

rule out infection prior to revision surgery. They observed that the PJI rate, occurring within three months after revision surgery, was lower in the long prophylaxis group compared to the short prophylaxis group (2.2% vs. 6.9%, $p = 0.049$). In addition, prolonged antibiotic prophylaxis was the only variable independently associated with a lower rate of PJI in their analysis (odds ratio (OR): 0.27, 95% confidence intervals (CI): 0.07–0.99). These data suggest that there might be a protective effect of prolonging antibiotic prophylaxis. However, although no other protocol modifications were made during the study period according to the authors, bias cannot be completely ruled out due to the retrospective nature of the study, especially as diagnostic methods to rule out an infection prior to revision surgery have been improved over recent years. Thus, there is a need for a randomized controlled trial that can examine this question. The PARITY trial, an international prospective randomized controlled trial currently conducted in the field of orthopaedic oncology, may provide us with additional evidence about the potential benefit of extended antibiotic prophylaxis in high-risk patients undergoing joint arthroplasty [16].

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QUESTION 6: Should duration and the type of antibiotic prophylaxis be altered in patients with a prior periprosthetic joint infection (PJI)?

RECOMMENDATION: Antibiotic prophylaxis should be tailored in patients with prior PJIs who are undergoing another subsequent elective primary or revision joint arthroplasty. Antibiotic prophylaxis should cover the initial causative organism(s) as well as the most common pathogens that can cause PJI with either single or dual antibiotics.

LEVEL OF EVIDENCE: Limited

DELEGATE VOTE: Agree: 93%, Disagree: 6%, Abstain: 1% (Super Majority, Strong Consensus)

RATIONALE

Patients with prior PJIs have a significantly higher risk for PJI in another prosthetic joint. Murray [1] described for the first time the risk of metachronous infections in multiple joints due to hematogenous spread. Studies by Parvizi et al. [2] and Leung et al. [3] both demonstrated that the majority of recurrent infections following PJI due to methicillin-resistant *Staphylococcus aureus* (MRSA) were reinfecting with the same organism (66.7 and 89.9%, respectively).

Preexisting PJI was identified as a significant risk factor for a subsequent infection in a study by Luessenhop et al. in 1996 [4]. The presence of rheumatoid arthritis and a prior sepsis were shown to be significantly associated with a higher risk for development of subsequent PJI ($p < 0.001$ and $p < 0.0001$, respectively).

Another study by Jafari et al. [5] retrospectively identified 55 patients with PJI who had another prosthetic joint in place at the

time of presentation. Eleven of them (20%) developed a PJI in a second joint, with the same bacteria in 36% of cases. Zmistowski et al. [6] found that recurrent PJI was due to the same organism as the index infection (PJI persistence) in 31.5% of 92 relapsed cases, following two-stage arthroplasty failure. A new organism (PJI reinfection) was observed in 68.5% of these cases. The only independent predictor of PJI persistence versus new infection was the original infecting organism, specifically *Staphylococci* (MRSA in particular). Moreover, polymicrobial PJIs were more frequently involved in immunocompromised hosts.

Bedair et al. [7] confirmed these observations in a multicenter, retrospective cohort study with 90 patients previously treated for PJI undergoing a second primary total hip or knee arthroplasty (THA or TKA). The study showed that patients with a history of PJI had a

higher risk of developing PJI in a subsequent THA or TKA (10 of 90, versus 0 of 90 in the control group; risk ratio: 21.00; 95% confidence interval (CI), 1.25-353.08; $p = 0.04$). The authors found that a second PJI occurred more frequently in those whose initial infection was by a staphylococcal species (odds ratio (OR), 4.26 $p = 0.04$). The infecting organisms were the same species in the first and second PJI in 40% of cases, and all four of these were caused by Staphylococci.

