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Prevalence of low-grade infection in uncomplicated fracture osteosynthesis

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ABSTRACT

Subclinical bacterial colonization of osteosynthesis implants has been suggested as a potential contributor to subsequent periprosthetic joint infection, yet its frequency in clinically uneventful fracture healing remains unclear. This prospective cohort study aimed to determine the prevalence of unexpected positive intraoperative cultures (UPIC) during elective hardware removal after uncomplicated fracture union.

Adult patients undergoing elective implant removal after radiographic union were prospectively enrolled. Inclusion required absence of signs of clinical infection and no antibiotic therapy within 48 hours before surgery. Three deep tissue samples were collected from the implant-bone interface prior to irrigation. Samples were homogenized and inoculated into aerobic and anaerobic blood culture bottles. UPIC were defined as culture growth without clinical suspicion. Microbiological confirmation required at least two concordant isolates according to the FRI consensus definition.

Sixty-nine patients were included. Any bacterial growth occurred in 32 patients (46.4%). Seventeen patients (24.6%) had two or more concordant isolates fulfilling microbiological criteria, whereas 15 (21.7%) had a single low-virulence isolate interpreted as contamination. UPIC were most frequent in the shoulder, predominantly Cutibacterium acnes, followed by the elbow with mainly coagulase-negative staphylococci. No postoperative infections, wound complications, or reoperations occurred.

Nearly one quarter of clinically unremarkable hardware removals yielded multiple concordant isolates, indicating a substantial rate of low-grade infection. Although no short-term clinical consequences were observed, the potential relevance of UPIC for future arthroplasty remains uncertain.

Keywords: Fracture fixation, hardware removal, unexpected intraoperative positive cultures, low-grade infection, implant colonization.

INTRODUCTION

Periprosthetic joint infection (PJI) is a devastating complication after joint arthroplasty, with reported incidences of 0.55-1.55% following primary procedures[1,2]. Several studies have demonstrated a substantially higher risk in patients with prior periarticular hardware, with reported PJI rates of 2.5-8% following conversion arthroplasty[3-6]. The underlying reasons for this excess risk remain debated. While longer and more complex surgical procedures may contribute, subclinical colonization of retained implants has also been proposed as a potential explanation.

Unexpected positive intraoperative cultures (UPIC) during elective hardware removal have been described in 20-40% of cases, even in patients without clinical signs of infection[7,8]. These findings are most common in the upper limb, particularly clavicle and shoulder implants, where Cutibacterium acnes is frequently isolated[9]. Case reports also highlight atypical pathogens such as Corynebacterium simulans[10]. Although most UPIC involve low-virulence organisms and patients remain clinically asymptomatic, their presence raises concern regarding potential implications should arthroplasty subsequently be performed at the same anatomical site.

The interpretation of microbiological findings in fracture fixation remains challenging, particularly in the absence of standardized diagnostic criteria. To address this issue, an international consensus definition of fracture-related infection (FRI) was published in 2018, introducing confirmatory and suggestive criteria to harmonize clinical practice and research reporting. However, subsequent literature has demonstrated considerable variability in the application and validation of these criteria in daily practice, underscoring the ongoing diagnostic challenges in FRI[11]. Consequently, uncertainty persists regarding the clinical significance of isolated microbiological findings in patients without overt signs of infection.

Despite increasing awareness of this phenomenon, prospective cohort data remain limited, particularly in patients with otherwise uncomplicated fracture healing.

The objective of this single-center prospective observational cohort study was to determine the prevalence of UPIC in patients undergoing elective implant removal after uneventful fracture healing.

MATERIALS AND METHODS

The study protocol was approved by the ZAS Ethics Committee (Ref. 230402ACADEM BUN 2023099000001). All patients provided written informed consent prior to inclusion.

Patient selection

This single-center prospective observational study included adult patients scheduled for elective implant removal after uneventful fracture healing. Indications for implant removal were patient-driven and primarily related to mechanical discomfort, soft tissue irritation, or friction from subcutaneous hardware after confirmed radiographic fracture union. Common reasons included local pressure symptoms, irritation from prominent plates or screws, and patient preference following complete fracture healing. Importantly, no removals were performed for suspected infection, implant loosening, non-union, or inflammatory symptoms suggestive of fracture-related infection. Inclusion required radiographic union, absence of clinical signs of infection, and no antibiotic therapy within 48 hours before surgery. No perioperative prophylactic antibiotics were administered at the time of anesthesia induction or during surgery. Exclusion criteria were clinical suspicion of infection (e.g., fistula, erythema), prolonged antibiotic use, avascular necrosis, non-union, perioperative wound complications, or delayed healing. Data on race and ethnicity were not collected, as these variables are not routinely recorded in the medical records of our institution and were not prespecified variables in the study protocol.

