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QUESTION 5: What type, dose and duration of prophylactic antibiotic(s) should be administered to patients undergoing oncologic endoprosthetic reconstruction who have received or will be receiving chemotherapy and/or radiation?

RECOMMENDATION: Antibiotic prophylaxis should be given in accordance with existing guidelines for standard arthroplasty surgery and other orthopaedic surgical procedures with foreign body placement.

LEVEL OF EVIDENCE: Consensus

DELEGATE VOTE: Agree: 93%, Disagree: 0%, Abstain: 7% (Super Majority, Strong Consensus)

RATIONALE

Studies examining the effect of chemotherapy and radiation on risk of postoperative infection in tumor patients have found an increased risk of surgical site infection (SSI) following radiation therapy (thoracic, head and neck, gynecological, breast malignancies) and chemotherapy (thoracic, head and neck, breast malignancies) [1,2]. No studies have been conducted to compare different prophylactic antibiotic regimens for patients who received radiation or chemotherapy prior to surgery; in a single randomized, controlled trial comparing prophylactic antibiotics with placebo in breast cancer patients, no significant difference was seen in the risk of developing postoperative infection between patients who received neoadjuvant chemotherapy and those who did not [3].

Studies examining the effect of chemotherapy and radiation on risk of postoperative infection specifically in patients with bone tumors and metastases have shown differing results based on the type and location of disease. A study of patients who underwent a variety of lower-extremity oncological operations did not find either chemotherapy or radiation to increase the risk of infection [4]. Similarly, in a cohort of patients undergoing surgery for primary bone tumor, mostly involving the lower limb, chemotherapy was not a risk factor for infection, nor was it in a group of patients who underwent endoprosthetic reconstruction for tumors around the knee [5,6]. On the other hand, a study of patients with spinal metastases found that postoperative radiation was associated with increased risk of infection [7].

As no studies have been conducted addressing the tailoring of antibiotic prophylaxis in oncologic patients undergoing tumor surgery pre- or post-radiation or chemotherapy, including endoprosthetic reconstruction, prophylaxis should be given in accordance with existing guidelines for arthroplasty and other orthopaedic surgical procedures with foreign body placement [1,8]. In the event of colonization with methicillin-resistant *Staphylococcus aureus*, the choice of intravenous antimicrobial prophylactic agent should be adjusted accordingly.

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QUESTION 6: Does the type, dose, and duration of antibiotic prophylaxis differ for patients undergoing oncologic endoprosthetic reconstruction compared to conventional total joint arthroplasty (TJA)?

RECOMMENDATION: No. There is no recommendation to adjust type, dose or duration of antibiotic prophylaxis in patients undergoing oncologic endoprosthetic reconstruction from that which is routinely administered in conventional TJA.

LEVEL OF EVIDENCE: Consensus

DELEGATE VOTE: Agree: 93%, Disagree: 0%, Abstain: 7% (Super Majority, Strong Consensus)

RATIONALE

Rates of infectious complications following knee and hip arthroplasty are generally less than 2% [1]. However, rates of infectious complications following lower-extremity limb salvage therapy with endoprostheses are approximately 10% [2]. The reason for this difference remains unclear, possibly due to systemic factors not directly related to the presence of localized malignancy [3].

Preoperative parenteral antibiotics have been demonstrated to reduce wound infections following TJA [4]. In a meta-analysis of antibiotic prophylaxis in TJA, which included 7 studies with 3,065 participants, the relative risk of infection was reduced by 81% compared to placebo [4]. None of the studies included in the meta-analysis or accompanying systematic review specifically addressed prophylaxis in patients undergoing orthopaedic endoprosthetic reconstruction.

Based on the preponderance of evidence, clinical guidelines recommend the use of perioperative parenteral antibiotics before TJA and other orthopaedic surgeries with foreign body placement [5,6]. No data exist regarding the tailoring of prophylaxis in oncologic patients with endoprosthetic reconstruction. Therefore, antibiotics should be given in accordance with accepted regimens.

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1.2. PREVENTION: CHEMOTHERAPY

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QUESTION 1: Do we need to evaluate the gut and skin microbiome of patients after chemotherapy to assess the risk for potential infection after endoprosthetic reconstruction?

RECOMMENDATION: Unknown. There is no evidence in the literature to suggest that evaluation of the gut and/or skin microbiome following chemotherapy aids with risk stratification for potential infection in patients undergoing endoprosthetic limb salvage surgery.

LEVEL OF EVIDENCE: Consensus

DELEGATE VOTE: Agree: 100%, Disagree: 0%, Abstain: 0% (Unanimous, Strongest Consensus)

RATIONALE

In the orthopaedic oncology literature, infection rates following metallic endoprosthesis limb salvage surgery are high and vary from 2.2–34% [1–4]. In a systematic review of the literature, Henderson et al. found the overall rate of infection-related failure of endoprostheses to be 7.8% and infection as the most common mode of failure in their current investigation of primary endoprostheses. Proximal tibia replacements and total femur replacements were noted to be at particular risk, requiring infection-related revision surgery in 19.7% and 17.5% of cases, respectively [1].

While not fully understood or rigorously investigated, the causes of these high rates of infection are likely multi-factorial, including extensive surgical dissection and resection, increased operation time, substantial loss of blood, inadequate soft tissue coverage, implantation of large constructs with foreign material and, often in the case of oncology patients, a poor nutritional and compromised immune status [5].

Perioperative chemotherapy has been shown to increase the total revision rates of endoprosthetic reconstruction to 40% from 10% due to its reduction of osseointegration [6]. The impact of chemotherapy on the rates of infection following endoprosthetic reconstruction remains unclear. There are conflicting reports on whether immunological deficiency following chemotherapy is a risk for postoperative infection of endoprostheses. In a review, Kapoor and Thiyam documented that a compromised immune status after neoadjuvant chemotherapy may result in postsurgical infection having an increased infection rate of 20% [5]. While in a multicenter retrospective review, Morii et al. showed chemotherapy did not affect infection risk and suggested no drawbacks related to chemotherapy in regards to postoperative infection control of endoprostheses [2]. It was shown that some patients who developed infection during postoperative chemotherapy were controlled by amelioration of myelosuppression alone, while others required revision and antibiotic therapy [7].

Any measure that leads to decreased infection rates of metallic endoprosthesis reconstruction would be desirable. Given the prevalence of the problem and the severity of the consequences of deep infection, even weak evidence supporting a decrease in postoperative infection rates would be worth considering. While a few interven-