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The identification of low-pathogenic bacteria on removed spinal implants and implications for antimicrobial prophylaxis

Ann-Kathrin Joerger [a,*], Vicki M. Butenschoen [a], Susanne Feihl [b], Sebastian Rühling [c], Jan S. Kirschke [c], Bernhard Meyer [a], Sandro M. Krieg [d]

[a] Department of Neurosurgery, Technical University of Munich, Ismaninger Str. 22, 81675, Munich, Germany
[b] Institute for Medical Microbiology, Immunology and Hygiene, Technical University of Munich, Trogerstr. 30, 81675, Munich, Germany
[c] Department of Neuroradiology, Technical University of Munich, Ismaninger Str. 22, 81675, Munich, Germany
[d] Department of Neurosurgery, Ruprecht-Karls-University Heidelberg, Im Neuenheimer Feld 400, 69120, Heidelberg, Germany

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ABSTRACT

Introduction: The role of low-pathogenic bacteria cultured from removed spinal implants is unclear and the efficacy of perioperative single-dose antibiotics against such bacteria remains underexplored.
Research question: This study aims to investigate whether pedicle screw loosening is associated with pathogens and if the choice of perioperative antibiotics can prevent these bacteria.
Methods: A retrospective analysis was conducted on 93 patients with implants removed between 01/01/2018 and 03/31/2020. Patients with both loosened and non-loosened implants were included. The latter group was subdivided into cases where implants were exchanged due to adjacent segment degeneration (ASD) and those with elective implant removal after fracture healing. Bacterial cultures from removed implants were analyzed for resistance profiles against the prophylactic single-shot antibiotics administered during implantation. Patients with acute infection, spondylodiscitis, deep wound infection, empyema, and carbon/polyetheretherketone spinal implants were excluded.
Results: Bacterial isolates were detected in both loosened (41%) and non-loosened (27%) implants ($p = 0.23$). The most frequently cultivated bacteria were *Cutibacterium acnes* and *Staphylococcus epidermidis*. Sensitivity to the administered antibiotics was 75%. While *Cutibacterium acnes* was entirely sensitive, *Staphylococcus epidermidis* was completely resistant. Patients with loosened implants without bacteria had a significantly lower bone mineral density (BMD) than patients with implants removed due to ASD. However, patients with loosened implants and positive bacterial cultures had comparable BMD to ASD patients.
Conclusions: The high rate of sensitive *Cutibacterium acnes* and resistant *Staphylococcus epidermidis* on removed spinal implants suggests a need to revisit current antimicrobial prophylaxis. Further research is required to determine the clinical significance of low-virulence bacteria, especially on non-loosened implants.

1. Introduction

Over the past decade, there has been growing interest in low-pathogenic bacteria such as *Cutibacterium acnes* and *Staphylococcus epidermidis,* causing low-grade infections in orthopedic and spinal surgery (Dodson et al., 2010; Hahn et al., 2005; Leitner et al., 2018; Shiban et al., 2020; Levy et al., 2008). Better diagnostic methods, such as prolonged cultivation and sonication, have led to more frequent detection of these infections (Schafer et al., 2008; Trampuz et al., 2007). Traditionally, *Cutibacterium acnes* and *Staphylococcus epidermidis* were considered skin commensal, predominantly found in sebaceous gland-rich areas like the nose, ears, glabella, neck and back (Grice et al., 2009). However, in recent years, these bacteria have been implicated in catheter-associated infections, periprosthetic joint infections (PJI), endocarditis and endophthalmitis (Cogen et al., 2008). Especially for *Cutibacterium acnes,* there is still an ongoing debate if its isolation from microbiological samples obtained during surgery results from iatrogenic translocation from the skin to the surgical field or if it genuinely resides in the deep tissue (Capoor et al., 2017; Levy et al., 2013).

Perioperative prophylactic antibiotics are administered just before

* Corresponding author.
E-mail address: annkathrin.joerger@tum.de (A.-K. Joerger).