Surgical technique

All procedures were performed under laminar airflow using a standardized sterile technique and the same surgical approach as for primary fixation procedures. Three separate deep tissue samples were collected from the implant–bone interface using new sterile instruments for each sample to minimize cross-contamination. The use of three independent samples was chosen in accordance with established orthopaedic infection diagnostic principles, as multiple concordant samples increase diagnostic specificity and reduce the risk of false-positive results due to contamination. All samples were obtained before irrigation or wound closure to avoid contamination or dilution of potential microorganisms. Hardware was removed aseptically, but the implants themselves were not cultured. All collected tissue samples were transferred immediately to the microbiology laboratory in double-wrapped sterile containers with beads for further analysis.

Microbiological analysis

Tissue samples were collected in the operating room in double-wrapped sterile containers with 5 mL saline solution (0.85%) and glass beads (EOLabs). Upon arrival in the laboratory, the tissue samples were homogenized by vortexing for 3 minutes using a mechanical cell disruptor (Bead Genie (Scientific Industries)) without opening the container to minimize contamination. After homogenization, samples were opened in a microbiological safety cabinet. Two millilitres (mL) of the suspension were then inoculated into an aerobic blood culture bottle (FA-Plus bottle, Biomerieux) and 2 mL into an anaerobic blood culture bottle (SN bottle, Biomerieux). Inoculation into blood culture bottles was selected based on evidence suggesting improved sensitivity for low-virulence and biofilm-associated organisms in orthopaedic device-related infections. The bottles were subsequently incubated in a blood culture incubator (Virtuo, Biomerieux). Cultures were reported as negative; no growth occurred after 7 days (aerobic bottles) or 14 days (anaerobic bottles). If the blood culture bottles detected growth, the bottles were subcultured onto agar plates, identified with MALDI-TOF (Bruker). Susceptibility testing was performed with Vitek (Biomerieux).

Definitions

Unexpected positive intraoperative cultures (UPIC) were defined as the growth of any microorganism in the absence of clinical suspicion of infection.

We applied the Fracture-Related Infection (FRI) consensus definition. Microbiologically confirmatory infection was defined as the isolation of phenotypically indistinguishable microorganisms from at least two separate deep tissue samples obtained during the same procedure[12].

In this study, cases fulfilling the microbiological confirmatory criteria of the FRI consensus definition (≥2 concordant isolates) were referred to as "low-grade infection", in the absence of clinical confirmatory criteria such as fistula, purulence, or implant loosening. All included patients demonstrated radiographic fracture union and no clinical signs of infection at the time of implant removal.

Single low-virulence isolates, such as Cutibacterium acnes or coagulase-negative staphylococci, were interpreted as probable contaminants in the absence of clinical signs of infection. To minimize misclassification due to skin commensal contamination, concordant growth in at least two independent samples was required to define microbiological confirmation. Potential contamination sources include skin flora, intraoperative sampling contamination, or laboratory processing contamination.

However, a single positive culture with a high-virulence organism, for example Staphylococcus aureus or β-hemolytic streptococci, was considered clinically relevant. This interpretation follows current FRI and PJI guidelines, as these pathogens are rarely contaminants and have been associated with true infection even when isolated only once[13].

Postoperative follow-up consisted of routine outpatient evaluation until satisfactory wound healing was achieved, typically at approximately two weeks after surgery. Additional visits were documented if patients re-presented with wound-related concerns.

RESULTS

Cohort

Between January 2023 and December 2024, 69 patients were included (Table I). Median age was 41 years (range 18–86), and median time from osteosynthesis to hardware removal was 13 months (range 2–83 months).

Unexpected positive cultures

Bacterial growth was observed in at least one culture in 32 of 69 patients (46.4%). Fifteen patients (21.7%) had only a single positive sample, which was classified as contamination. In 17 patients (24.6%), two or more cultures yielded the same microorganism, meeting the microbiological confirmatory criterion according to the FRI consensus definition.

Microbiology

Low-virulence skin commensals predominated among the isolates. Cutibacterium acnes and coagulase-

Table I. — Patient characteristics.

