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1.3. PREVENTION: RESEARCH CAVEATS

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QUESTION 1: What are the significant risk factors for surgical site infection/periprosthetic joint infection (SSI/PJI) of an oncologic endoprosthesis following resection of a malignant bone tumor?

RECOMMENDATION: Patient-related risk factors for SSI/PJI of an oncologic endoprosthesis include increased patients' body mass index, overall presence of comorbidities, coexistence of superficial SSI or skin necrosis and lower preoperative hemoglobin or albumin levels. Disease-related risk factors for SSI/PJI of an oncologic endoprosthesis include lesion localization in proximal tibia, pelvis and lesion extending to pelvis from proximal femur. In addition, procedure related risk factors for SSI/PJI include preoperative hospitalization longer than 48 hours, resection of greater than 37% of the proximal tibia, resection of 3 or 4 heads of the quadriceps muscle in distal femoral lesions compared to 1 or 2 heads, increasing surgical time (longer than 2.5 h), use of cemented oncologic endoprosthesis, need for postoperative admission to the intensive care unit, increased postoperative blood transfusion requirement (2 or more units of allogeneic packed cells), presence of postoperative hematoma and the need for additional surgical procedures after the megaprosthesis implantation.

LEVEL OF EVIDENCE: Moderate

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

RATIONALE

Periprosthetic joint infection represents one of the most challenging complications following any joint replacement and may result in devastating consequences. According to a recent systematic review, the mean rate of periprosthetic infection of a megaprosthesis (PMI) is 10% after primary procedure and 43% after revision procedures of infected cases [1,2].

Despite the lack of multiple randomized clinical trials, several retrospective studies (Level IV) showed significant risk factors for SSI/PJI of an oncologic endoprosthesis following resection of a malignant bone tumor. In a systematic review of the literature, De Gori et al. examined risk factors for PMI [3]. A total of 8 articles, all retrospective, including 2,136 patients, met the inclusion criteria and were analyzed [4–11]. The overall PMI rate was 14.2%. Patient-related factors associated with a significantly higher risk of PMI included increasing patients' body mass index and overall presence of comorbidities (but not the American Society of Anesthesiolgists (ASA) score or diabetes mellitus specifically) and coexistence of superficial surgical site infection or skin necrosis. Disease-related factors associated with increased risk for PMI included lesion localization in proximal tibia, pelvis and lesion extending to pelvis from proximal femur. In contrast, lesions localized in the distal femur appear to be protective for PMI occurrence. There was no association between primary tumor histological features or metastatic spread and PMI. In addition, there was no significant effect of chemotherapy and radiotherapy for the development of PMI, which is in contrast to several studies [12–15] which report increased incidence of infection rate associated with chemotherapy and radiotherapy. Controversy also still exists regarding whether primary or metastatic lesions have higher risk for PMI [3,12]. In this systematic review, procedure-related factors associated with higher risk of PMI included preoperative hospitalization longer than 48 hours, resection of greater than 37% of the proximal tibia, resection of 3 or 4 heads of the quadriceps muscle in distal femoral lesions compared to 1 or 2 heads, increasing surgical time (longer than 2.5 h), need for postoperative admission to the intensive care unit, increased postoperative blood transfusion requirement (2 or more units of allogenic packed cells), presence of postoperative hematoma and the need for additional surgical procedures after the megaprosthesis

implantation. According to this systematic review, features of perioperative antibiotic prophylaxis do not affect PJI rates, i.e., choice of antibiotic used, dosing, number of antibiotics used postoperatively or length of prophylaxis, which is in contrast to previous systematic review conclusions [1]. In addition, width of resection margins, bone resection length and extracapsular resection of knee tumors were not associated with increased rates of PMI. There was no difference in PMI rates according to prosthesis type or hinge movement, but two studies have shown that cemented megaprostheses have led to a higher PMI rate compared to uncemented ones, thus contradicting information regarding conventional arthroplasties. Routine use of gastrocnemius flap for anterior reconstruction and megaprosthesis coverage following proximal tibia resection has led to a reduced rate of PMI. Data of this systematic review supports the idea that soft tissue condition merely influences the PMI rate [16].

According to a most recent Level III retrospective cohort study on 150 patients, reported by Meijer et al., factors associated with infection after reconstructive shoulder surgery for proximal humerus tumors were lower preoperative hemoglobin or albumin levels and these patients should undergo optimization before surgery [17]. In addition, a lower WBC count and positive resection margins were associated with superficial infection and younger age with deep infection [17]. Furthermore, the location of the endoprosthesis may also influence the infection risk as the lower extremities have been demonstrated to have a greater risk of infection than the upper extremities [15].

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QUESTION 2: What metrics should be used to determine the optimal timing of reimplantation for patients with a resected oncologic endoprosthesis?

RECOMMENDATION: Prior to reimplantation of an oncologic endoprosthesis after a previous resection, surgeons must ensure that the infection has been eradicated from the surgical bed. This would be determined via a sterile aspirate from the joint cavity following the antibiotic treatment.

LEVEL OF EVIDENCE: Moderate

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

RATIONALE

Periprosthetic infection following oncologic endoprosthestic limb salvage surgery is a well-recognized and devastating complication [1]. Surgeons who treat oncologic patients with endoprostheses need to have a low tolerance to suspected periprosthetic infection. Oncology patients are at greater risk of infection than general arthroplasty patients, up to 15% of oncological endoprosthetic reconstructions compared to 1-2% within the general population [2,3]. Early diagnosis and treatment are key to outcome. Surgical treatment options include amputation, irrigation and debridement, excision arthroplasty, and one- and two-stage revision, along with targeted antibiotic therapy. Two-stage revision involves initial irrigation, debridement, removal of the endoprosthesis with implantation of a cement spacer and later reimplantation of the device. Despite the established acknowledgement that the two-stage revision is the gold standard for surgical treatment [4], there is a limited amount of information on the clinical parameters that should be used to optimize the reimplantation of an endoprosthesis following initial staged debridement and resection.

A search of the literature found nine retrospective studies, six retrospective cohort studies and three retrospective case studies