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skin incision to reduce the risk of surgical site infections (Classen et al., 1992). However, perioperative single-shot antibiotics' ability to eradicate low-virulent bacteria has yet to be thoroughly studied. Recent studies have shown that conventional topical antiseptics and perioperative antibiotics could not effectively eliminate *Cutibacterium acnes* (Koh et al., 2016; Anagnostopoulos et al., 2018; Matsen et al., 2015; Pauzenberger et al., 2019). The underlying reasons for this are not well understood. A key virulence factor of *Cutibacterium acnes* and *Staphylococcus epidermidis* is their ability to produce a biofilm (Bruggemann et al., 2004; Buttner et al., 2015), which makes them less susceptible to standard antibiotics (Ramage et al., 2003). Additionally, it has been shown that patients undergoing revision total hip arthroplasty have skin bacteria significantly more resistant to standard perioperative antibiotics than patients undergoing primary surgery (Muhlhofer et al., 2017).

Osteoporosis and low bone mineral density (BMD) are well-known risk factors for pedicle screw loosening (Weiser et al., 2017; Schomig et al., 2023; Marie-Hardy et al., 2020) as the axial pull-out force of pedicle screws is considerably lower compared to normal spines (Halvorson et al., 1994). To what extent low-grade infection may be responsible for pedicle screw loosening is still a matter of debate.

This study aims to investigate two main aspects. First, it will examine the association between pedicle screw loosening and pathogens. Second, it will assess whether the choice of perioperative antibiotic during implantation is effective against these bacteria at all. Therefore, the rate of positive bacterial cultures from removed spinal implants and the sensitivity profile of these bacteria to the prophylactic antibiotics administered during the initial implantation (index operation) were studied. Patients with loosened and non-loosened spinal implants were enrolled to evaluate the role of bacteria in implant loosening. To assess the impact of bone quality on pedicle screw loosening, BMD was calculated based on the available CT images.

2. Methods

2.1. Study design

We conducted a retrospective analysis of the neurosurgical department of a tertiary care university hospital. Patients who underwent removal or exchange of posterior instrumentation between January 1st, 2018, and March 31st, 2020, were included. Patients were divided into two groups: those who had implant removal due to pedicle screw loosening and those without loosening. The latter group was subdivided into cases where implants were exchanged due to adjacent segment degeneration (ASD) and those with elective implant removal after fracture healing. Loosened implants were removed when patients became symptomatic with pain associated with the loosened implants. The presence of a low-grade infection was expected in most (37) of these cases, while a purely mechanical failure was anticipated in 11 cases. Patients with ASD underwent surgery when they presented with appropriate clinical symptoms and corresponding MRI findings and when CT ruled out implant loosening. Elective implant removal after fracture healing was performed when follow-up CT imaging demonstrated sufficient fracture consolidation, usually after at least 12 months. In patients with ASD and healed fractures, a low-grade infection was not initially expected.

During implant removal, swabs were taken, and sonication was performed on the removed implants. Results were validated after 14 days. Patients with acute infection, spondylodiscitis, deep wound infection, empyema, and carbon-fiber-reinforced polyetheretherketone (CFR PEEK) stabilization were excluded.

The administered prophylactic antibiotics were collected and analyzed during the index implant operation, as well as the type of bacteria cultivated from swabs, biopsies, and sonication of removed implants along with their respective antibiotic resistance profiles. The sonication process was introduced according to the publication by Trampuz et al. (2007). Details of microbiological work-up and sonication procedure have recently been described (Shiban et al., 2020). An adapted version of the criteria published by Renz et al. (2017) was used to interpret the microbiological results.

The detection of bacteria was considered significant based on the following criteria: (1) for high-pathogenic bacteria (e.g. *Staphylococcus aureus, Escherichia coli*): at least one positive sample; (2) for low-pathogenic bacteria (e.g. *Cutibacterium acnes*, *Staphylococcus epidermidis*): more than 50 colony forming units (CFU) per milliliter (ml) cultivated in at least one sample or less than 50 CFU/ml cultivated in at least two samples or less than 50 CFU/ml cultivated in one sample and histopathologic analysis confirming infection. The cut-off of 50 CFU/ml was determined based on the landmark paper by Trampuz et al. (2007). In all other cases, the isolation was classified as contamination and excluded from our analysis.