Age, years	
Median (range)	41 (18–86)
Sex	
Male, n (%)	28 (40.6%)
Female, n (%)	41 (59.4%)
Anatomical location of hardware, n (%)	
Distal tibia + ankle	31 (45.0%)
Elbow	14 (20.3%)
Shoulder	10 (14.5%)
Knee	6 (8.7%)
Hand/Wrist	5 (7.2%)
Femur	3 (4.3%)
Time from osteosynthesis to hardware removal	
Median	13 months
Range	2–83 months
Culture results, n (%)	
Any positive culture	32 (46.4%)
≥2 concordant cultures	17 (24.6%)
Contaminants	15 (21.7%)

negative staphylococci accounted for the majority of UPIC cases (Table II). C. acnes was repeatedly isolated in the shoulder region.

In the elbow region, most isolates consisted of coagulase-negative staphylococci, with S. epidermidis being the only organism recovered in more than one case. Other organisms such as C. acnes and Bacillus species occurred only sporadically.

A single case involving the proximal femur showed mixed growth of S. epidermidis and Staphylococcus aureus. Given the known virulence of S. aureus, this finding was considered clinically relevant[13].

Distal tibia and ankle likewise involved low-virulence skin commensals but showed no consistent microbiological pattern.

No other high-virulence organisms or polymicrobial infections were detected. This microbiological pattern supports the hypothesis that persistent colonization of osteosynthesis implants is largely due to indolent skin commensals with limited pathogenic potential rather than overt infection.

Clinical outcomes

None of the patients exhibited clinical signs of infection at the time of hardware removal. All fractures demonstrated radiographic union without signs of implant loosening. Postoperative follow-up consisted of routine outpatient evaluation until satisfactory wound healing was achieved, typically at approximately two weeks. No wound complications, surgical site infections, or reoperations occurred during this period.

No patients required antibiotic therapy based on intraoperative culture results, as no clinical signs of infection developed during follow-up.

DISCUSSION

Our findings demonstrate that unexpected positive intraoperative cultures (UPIC) are relatively common, even in the absence of clinical signs of infection. Nearly a quarter of patients had two or more identical isolates, meeting the microbiological confirmatory criterion according to the FRI consensus definition. This 24.6% rate of low-grade infection falls within the broad range reported by previous studies and underscores the subclinical nature of these findings. The predominant organisms were indolent skin commensals, notably Cutibacterium acnes and coagulase-negative staphylococci, consistent with previous reports of hardware colonization[9,14]. In particular, upper-extremity implants (e.g., clavicle and proximal humerus) demonstrated the highest proportion of UPIC, with a predilection for C. acnes, mirroring the high bacterial load of the shoulder region. This pattern supports the hypothesis that persistent biofilm-forming commensals may persist on orthopedic implants without causing clinically overt infection. Indeed, C. acnes has been well characterized as an opportunistic pathogen capable of forming biofilms on implants, transitioning from a benign skin resident to a source of implant-related infection under the right conditions[9].

Interestingly, several UPIC cases in our series occurred after relatively short implantation times of less than six months. One UPIC case occurred after only two months in situ. These patients underwent early hardware removal due to mechanical discomfort or local intolerance, without any clinical or radiographic signs of infection. This observation supports the idea that positive cultures can arise even without prolonged implant exposure and suggests early colonization by low-virulence skin flora rather than established biofilm-driven infection.

An important question is the clinical relevance of these UPICs. On one hand, none of the patients developed postoperative infections during follow-up, suggesting that many isolates may represent colonization or contamination rather than clinically meaningful infection. Similar challenges in interpreting infection-related findings after fracture fixation have been reported in previous trauma series[15]. Furthermore, no clinical deterioration, delayed wound healing, or secondary interventions were observed, reinforcing the absence of short-term

Table II. — Distribution of Unexpected Positive Intraoperative Cultures (UPIC) by Anatomical Site.

Anatomical site	No. of removals (n)	UPIC-cases, n (%)	Predominant organism(s)
Shoulder	10	8 (80.0%)	C. acnes, S. epidermidis
Elbow	14	5 (35.7%)	S. epidermidis
Proximal femur	3	2 (66.7%)	None specific
Distal tibia + ankle	31	2 (6.5%)	None specific
Knee	6	0 (0%)	—
Hand + wrist	5	0 (0%)	—
Total	69	17 (24.6%)	

clinical correlation with microbiological findings. This viewpoint is supported by other studies in which patients with positive cultures after hardware removal had benign clinical courses[9,16]. On the other hand, the presence of low-grade pathogens is concerning, particularly when they are biofilm-forming organisms such as C. acnes and coagulase-negative staphylococci. These bacteria may contribute to future periprosthetic joint infection (PJI), especially in patients undergoing conversion arthroplasty. C. acnes is a well-established cause of indolent PJI, most notably in the shoulder. It can persist in biofilms without triggering an overt inflammatory response[14,17,18].

