

G7: Should the administration of prophylactic antibiotics be weight-based?

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Response/Recommendation:

Yes. Administration of all prophylactic antibiotics needs to be weight-based.

Level of Evidence: Strong.

Delegate Vote:

Rationale:

Obesity is a well-established major risk factor for surgical site infection (SSI) and periprosthetic joint infection (PJI), contributing to higher infection rates through multiple physiological and pharmacokinetic mechanisms. [1–4] One major way in which obesity increases the risk of SSI/PJI is by making it more challenging to achieve adequate therapeutic tissue and serum concentrations with standard antibiotic dosing. Obese patients have an increased volume of distribution and altered drug metabolism, which can result in subtherapeutic antibiotic levels when fixed dosing regimens are used. Studies have demonstrated that patients who have a body mass index (BMI) ≥ 35 or who weigh ≥ 120 kg face a markedly higher risk of PJI. A retrospective cohort study found that underdosed patients in this weight category had a 1-year PJI rate of 3.25%, while those who received weight-adjusted dosing experienced a significantly lower rate of 0.83%. [5,6]

Beyond pharmacokinetic challenges, obesity predisposes patients to infection through poor vascular perfusion, which limits antibiotic penetration to the surgical site, and increased subcutaneous tissue, which creates a favorable environment for bacterial colonization. [7,8] Additionally, obesity is associated with higher rates of wound complications, delayed healing, and chronic systemic inflammation, further compounding the risk of PJI. [9–11] Given these multifaceted challenges, weight-based antibiotic dosing is essential to ensure effective prophylaxis and improve surgical outcomes in obese patients.

Weight-based dosing ensures adequate drug levels in both serum and bone tissue, which is critical for effective infection prophylaxis in total hip and knee arthroplasty. Antibiotics like cefazolin must reach sufficient concentrations not only in the bloodstream but also in the bone and soft tissues surrounding the surgical site to prevent bacterial colonization and subsequent PJI. [12,13] Studies evaluating the trabecular bone concentrations of cefazolin have demonstrated that fixed dosing frequently results in subtherapeutic levels, particularly in obese patients. This is attributed to the increased volume of distribution in individuals who have higher body weights, which dilutes the antibiotic concentration in both serum and tissue compartments. [14] For example, one study found that fixed-dose cefazolin failed to achieve the minimum inhibitory concentration (MIC) for common pathogens such as methicillin-sensitive *Staphylococcus aureus* (MSSA) in a significant proportion of obese patients. Conversely,

weight-adjusted dosing protocols, such as administering two g of cefazolin for patients weighing 60 to 120 kg and three g for those over 120 kg, have been shown to maintain adequate serum and tissue levels, effectively reducing the risk of PJI.[15]

Moreover, adequate antibiotic penetration into bone tissue is particularly important for combating low-virulence organisms that can persist in the avascular or poorly perfused areas surrounding prosthetic implants. A weight-based approach ensures that therapeutic concentrations are achieved uniformly across patient populations, mitigating the risk of underdosing in heavier individuals and the associated complications. This strategy not only improves prophylactic efficacy but also reduces the likelihood of bacterial resistance arising from subtherapeutic dosing.[6,9,14]

Weight-based antibiotic dosing is endorsed by professional organizations such as the American Academy of Orthopaedic Surgeons (AAOS), International Consensus Meeting (2018), and the Centers for Disease Control (CDC), which recommend adjusting cefazolin and vancomycin doses based on body weight to optimize efficacy. [18] Beyond clinical benefits, this approach is also cost-effective. By reducing the incidence of PJIs, weight-adjusted dosing minimizes the need for costly revision surgeries and extended hospital stays, with PJI treatment costs often exceeding \$50,000 per case. Implementing these evidence-based dosing strategies enhances both patient outcomes and healthcare resource utilization.[15]

Conclusion:

Weight-based antibiotic administration is a crucial component of effective surgical prophylaxis in orthopaedic surgery. By ensuring optimal drug concentrations in serum, bone, and periarticular soft tissues, this approach significantly reduces the risk of SSI/PJI, particularly in obese and high-risk patients. Evidence from clinical studies supports its role in improving infection prevention, surgical outcomes, and overall patient safety. Furthermore, adopting weight-adjusted dosing protocols aligns with evidence-based best practices and professional guidelines, reinforcing their necessity in modern orthopaedic surgery.

Practical Considerations:

- Weight-adjusted dosing protocols should be implemented as standard practice for antibiotic prophylaxis in arthroplasty.
- Dosing adjustments should account for patient-specific factors such as BMI and comorbidities.

To achieve optimal prophylaxis, the following dosing guidelines are recommended:

Cefazolin: Two g for patients <120 kg, three g for patients $\geq$ 120 kg

Vancomycin: 15 mg/kg, timed to ensure peak levels at incision

Intraoperative redosing: Additional doses for procedures exceeding three to four hours or with major blood loss

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