All patients received a perioperative single-shot antibiotic prophylaxis. This was usually administered 30 min before the incision and repeated after 4 h if the surgery lasted that long. In cases where a low-grade infection was suspected, the perioperative antibiotic prophylaxis was withheld until microbiological samples were collected. These cases also received a 14-day postoperative intravenous antibiotic therapy. This was initially started on an empirical basis and subsequently de-escalated according to the antibiogram upon identification of a pathogen. If a pathogen was detected, the antibiotic therapy was continued with a 10-week oral regimen. In patients without pathogen detection after the 14-day cultivation period, no 10-week oral antibiotic therapy was administered. Patients with ASD and elective material removal received only the perioperative single-shot antibiotic prophylaxis. No further antibiotic therapy was given thereafter unless significant pathogen detection occurred in the intraoperative samples. In the case of a positive pathogen detection in patients with ASD, a 2-week intravenous antibiotic therapy was also initially administered, followed by a 10-week oral regimen. In patients with elective material removal and a positive low-grade pathogen detection, no further antibiotic therapy was provided, as all foreign material was explanted.

2.2. Measurement of bone mineral density

Volumetric bone mineral density (BMD) was measured using routine CT imaging data, including the thoracolumbar spine. BMD was measured using SpineQ software v1.0 (Bonescreen, Munich, Germany) as previously described (Loffler et al., 2021; Ruhling et al., 2022). Briefly, the SpineQ software was used for automated spine processing, allowing for the separate characterization of trabecular and cortical vertebral compartments. Vertebrae with the following criteria were excluded from subsequent BMD measurements: (1) presence of any fracture, including those of malignant, traumatic, or osteoporotic origin, (2) severe degenerative changes such as sclerotic alterations of the endplates, (4) vertebrae with hardware. Volumetric BMD (expressed in mg/cm^3) was extracted from the trabecular region in measurable vertebrae. All CT scanners were calibrated using asynchronous phantom measurements with a European Spine Phantom (ESP)(Sollmann et al., 2022). BMD values were averaged over measurable lumbar vertebrae L1–L3 (Taco, 2023). If none of these vertebral levels could be assessed because of the exclusion criteria mentioned above, BMD values were averaged over available vertebrae within Th12–L5.

2.3. Ethical agreement

The study was approved by the ethical committee of our University Hospital (reference number 318/20S) and conducted in accordance with the Declaration of Helsinki. Due to its retrospective nature, patient consent was not required and was waived by the local ethics committee.

2.4. Declaration on the use of AI

While preparing this work, the authors used ChatGPT3.5 (OpenAI,

San Francisco, California, USA) and Grammarly (Grammarly, Inc., San Francisco, California, USA) to check spelling, grammar, and style. After using this service, the authors reviewed and edited the content as needed and take full responsibility for the publication's content.

2.5. Statistical analysis

A student's t-test was used to compare the BMD between patients with and without loosened implants. To compare the BMD of the four groups (ASD, elective removal, pedicle screw loosening + bacteria, pedicle screw loosening - bacteria) Kruskal-Wallis test was used. Fisher's exact test was used to compare the rates of positive bacterial cultures and re-revision rates. $P < 0.05$ was regarded as statistically significant. Statistical calculation was performed by GraphPad Prism Version 10.2.3 (GraphPad Software, La Jolla, California, USA).

3. Results

3.1. Population

A total of 93 patients with removed spinal implants were included in the study (Fig. 1). To investigate the role of bacteria in pedicle screw loosening, patients with loosened implants were compared to those without implant loosening. In 48 cases, implants were removed for pedicle screw loosening shown by CT imaging. The initial indications of posterior instrumentation for these patients were primarily degenerative reasons (37 cases), followed by trauma (10) and pathological (metastatic) fracture (1). These patients were compared to 45 cases with implants removed for reasons other than pedicle screw loosening (Fig. 1). These cases were subdivided into 29 cases with adjacent segment degeneration (ASD) and 16 cases with elective implant removal after fracture healing. The initial indications of posterior instrumentation for patients with ASD were degenerative spine disease in 27 cases and trauma in two cases.

