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

Study Name	Study Type	Total Number of Patients	Number of Patients Who Developed Infections	Infected Patients Who Underwent Two-stage Revision	Patients With Infections Controlled Successfully (%)
Jeys et al., 2005	Retrospective cohort study	1264	136	58	42 (72%)
Funovics et al., 2011	Retrospective cohort study	170	12	2	2 (100%)
Hardes et al., 2006	Retrospective case study	30	30	15	12 (80%)
Donati et al., 1998	Retrospective cohort study	35	20	19	14(74%)
Rao et al., 2006	Retrospective cohort study	9	9	9	8 (89%)
Manoso et al., 2006	Retrospective case series	11	11	11	10 (91%)
Grimer et al., 2002	Retrospective case series	34	34	34	25(74%)

TABLE 1. Endoprosthetic infection two-stage revision study data

[5–13]. Seven of these studies required clearance of residual infection as determined by a sterile aspirate sample from the periprosthetic space before the revision endoprosthesis could be reinserted [5-11]. These studies showed the success rate of preventing reinfection ranged between 72-100% if reimplantation was conducted using this metric.

The results of four studies following one-stage revision to control infection varied. This approach was performed when the operating surgeons deemed the infection was early in its course or low grade. Funovics et al. reported success rate of 62.5% (5 out of 8 patients) [6]. Jeys et al. found 47% (15 out of 32) of one-stage revisions eradicated the infection [5]. Hardes et al. only found success in 1 out 3 patients (33%) treated with this technique [11]. Holzer et al. reported a success rate comparable to those reported by two-stage revisions at 78% (14 out of 18 patients cleared their infections) [12]. The results of these studies show that the efficacy of one-stage revisions in treating infected oncological endoprotheses is inferior to that of a two-stage approach following negative aspirates. However, the low sample numbers make it difficult to draw a definitive conclusion.

Finally, four of the studies also reported on the importance of adequate soft tissue coverage prior to reimplantation [9-11,13]. This was used as a subjective clinical parameter. Three studies noted that the decision to proceed to the second stage was delayed until adequate soft tissue coverage and wound healing was seen [10,11,13]. Rao et al. noted the influence of different types of soft tissue flaps on infection control in two-stage revisions [9].

Despite the lack of higher quality literature, there has been consistent support by several retrospective studies for using sterile periprosthetic cavity aspirates as a clinical metric to indicate optimal timing for oncological endoprosthesis reimplantation. Other subjective parameters, such as soft tissue coverage and stage of infection, were also recorded. While clearer parameters exist in revision cases for general arthroplasty, more robust evidence, including larger sample sizes and randomized clinical trials, are desired for oncological endoprosthesis. Thus, only a moderate strength recommendation can be provided.

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