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Authors: Karan Goswami, Hannah Groff

QUESTION 3: Is there a difference in the type of pathogens that can cause surgical site infections/periprosthetic joint infections (SSIs/PJIs) between hip and knee arthroplasty?

RECOMMENDATION: There is limited evidence to support a difference in the organism profile causing SSIs and PJIs between hip and knee arthroplasty. Isolated studies have reported an increased prevalence of *Streptococcal* and culture-negative PJI around the knee, whereas, *Staphylococcal, Enterococcal, Pseudomonal* PJIs may be more prevalent around the hip. Further work regarding the different flora in these respective body regions is needed, as it may determine antibiotic selection.

LEVEL OF EVIDENCE: Limited

DELEGATE VOTE: Agree: 92%, Disagree: 4%, Abstain: 4% (Super Majority, Strong Consensus)

RATIONALE

Several studies have investigated the profile of organisms causing SSI and PJI following orthopaedic procedures with varying results. *Staphylococci* species are the most commonly isolated agents in orthopaedic prosthetic infections. According to recent literature, these pathogens are the primary source of up to 72% of infections [5–8]. Bacterial resistance has become a significant problem with certain studies reporting up to 27% of PJI are caused by methicillin-resistant organisms [9,10]. The prevalence of resistance also appears to be rising [11].

The published literature depicts *Staphylococcus aureus* (*S. aureus*) as the leading cause of PJI after total joint arthroplasty (TJA) [7,12,13]. A 14-year study evaluating the microbiological profile of PJI after two-stage revision from 1998-2011 found increased infection rates of methicillin-resistant *S.aureus* (MRSA), *Cutibacterium acnes* (*C. acnes*) and *Streptococcus viridans* (*S. viridans*) with no change in gram-negative, gram-positive or fungal infections [14]. Another study investigating 121 patients diagnosed with PJI after total knee arthroplasty (TKA) identified an increase in the prevalence of coagulase-negative *Staphylococcus* (CoNS) between 1994 and 2008, while *S. aureus* appeared to decrease [15]. A separate study conducted by Uçkay et al. evaluated resistance in CoNS orthopaedic infection over a 13-year period and did not identify any change in methicillin-resistance rates associated with CoNS [16].

Aggarwal et al. identified two different organism profiles when comparing 772 cases of PJI from the Rothman Institute in the United States (US) to 898 cases at HELIOS ENDO-Klinik, Hamburg in Europe [12]. The center in Europe had fewer *S.aureus* infections (13.0% vs. 31.0%), but more CoNS PJI than the US site (39.3 vs. 20.2%). There was also a significantly higher incidence of MRSA at the US center (48.1 vs. 12.8%; $p<0.0001$). However, there appears to be conflicting evidence regarding increasing prevalence of resistance in PJI [11].

The incidence of PJI affecting TKA versus total hip arthroplasty (THA) has been estimated at 1-3% and 0.3-2%, respectively [12–14]. Several studies have examined the organism profile causing PJI after arthroplasty, but few have identified any significant difference in profile between hip and knee arthroplasty.

Pulido et al. noted a higher rate of PJI in patients undergoing TKA (1.1%; 48 of 4185) compared to THA (0.3%; 15 of 5060; $p<0.0001$) [13]. A 14-year study identified a linear increase in MRSA, *S.viridans*, and *C.acnes* causing PJI after arthroplasty from 1998 to 2011. However, they identified no difference between organisms causing PJI in TKA and THA ($p> 0.05$) [14]. *Enterococcus* was found in the majority of THA (68%), but was not considered significant after a Bonferroni correction was performed comparing THA and TKA [14].

In a large multi-institutional study evaluating the organism profile causing PJI at two different academic centers, it was found that knees had more culture-negative infections at one of the two centers compared to hips. However, there were no other significant differences in organism profile when comparing hips and knees [12]. Drago et al. evaluated the organism profile and antibiotic susceptibilities of 429 patients diagnosed with PJI from 2013 to 2015 including 229 knee and 200 hip infections. Again, the authors found no difference in pathogen profile between hips and knees. *Staphylococci* were still the predominant organism affecting hips and knees followed by *Enterobacteriaceae* and *C.acnes*. However, methicillin resistance in CoNS was twice as prevalent around the knee versus the hip. Increased resistance to glycopeptides and fluoroquinolones was also observed around the knee in comparison to the hip [17]. Future

studies should aim to further investigate these potential differences in the organism and resistance profiles in hips and knees diagnosed with SSI and PJI.

Groff *et al.* recently examined 1,214 PJI cases (501 hips and 713 knees) over a 17-year timeframe and found significant differences in pathogens causing PJI in the hip and the knee. A higher incidence of *Streptococcal* species (odds ratio (OR) 1.82, 95% confidence interval (CI), 1.23-2.67) and culture-negative PJI (OR 1.53, 95% CI, 1.12-2.09) were identified in TKA compared to THA. In contrast, *Pseudomonas* (OR 2.123, 95% CI, 1.04-4.34), *Enterococcus* (OR 1.72, 95% CI, 1.03-2.86), resistant species (OR 1.64, 95% CI, 1.19-2.25), *Staphylococcus aureus* (OR 1.40, 95% CI, 1.11-1.77) and gram-positive (OR1.37, 95% CI, 1.05-1.78) organisms were more prevalent in hips. The authors suggested that the higher rates of urogenital-associated pathogens causing PJI in hips may have been related to the close proximity of the incision to the flexural creases and the groin region.

Although most studies have not demonstrated a definitive difference in organism profile between hips and knees, some have identified differences in virulence patterns, culture-negative rates, urogenital and fecal bacteria, as well as the overall rates of PJI in bilateral compared to unilateral TKA [12–14,17]. It is important to further delineate the differences in organism profile at these anatomic sites in order to establish adequate protocols and select antimicrobials accordingly, that may account for potential differences in the pathogenic flora and mitigate the risk of SSI/PJI.

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Authors: Paul M. Courtney, Nemandra A. Sandiford, Daniel Kendoff

QUESTION 4: Is there a difference in the organism profile that causes periprosthetic joint infections (PJIs) in different countries?

RECOMMENDATION: Yes, there is a difference in the organism profile causing PJIs in different countries and regions of this world. There seems to be a higher incidence of PJI caused by methicillin-resistant *Staphylococcus aureus* (MRSA) in the United States and Australia compared to Europe.

LEVEL OF EVIDENCE: Moderate

DELEGATE VOTE: Agree: 97%, Disagree: 1%, Abstain: 2% (Unanimous, Strongest Consensus)

RATIONALE

General strategies to prevent occurrence of PJIs have become more relevant over the last few years. As one recommendation of the International Consensus Meeting on Periprosthetic Joint Infection in 2013, surgical antibiotic prophylaxis with either single or 24-hour dose of cephalosporin should be performed. However, antibiotics (prophylactic and therapeutic) should be selected to cover the most frequently encountered pathogens, which might vary regionally, nationally and internationally (and could be affected as well by other factors) and not simply be administered empirically.

To date, several authors have described the bacterial incidence in isolated series of PJI with either single- or multicenter studies. However, the comparison of organism profiles causing PJI between countries or world regions has been evaluated by relatively few studies.

A study comparing organism profiles between PJI referral centers in the United States (US) (Rothman Institute) and Europe (HELIOS ENDO-Klinik) found that the percentage of MRSA pathogens was significantly higher in the US than in Europe [1]. In addi-