3.2. Bone mineral density

BMD measurement was available for 76 out of 94 (81%) patients. Mean BMD of patients without pedicle screw loosening (136±53 mg/cm^3) was significantly higher compared to patients with loosened implants (95±32 mg/cm^3) ($p = 0.0001$) (Fig. 2A).

Comparing patients with ASD and elective implant removal, mean BMD of patients with elective implant removal (178±58 mg/cm^3) was significantly higher than mean BMD of patients with ASD (118±40 mg/cm^3) ($p = 0.0427$) (Fig. 2B). Mean BMD of patients with ASD (118±40 mg/cm^3) was significantly higher than mean BMD of patients with pedicle screw loosening without positive bacterial cultures (84±25 mg/cm^3) ($p = 0.0164$), while there was no significant difference between mean BMD of patients with ASD and patients with pedicle screw loosening and positive bacterial cultures (114±36 mg/cm^3) ($p > 0.9999$).

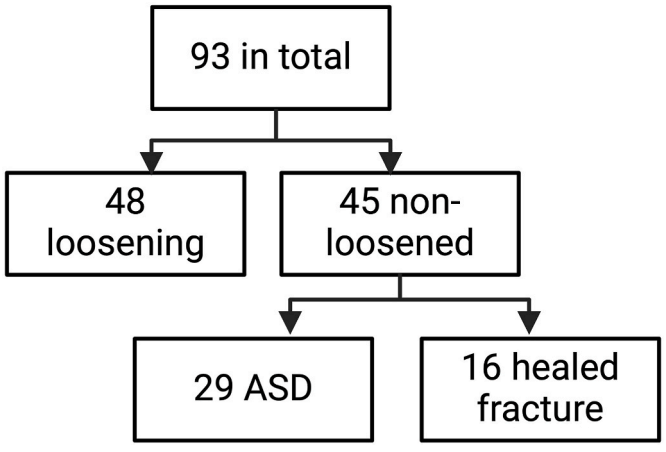

Fig. 1. Overview of different indications for implant removal. Created with Biorender.
ASD = adjacent segment degeneration.

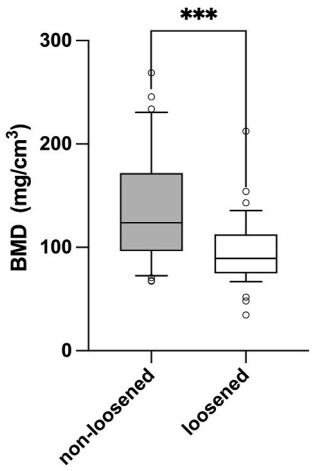

Fig. 2A. Bone mineral density measurement of patients with removed spinal implants comparing loosened and non-loosened implants. Student's t-test was used. $P = 0.0001$.
BMD = bone mineral density.

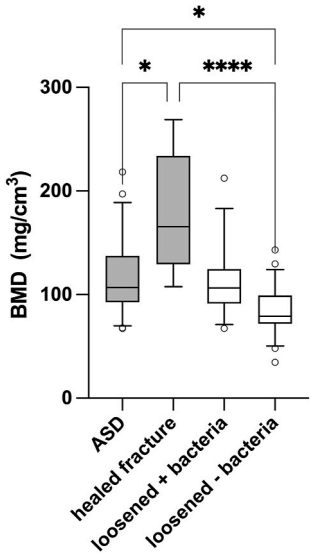

Fig. 2B. Bone mineral density measurement of patients with removed spinal implants comparing patients with adjacent segment degeneration, with healed fractures and with pedicle screw loosening. Kruskal-Wallis test was used. * ASD vs. healed fracture: $p = 0.0427$; * ASD vs. loosend – bacteria: $p = 0.0164$; **** healed fracture vs. loosened: $p < 0.0001$.
BMD = bone mineral density, ASD = adjacent segment degeneration.

