, confirming the efficacy of peroxide-containing solutions in reducing *C. acnes* bioburden, despite the presence of heterogeneity in the study designs. In conclusion, the application of topical BPO to the incision site as a preventive measure during surgery can effectively reduce the bacterial burden of *C. acnes*, in addition to standard preparation protocols.[67] The future challenge lies in determining which of the various protocols used to date is most effective in reducing the risk of postoperative *C. acnes* infections.

CONCLUSION

C. acnes is the most commonly cultured bacterium following shoulder joint surgery and is mainly considered a skin commensal. However, its indolent nature makes the clear identification of clinical symptoms challenging. Laboratory findings are often nonspecific and can be confused with postoperative changes, further contributing to the diagnostic difficulty. Furthermore, the time required for culture, combined with the inherent risk of contamination owing to its skin commensal nature, reduces the reliability of culture results. In response, emerging technologies such as NGS and polymerase chain reaction-based methods are being considered to improve diagnosis. Furthermore, arthroscopic soft-tissue culture has shown promising results in enhancing the diagnostic accuracy for shoulder infections, providing a more sensitive and specific method in the identification of *C. acnes*.

Given its propensity to form biofilms, there is a general consensus that implant removal should be prioritized when infection is suspected. However, the role of antibiotics, such as rifampicin, in treatment remains controversial. Many attempts have been made to reduce bacterial burden using appropriate preoperative measures, with BPO reported to be effective in reducing burden compared with other methods.

In the future, alternative, accurate, and rapid diagnostic methods beyond culture testing when *C. acnes* infection is suspected need to be explored. Furthermore, a more detailed study of the pathogenicity of *C. acnes* is warranted to accurately gauge the extent of its threat. Consensus is needed on treatment methods when infection requires intervention, and discussions regarding appropriate measures for preventing preoperative infections are necessary.

CONFLICT OF INTEREST

No potential conflict of interest relevant to this article was reported.

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ORCID

Jong Pil Yoon https://orcid.org/0000-0001-6446-6254
Kang-San Lee https://orcid.org/0000-0001-7932-0426
Sung-Jin Park https://orcid.org/0009-0008-6869-0788
Dong-Hyun Kim https://orcid.org/0000-0001-9078-5953
Junsung Kim https://orcid.org/0009-0008-7994-0666
Yoon Seong Choi https://orcid.org/0009-0006-1483-0023
Hyun Joo Lee https://orcid.org/0000-0003-2837-3434
Seok Won Chung https://orcid.org/0000-0002-8221-9289

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