Based on the available data, it appears that patients with a prior PJI who are undergoing elective arthroplasty are at higher risk of subsequent infection. The infecting organism for the second joint is most of the time same as the first infecting organism. Taken together, we feel that antibiotic prophylaxis for patients with a prior PJI who are undergoing an elective primary or revision arthroplasty needs to be altered. These patients may require administration of an alternative or additional antibiotic(s). For example, patients with a prior PJI by a gram-negative organism should receive prophylactic antibiotics against gram-negative bacteria. The same applies to patients with a prior MRSA infection and so on.

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QUESTION 7: Should prophylactic antibiotic therapy be administered for an extended duration in patients admitted to the Intensive Care Unit (ICU)?

RECOMMENDATION: Surgical prophylactic antibiotic therapy should not be administered for an extended duration in patients admitted to the ICU.

LEVEL OF EVIDENCE: Limited

DELEGATE VOTE: Agree: 82%, Disagree: 13%, Abstain: 5% (Super Majority, Strong Consensus)

RATIONALE

The literature on surgical site infections (SSIs) classifies SSI risk factors into intrinsic (patient) related (e.g., age and underlying morbidity) and extrinsic (procedure) related (procedure, facility, pre-and intraoperative factors), both being either modifiable or not [1]. Admittance to the ICU is not treated as an independent risk factor, although risk factors for SSIs and risk factors for ICU admittance are correlated (age, co-morbidity, complexity of procedure). Using the published search algorithm from the World Health Organization (WHO) guideline's literature review and narrowing it with the term "ICU" and expanding it with the term "observational study," 180 articles were retrieved from October 1, 2015 until present (PubMed 39, Embase 84, Central 57). All abstracts were screened, but none found relevant for the question of extending antibiotic duration in patients admitted to the ICU. Using the unaltered WHO search algorithm (without narrowing with "ICU" and expanding with "observational study"), another 23 PubMed articles not covered within the first search were identified, but none of the screened abstracts were relevant. An unsystematic search in the PubMed Clinical Queries search was then performed with the terms "(Therapy/Broad [filter]) AND (antibiotic prophylaxis extended)" returning 245 articles. All titles were screened and abstracts of putative relevance reviewed and none were found to be relevant. The 34 articles retrieved with a modified search term (Therapy/Broad [filter]) AND (antibiotic prophylaxis prolonged ICU) were not found to be relevant either. Thus, no studies were found examining extended antibiotic prophylaxis in ICU patients when these patients are considered as a separate patient

category and there are no data to support or refute an extended duration for preventing SSIs solely based on the admittance to the ICU.

However, ICU patients are included in the core randomized controlled trials (RCTs) showing no benefit of extending antibiotic prophylaxis past wound closure [2,3] albeit not specifically for arthroplasty patients. Since the publication of the Proceedings of the International Consensus Meeting on Periprosthetic Joint Infections in 2013, three major literature reviews and guidelines on prevention of SSI have been published from WHO [2], Centers for Disease Control and Preventiopl (CDC) [3], and the American College of Surgeons and Surgical Infection Society (ACS/SIS) [1], respectively. The CDC and WHO guidelines agree on not extending prophylaxis past wound closure based on a comprehensive systematic literature review, but the strength of the data supporting the recommendation for arthroplasty have been questioned [4-11]. The ACS/SIS makes an exception for prophylactic antibiotics past wound closure for joint arthroplasty, on the grounds that optimal antibiotic therapy for these patients remains unknown, but refers to the American Society of Health-System Pharmacists (ASHP); Infectious Diseases Society of America (IDSA); Surgical Infection Society (SIS); and the Society for Healthcare Epidemiology of America (SHEA) guidelines for a total antibiotic prophylaxis duration ≤ 24 hours [12]. A recently published meta-analysis and review on postoperative antibiotic prophylaxis in knee and hip arthroplasty did not find evidence to show efficacy of extended antibiotic prophylaxis for the prevention of SSI in patients undergoing total hip or knee arthro-