3.3. Microbiology

To assess whether pedicle screw loosening is associated with bacterial presence, swabs and samples from the screw channels as well as the sonication fluid of the removed implants were analyzed for bacteria and compared between patients with and without screw loosening. Detection of bacteria was regarded as significant according to the criteria mentioned above. Cases in which neither sonication nor swabs were performed were excluded. Among cases with implant loosening,

bacteria were cultured in 41% (29 out of 46) of patients, compared to 27% (8 out of 30) of patients without loosening (p = 0.23) (Table 1). Further subdivision of cases without loosening into those with implant removal due to ASD and those with elective implant removal after fracture healing revealed positive bacterial cultures in 29% (6 out of 21) and 22% (2 out of 9) of cases, respectively (p > 0.99) (Table 1). The most frequently isolated bacterium in patients with implant loosening was *Cutibacterium acnes*, followed by *Staphylococcus epidermidis* (Table 2); in patients without implant loosening, only *Cutibacterium acnes* was found (Table 2).

Of the 48 patients with implant loosening, 37 (77%) received postoperative antibiotics. Those who did not were regarded as having clear mechanical failure, and cultures were negative. In contrast, none of the 16 patients who underwent elective implant removal following fracture healing, and only 8 of the 29 patients (28%) with ASD, received postoperative antibiotics.

To examine whether the perioperative antibiotics administered during implantation were effective against the identified bacteria and could have prevented them, the bacteria's resistance profile was compared with the administered perioperative antibiotics. Prophylactic perioperative antibiotics of the index operation were 1st or 2nd generation cephalosporins (cefazolin and cefuroxime) or clindamycin in case of allergy (two cases). In six cases with significant bacterial cultures, the specific perioperative antibiotics used were unknown. Overall, sensitivity to the perioperative antibiotics of all bacteria cultured from removed spinal implants was 75% (18 out of 24) and resistance 25% (6 out of 24) (Table 3). While *Cutibacterium acnes* was found to be entirely sensitive to the applied antibiotics, *Staphylococcus epidermidis* showed complete resistance. For all resistant cases, alternative antibiotics existed, e.g., vancomycin or linezolid.

3.4. Re-revision rates and microbiology

Ultimately, the clinical significance and an optimal treatment strategy for detecting low-grade bacteria on non-loosened implants remain a question of debate. To explore this further, we conducted a follow-up analysis of patients with removed implants and re-instrumentation due to ASD and examined them for additional revision due to pedicle screw loosening. Of the 29 patients with ASD, 22 had a minimum follow-up of eight weeks and were included in this analysis. Among the six cases where significant bacterial cultures were obtained from implants during the first revision, three patients (50%) required additional revision due to pedicle screw loosening. This was compared to two out of 16 patients (13%) without initial detection of bacteria (p = 0.10) (Fig. 3). In the three cases with additional revision and initially positive bacterial cultures, one patient received twelve weeks of antibiotic treatment after the first revision. Comparatively, in the three cases with positive bacterial cultures but no additional revision, two patients received antibiotic treatment following the first revision (p > 0.99). Microbiological cultivation of cases with additional revision and initially positive cultures found *Cutibacterium acnes* and *Staphylococcus epidermidis* (both sensitive to the perioperative prophylactic antibiotics of the first revision) in one case during additional revision, *Cutibacterium acnes* (sensitive) and *Staphylococcus epidermidis* (resistant) in the second case and *Staphylococcus epidermidis*, *Bacillus cereus* and *Dermabacter hominis* (all three not tested for sensitivity/resistance) in the third case (Table 4). In the two cases without positive bacterial cultures from the first revision, the additional revision revealed *Cutibacterium acnes* (sensitive) in one case. In contrast, bacterial cultures remained negative in the second case (Table 4).

Table 1
Significant positive bacterial cultures by swabs and sonication from removed spinal implants.