While causality cannot be assumed, the association between prior fracture fixation and elevated PJI rates following conversion arthroplasty has been consistently observed[19]. Residual bacterial colonization of hardware or surrounding soft tissue is one proposed mechanism. Detecting UPIC in clinically well patients could, therefore, reflect a latent risk factor rather than an incidental finding. This possibility deserves greater attention, especially in surgical planning for patients anticipating arthroplasty near previously treated joints, most notably the hip, knee and shoulder, with an emerging role for total ankle arthroplasty.

The optimal response to UPIC remains debated. Observation may suffice for single low-virulence isolates without clinical signs, whereas multiple concordant cultures may warrant treatment. A recent systematic review suggests that single positive cultures, particularly with C. acnes, can often be safely ignored in the absence of other confirmatory infection criteria[20]. Conversely, persistent recovery of the same organism in multiple samples is more likely to represent true infection and may justify a limited antibiotic course[16,20]. Our results align with this pragmatic approach. Currently, no standardized protocol exists for the management of UPIC, leading clinicians to extrapolate from broader orthopaedic infection frameworks, including FRI and PJI definitions and contemporary concepts of debridement-based infection managemen[21].

The integration of our findings within this broader clinical framework highlights a delicate balance. Overtreating a biologically insignificant colonization exposes patients to unnecessary antibiotics, whereas undertreating a smoldering low-grade infection could carry consequences, particularly for those expected to undergo future joint replacement. This tension mirrors the broader debate in fracture surgery about what truly constitutes "infection" in a healed bone. Clinically, these cases behaved as sterile fracture unions. However, they fulfilled microbiological confirmation criteria according to the FRI definition, highlighting the disconnect between laboratory findings and clinical presentation.

Furthermore, the detection of low-grade organisms without overt symptoms raises important questions about their natural history. Some UPIC likely represent harmless colonization, whereas others may act as biologically relevant reservoirs with the potential to influence later surgical outcomes. At present, distinguishing between these possibilities is not feasible, highlighting the need for prospective longitudinal research to determine whether UPIC predispose to future PJI or whether timely intervention might mitigate that risk.

The strengths of this study include its prospective design and the focused inclusion of patients with radiographically confirmed fracture union and no clinical suspicion of infection, thereby minimizing confounding from non-union, implant failure, or overt fracture-related infection. An additional methodological strength is the standardized aseptic sampling technique and incubation of homogenized tissue in blood culture bottles, a method shown to improve detection of low-virulence organisms while reducing false-positive results[22].

Several limitations must be acknowledged. Although prospectively conducted, this was an observational study without a control group. The sample size was modest and anatomical locations were heterogeneous, which may limit generalizability. Furthermore, only patients undergoing elective implant removal were included, introducing potential selection bias and limiting extrapolation to the broader fracture fixation population. A comprehensive standardized fracture-related infection diagnostic workup was not performed. Histological analysis and sonication of explanted hardware were not available, and inflammatory laboratory markers such as C-reactive protein or leukocyte count were not systematically assessed preoperatively in clinically asymptomatic patients. Consequently, differentiation between low-grade infection, implant colonization, and contamination remains inherently limited, and subclinical systemic inflammatory responses cannot be entirely excluded. Follow-up was restricted to short-term postoperative clinical evaluation. Therefore, the study does not allow conclusions regarding the long-term clinical relevance of unexpected positive intraoperative cultures, particularly in relation to subsequent fracture-related infection or future periprosthetic joint infection. Finally, race and ethnicity data were not collected, which may limit the generalizability of our findings to populations with different demographic compositions.

CONCLUSION

Unexpected positive intraoperative cultures were found in nearly one quarter of routine hardware removals after fracture union, predominantly involving low-virulence skin commensals. Although these findings did not translate into short-term clinical infection, they challenge the assumption that an uneventful clinical course equates to a sterile environment. The long-term significance of UPIC remains uncertain, particularly for patients who may later undergo arthroplasty, where indolent organisms could potentially contribute to prosthetic joint infection. Further prospective studies are essential to clarify which UPIC represent harmless colonization, and which may warrant intervention, enabling clinicians to approach this diagnostic grey zone with greater precision.

Level of evidence IV: Observational study.

Conflict of Interest: The authors declare that they have no commercial associations (e.g., consultancies, stock ownership, equity interest, patent/licensing arrangements, etc.) that might pose a conflict of interest in connection with the submitted manuscript.

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