

Authors: Christina Gutowski, Michelle Ghert, Anthony Bozzo, Marc Levine

QUESTION 2: When should a surgical drain be removed to minimize the risk of subsequent surgical site infection/periprosthetic joint infection (SSI/PJI) in patients who have received endoprosthetic reconstruction (EPR) following resection of a musculoskeletal tumor?

RECOMMENDATION: Based on the available literature, we recommend drains be removed within 24 hours of surgery.

LEVEL OF EVIDENCE: Limited

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

RATIONALE

Drains are plastic tubes that are used to prevent the formation of surgical site serous pockets (seromas) and blood pockets (hematomas), both of which may act as a space for potential surgical site infection in addition to causing pain [1]. In orthopaedics, drains are commonly used to reduce collection of fluid around the joint and potentially reduce subsequent SSIs despite little evidence showing their benefit [2,3]. The utilization of closed suction drainage systems in primary arthroplasty has been debated for many years. Anecdotally, the benefits of a drain are thought to be prevention of hematoma formation and therefore improved wound healing and decreased infection rates [2]. The main disadvantage is the creation of a communication between the deep tissues and the surrounding environment, providing a conduit for bacterial contamination [2]. In fact, drains are known to be risk factor for SSIs [4]. Patel et al. have reported a relative risk increase in SSIs of 42% with each additional day of wound drainage [5]. Despite the scarcity of evidence supporting their benefit and known risks, orthopaedic surgeons continue to utilize drains in their procedures [6].

PJI rates after elective total joint replacement are reported between 1-2% [7,8]. However, the risk of PJI following EPR is even higher with rates ranging between 10-25% [9,10]. Because drains are a known risk factor for SSIs, their use in orthopaedic oncologic procedures is of particular concern. Oncology patients are at increased risk because many of them are immunocompromised. Secondly, this patient population often develops a large dead space after tumor resection necessitating placement of a surgical drain to prevent hematoma formation in the postoperative period.

A large meta-analysis of all randomized controlled trials of drain use in orthopaedic surgery was published by Parker et al. in 2004. They found no significant difference between wounds treated with and without drains with respect to the development of wound infection, wound hematoma or reoperations for wound complications [11]. However, the drained wounds did have a significantly greater need for blood transfusion [11]. These overall findings have been shown in numerous other studies of patients undergoing arthroplasty, general surgical and orthopaedic trauma procedures [12-14].

In 2007, a Cochrane Systematic Review was conducted to assess the utilization of drains in orthopaedic surgery. Thirty-six studies involving 5,464 patients with 5,697 surgical wounds were included [2]. Many orthopaedic procedures were utilized, although there was no specific mention of oncologic patients in the review. Pooling of results showed no statistically significant difference in the incidence of wound infection, hematoma, dehiscence or reoperation between those who had a drain and those who did not [2]. The incidence of SSI was 1.9% in patients who received a closed suction drain and 2.4% in those who did not [2]. Blood transfusions were required

more frequently in those who received drains [2]. Previous literature has found an association between blood transfusion and infection in both the arthroplasty and orthopaedic oncology literature [15,16]. Despite the described findings of previous literature and the increased blood transfusions in the drain group, an independent relationship between drain placement and infection was not found in the Cochrane review [2].

In terms of the timing of drain removal, the literature remains inconclusive. In their prospective study of 214 uninfected orthopaedic operations, Sankar et al. found no significant correlation between wound infection and duration of drain retention [17]. Another prospective study examined total hip and knee arthroplasty patients who all received suction drains. Upon drain removal, the patients' drain-sites were swabbed and the drain tips were sent for culture [18]. This study demonstrated that the likelihood of bacterial colonization increased while wound drainage decreased over time; however, this does not necessarily translate to clinical development of SSI and their recommendation for removal at 24 hours must be cautiously considered [18].

Willett et al. attempted to further examine the timing of drain removal by removing drains at 24, 48 or 72 hours and culturing the aspirates taken from the drain tip; they found increasing rates of positive cultures in the groups where the drain was removed later. However, this difference was not statistically significant [19]. The authors of this study conclude that their data affirm the risk of retrograde influx of organisms along the drain track if the drain remains in place longer than 24 hours [19]. However, because their results were not statistically significant, they were incorrectly drawing this conclusion.

From the arthroplasty and surgical literature, there is no evidence of benefit to extending antibiotic duration until drains are removed; however, this has not specifically been evaluated in a musculoskeletal oncology patient population [20,21]. Due to the scarcity of quality literature in this area and the lack of evidence suggesting a relationship between utilization of drains and SSI, an evidence-based recommendation regarding the use of drains and the timing of their removal cannot be made for orthopaedic oncology patients.

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Authors: Richard O'Donnell, John Strony

QUESTION 3: Does the type of fixation (cemented vs. uncemented) of an oncologic endoprosthesis influence the incidence of subsequent surgical site infection/periprosthetic joint infection (SSI/PJI)?

RECOMMENDATION: There is conflicting evidence surrounding this topic. Multiple studies have demonstrated superiority with cemented fixation of an oncologic endoprosthesis while others have suggested superiority with uncemented fixation. Therefore, the choice of the method of fixation should be made on the basis of all clinical indications, other than the influence of fixation on subsequent SSI/PJI.

LEVEL OF EVIDENCE: Limited

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

RATIONALE

Limb salvage surgery has become the treatment of choice for musculoskeletal cancers due to advances within the field of orthopaedic oncology. The use of an oncologic endoprosthesis has become the procedure of choice in limb salvage surgery. Though there are many benefits in utilizing an endoprosthesis, the development of subsequent infection is one of the most common and feared complications.

Multiple studies have been conducted to examine the risk of postoperative infection associated with the type of fixation (cemented vs. uncemented). Moreover, the approval and universal use of antibiotic-impregnated cement has altered the landscape as it relates to the risk and type of infection.

A systemic review of 40 studies examining distal femoral replacement (DFR) cases and proximal tibial replacement (PTR) cases showed mixed results. One hundred and nine (5.8%) of 1,894 cemented DFR cases became infected while 65 (9.0%) of 721 uncemented DFR cases became infected. This difference was found to be statistically significant [1]. For cemented DFR replacements, linear regression analysis showed that the risk of infection increased over time ($p < 0.001$), but the risk for infection in uncemented DFR implants did not increase over time. The same systemic review showed that 109 (15.2%) of 716 cemented PTR cases became infected while 56 (14.1%) of 396 uncemented PTR cases became infected; this difference was not found to be statistically significant. The incidence

of infection in PTR cases did not increase over time, regardless of the fixation method [1].

Pala et al. [2] reported that 20 (9.1%) of 220 endoprostheses originally implanted in patients with either a lower extremity primary bone tumor or metastatic disease became infected. Of these 20 cases, 12 (10.3%) were cemented and eight (7.7%) were uncemented. In addition, survival of cemented endoprostheses to infection was 68% at 60 months, while survival of the uncemented endoprostheses was 82% at 60 months [2]. Finally, in both univariate and multivariate analyses, the only variable that was found to be a predictor of survival was uncemented fixation [2].

The infection rates of endoprostheses vary widely in the literature. Studies investigating the infection rate after cemented fixation of an endoprosthetic device yielded an infection rate ranging from 5.2% to 21.9% [3-7]; studies investigating the infection rate after uncemented fixation yielded rates ranging from 9.7% to 12% [8-10]. A condition of equipoise exists resulting from the conflicting data supporting cemented or uncemented fixation and the incidence of subsequent SSI/PJI.

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