	Screw loosening (n = 48)	Non-loosened (n = 45)	ASD (n = 29)	Healed fracture (n = 16)
Cultivation performed	46	30	21	9
Positive cultivation	19 (41%)	8 (27%)	6 (29%)	2 (22%)
Negative cultivation	27 (59%)	22 (73%)	15 (71%)	7 (78%)

Loosened vs. non-loosened: 41% vs. 27%, p = 0.23. Non-loosened cases were further divided into ASD and healed fractures (29% vs 22%, p > 0.99). In 17 cases no bacterial cultivation was performed. These cases were excluded from the analysis.

Table 2
Bacterial species isolated from intraoperative samples and sonication of removed spinal implants.

Bacterial species n (%)	Screw loosening (n = 22)	Non-loosened (n = 10)
Cutibact. acnes	10 (45.5%)	8 (100%)
Staph. epidermidis	6 (27.3%)	0
Staph. lugdunensis	2 (9.1%)	0
Cutibact. granulosum	1 (4.5%)	0
Staph. capitis	1 (4.5%)	0
Parvimonas micra	1 (4.5%)	0
E. coli	1 (4.5%)	0

Cutibact. = *Cutibacterium,* Staph. = *Staphylococcus*, E. = *Escherichia.*

Table 3
Sensitivity/Resistance rates of bacteria to prophylactic perioperative antibiotics of the index operation.

	All patients (n = 93)
All bacteria	30
Sensitive	18 (75%)
Resistant	6 (25%)
n/a	6
Cutibacterium acnes	18
Sensitive	15 (100%)
Resistant	0
n/a	3
Staph. epidermidis	6
Sensitive	0
Resistant	5 (100%)
n/a	1
Staph. capitis	1
Sensitive	0
Resistant	1 (100%)
n/a	0
Staph. lugdunensis	2
Sensitive	1 (100%)
Resistant	0
n/a	1
Cutibacterium granulosum	1
Sensitive	1 (100%)
Resistant	0
n/a	0
Parvimonas micra	1
Sensitive	1 (100%)
Resistant	0
n/a	0
E.coli	1
Sensitive	0
Resistant	0
n/a	1

Staph. = *Staphylococcus*, E. = *Escherichia.*

4. Discussion

In this retrospective analysis of a consecutive series of patients undergoing spinal implant removal of loosened and non-loosened implants, we analyzed if pedicle screw loosening was associated with pathogens and if the choice of perioperative antibiotic can prevent these

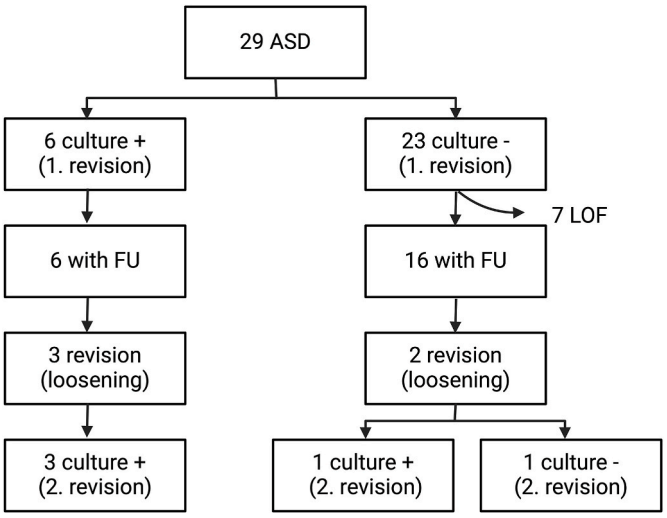

Fig. 3. Long-term follow-up of patients with non-loosened implants removed and re-instrumented for adjacent segment degeneration. Created with Biorender. ASD = adjacent segment degeneration, FU = follow-up, LOF = lost to follow-up.

Table 4
Bacterial species were detected during the first and second revision of cases with ASD and sensitivity to prophylactic antibiotics of index operation (op) and first revision, respectively.

Bacterium 1st revision	Sensitive to abx of index op?	Bacterium 2nd revision	Sensitive to abx of 1st revision?
Cutibact. acnes	yes	Cutibact. acnes	yes
		Staph. epidermidis	yes
Cutibact. acnes	yes	Cutibact. acnes	yes
		Staph. epidermidis	no
Cutibact. acnes	yes	Staph. epidermidis	not tested
		Bacillus cereus	not tested
		Dermabacter hominis	not tested
sterile	n/a	Cutibact. acnes	yes
sterile	n/a	sterile	n/a

Cutibact. = *Cutibacterium*, Staph. = *Staphylococcus*, abx = antibiotics.

bacteria during implantation.

4.1. High rates of positive cultures of non-loosened spinal implants

Low-pathogenic bacteria were not only detected with a high frequency in cases with screw loosening (41%) and assumed low-grade infection but also in cases with non-loosened implants (27%). Given the stringent criteria used to define significant bacterial isolation, the possibility of sample contamination can be ruled out. Recent studies demonstrated that bacteria, mostly low-pathogenic bacteria, were detected in 10–40% of samples (sonication of removed implants and swabs of surrounding tissue) taken from re-operated spine patients due to degenerative reasons (presumed aseptic cases) (Shiban et al., 2020; Shifflett et al., 2016; Burkhard et al., 2021). These findings suggest that the significance of detecting low-grade bacteria on spinal implants remains unresolved. While they appear to be more frequently found on loosened spinal implants, their presence on non-loosened implants raises questions about their pathological significance. This remains a critical question for future research. In our follow-up analysis, there was a trend for a more frequent additional revision due to screw loosening in initially culture-positive cases with ASD (i.e., non-loosened pedicle-screws) compared to the rate of initially culture-negative cases with ASD. However, this trend was not statistically significant. A recent study found the same rates of additional revision due to pedicle screw loosening when comparing initially culture-negative and culture-positive cases with all culture-positive cases treated antibiotically for three months (Burkhard et al., 2022). In our study, the additional revision rate for pedicle screw loosening of initially culture-positive patients with ASD did not differ significantly regarding whether patients received antibiotics after the first revision or not. However, this could also be due to the small number of cases. A valid statement on this requires further prospective studies with larger sample sizes.

4.2. The role of bone mineral density

BMD of patients without pedicle screw loosening was significantly higher compared to that of patients with loosened implants suggesting that low BMD may be the decisive factor for implant loosening. However, when comparing subgroups of patients without implant loosening, those with elective implant removal due to consolidated fractures had significantly better BMD than those with ASD. This is logical because implant removal in these patients only occurs when good bone quality is present, leading to fracture healing. Therefore, a selection bias favors better BMD in patients with non-loosened implants. When comparing only patients with ASD to those with loosened implants, a significantly better BMD was observed in patients with ASD compared to those with loosened screws and no pathogen detection, while BMD of patients with loosened screws and positive cultures was comparable to BMD of patients with ASD. This suggests that in patients with loosened pedicle screws without pathogen detection, reduced BMD is responsible for the screw loosening, whereas, in patients with loosened screws and positive bacterial cultures, BMD does not play a role. In these cases, the bacteria may actually be the decisive factor for the screw loosening. However, larger, prospective and randomized studies are necessary to better understand these dynamics and to quantify the influence of both BMD and bacterial presence on screw loosening.

4.3. High rates of Cutibacterium acnes despite sensitivity

The most frequently cultivated bacterium from the removed implants was *Cutibacterium acnes*, followed by *Staphylococcus epidermidis*, consistent with current literature (Leitner et al., 2018; Schafer et al., 2008; Trampuz et al., 2007; Burger et al., 2019).

While *Cutibacterium acnes* was entirely sensitive to the applied prophylactic antibiotics during implantation, we found complete resistance for *Staphylococcus epidermidis*. Despite a 100% sensitivity rate for *Cutibacterium acnes* to the prophylactic antibiotics administered during implantation, it was still found at high rates on removed implants. Our study cannot fully explain the reasons for this finding or the origin of this bacteria. An explanation could be that these bacteria are already in the deep tissue. Another hypothesis is that they were translocated from the skin into the depth during the first operation or revision surgery. Several widely discussed studies found *Cutibacterium acnes* in up to 44% of spinal disc tissue of patients undergoing first-time microdiscectomy (Capoor et al., 2017; Albert et al., 2013; Agarwal et al., 2011; Stirling et al., 2001) supporting the theory of deep tissue presence. However, a perioperative translocation from the skin into the deep cannot be definitively ruled out in these studies. McLorinan et al. (2005) examined samples of the skin and deep tissue of spinal surgery patients with immunofluorescence microscopy. They found identical phenotypes of *Cutibacterium acnes* in the deep tissue as on patients' skin, supporting the theory that these bacteria originate from the patient's skin.

Especially for coagulase-negative *Staphylococcus species*, previous research has shown that patients undergoing revision hip arthroplasty exhibited significantly more resistant strains on their skin than those undergoing primary surgery (Muhlhofer et al., 2017). The exclusive

detection of resistant *Staphylococcus epidermidis species* during revision surgery in our study suggests that these bacteria were translocated from the patient's skin to the deep tissue during the revision surgery.

4.4. The role of a dual antimicrobial prophylaxis

A high rate of *Cutibacterium acnes*, although sensitive, as well as a high rate of resistant *Staphylococcus epidermidis*, detected on the implants and presumably reaching there through translocation from the skin, should prompt us to revisit the current antimicrobial prophylaxis. Dual antibiotic prophylaxis has been widely discussed in the orthopedic field. For instance, no advantage was found in reducing acute surgical site infections after elective hip and knee arthroplasty when comparing a combination of vancomycin and cefazolin to cefazolin alon (Ponce et al., 2014; Sewick et al., 2012). However, in revision total knee arthroplasty, adding vancomycin to cefazolin significantly reduced the rate of periprosthetic joint infections (Liu et al., 2014).

Based on these results from orthopedics, dual antimicrobial prophylaxis supplemented with vancomycin could reduce the rate of bacteria cultivated from removed spinal implants. However, until the significance of detecting low-grade bacteria on non-loosened implants is clarified, no definitive recommendations can be made.

4.5. Limitations

A limitation of our study is its retrospective and non-randomized controlled design. Especially the time to re-operation, patients' age, and medical history differed substantially. Moreover, the impact of antibiotics taken for other reasons between the index operation and implant removal operation could not be accounted for. Additionally, the number of patients undergoing additional revision after revision for ASD was small and treatment regime of initially culture positive patients differed from case to case. A large-scale prospective randomized study is needed to determine the optimal treatment approach.

Finally, our study cannot explain why *Cutibacterium acnes* was isolated at such a high rate despite being entirely sensitive to the administered antibiotics. The clinical significance of low-grade bacteria found on non-loosened implants remains uncertain and further research is required to address this issue.

4.6. Strengths

To our knowledge, this is the first study to analyze a large consecutive series of patients with the removal of spinal implants performed at a single high-volume center using a standardized microbiological analysis and sonication.

5. Conclusion

This study has four key results. (1) Low-pathogenic bacteria were found not only on loosened implants but also in a significant number on non-loosened ones. (2) *Cutibacterium acnes* and *Staphylococcus epidermidis* were the most frequently detected bacteria. (3) While *Cutibacterium acnes* was entirely sensitive to the applied perioperative prophylactic antibiotics, *Staphylococcus epidermidis* was utterly resistant. (4) Not only a low BMD but also the detection of bacteria is associated with screw loosening.

Further prospective studies are warranted to clarify the significance of positive bacterial cultures on non-loosened spinal implants and to find the optimal antimicrobial prophylaxis strategy.

Author contributions

Conceptualization: SMK and AKJ; formal analysis: AKJ, VMB, SR, JSK and SF; investigation: AKJ and VMB; data curation: SMK, AKJ and VMB; writing—original draft preparation: AKJ and VMB; writing—review and editing: AKJ, VMB, SMK, SF, SR, JSK and BM; visualization: AKJ, SR; supervision: BM and SMK. All authors have read and agreed to the published version of the manuscript.

Data availability statement

The datasets generated during and/or analyzed during the current study are available from the corresponding author upon reasonable request.

Funding

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Declaration of competing interest

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