

Clinical Investigation: Sarcoma

Wound Complications in Preoperatively Irradiated Soft-Tissue Sarcomas of the Extremities

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Summary

Wound complications are a significant concern when soft-tissue sarcomas of the extremities are irradiated before resection. This retrospective study evaluated such patients and sought to determine what factors influence the occurrence of wound complications. We found that the frequency of wound complications remains concerning even with aggressive and careful interventions, but a trend suggested that complications are less frequent when plastic surgery performs closure.

Purpose: To determine whether the involvement of plastic surgery and the use of vascularized tissue flaps reduces the frequency of major wound complications after radiation therapy for soft-tissue sarcomas (STS) of the extremities.

Methods and Materials: This retrospective study evaluated patients with STS of the extremities who underwent radiation therapy before surgery. Major complications were defined as secondary operations with anesthesia, seroma/hematoma aspirations, readmission for wound complications, or persistent deep packing.

Results: Between 1996 and 2010, 73 patients with extremity STS were preoperatively irradiated. Major wound complications occurred in 32% and secondary operations in 16% of patients. Plastic surgery closed 63% of the wounds, and vascularized tissue flaps were used in 22% of closures. When plastic surgery performed closure the frequency of secondary operations trended lower (11% vs 26%; $P=.093$), but the frequency of major wound complications was not different (28% vs 38%; $P=.43$). The use of a vascularized tissue flap seemed to have no effect on the frequency of complications. The occurrence of a major wound complication did not affect disease recurrence or survival. For all patients, 3-year local control was 94%, and overall survival was 72%.

Conclusions: The rates of wound complications and secondary operations in this study were very similar to previously published results. We were not able to demonstrate a significant relationship between the involvement of plastic surgery and the rate of wound complications, although there was a trend toward reduced secondary operations when plastic surgery was involved in the initial operation. Wound complications were manageable and did not compromise outcomes. © 2013 Elsevier Inc.

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Introduction

Historically, without the use of additional therapy, amputations or large compartmental excisions were required to achieve acceptable local control rates for soft tissue sarcomas (STS) of the extremities (1). A randomized controlled trial in 1982 demonstrated that the addition of radiation therapy (RT) to limb-sparing surgery achieved acceptable local control rates when compared with amputation, with no difference in survival (2). Other randomized controlled trials have confirmed the value of RT as an integral part of limb-sparing treatment for high-grade or large STS (3, 4).

The timing of RT with respect to surgery is controversial. O'Sullivan et al randomized patients with STS to preoperative or postoperative RT. Results ultimately demonstrated no difference in local control or overall survival, although an early report suggested a survival benefit with preoperative radiation (5, 6). Although oncologic outcomes seem independent of radiation timing, several studies have shown significant differences in the rate of complications: major wound complications are more common with preoperative RT, and late complications may be more common with postoperative RT (5-9).

Our institutional preference has been to irradiate preoperatively STS that are high grade, large, or predicted to be difficult to resect with negative margins, such as those abutting major vessels or nerves. In an attempt to reduce the risk of wound complications, the plastic surgery service is routinely involved in choosing the wound closure approach and frequently performs closure, often with vascularized tissue flaps. We hypothesized that the use of vascularized tissue flaps and/or closure by the plastic surgery service would be associated with a lower rate of major wound complications. We therefore evaluated the frequency of major wound complications at our institution in patients with STS of the extremities who were preoperatively irradiated and determined which patient and tumor characteristics predict for such complications.

Methods and Materials

With the approval of our institutional review board (IRB #11-0019), a retrospective study was undertaken to evaluate wound complications in patients with STS of the extremities who underwent preoperative RT. Patients eligible for this study were older than 18 years, had at least 4 months of follow-up from the time of surgery, underwent primary surgery at our institution, and were treated with preoperative RT either at our or another institution. Rhabdomyosarcoma, Ewing sarcoma, and dermatofibrosarcoma protuberans were excluded from this study because these malignancies differ in therapy and natural history compared with standard adult extremity STS. Several existing patient databases at our institution were searched for eligible patients, and data were collected using electronic and print medical records, patient phone calls, and the social security death index.

Upper extremity sarcomas were defined as those between the fingers and the medial border of the scapula; lower extremity sarcomas were those between the toes and the upper border of the iliac crest (excluding internal pelvic tumors). Any discordance between the pathology (including grade) of the biopsy and the operative pathology was resolved by favoring the biopsy, because this tissue was unirradiated. If the biopsy yielded incomplete information, the pathology report from the surgery was used. Pathologists have used multiple approaches over the years of this

study for determining sarcoma grade at our institution. For the purposes of this article, any pathology labeled "high grade," "intermediate grade," "grade 3," or "grade 2" was considered "high grade"; and any pathology labeled "low grade" or "grade 1" was considered "low grade."

Wound closure approaches were placed into the following categories: primary closure (simple reapproximation of tissues), healing by secondary intention, local tissue rearrangement (ie, advancement flap), regional flap (ie, pedicled flap), and free flap. The term "unirradiated tissue flap" includes both regional and free flaps.

The definition of "major wound complication" was by design identical to that used in the O'Sullivan (2002) trial (5), reproduced here: "[M]ajor wound complication [was] defined as a secondary operation under general or regional anesthesia for wound repair (debridement, operative drainage, and secondary wound closure including rotationplasty, free flaps, or skin grafts), or wound management without secondary operation. Wound management included an invasive procedure without general or regional anaesthesia (mainly aspiration of seroma), readmission for wound care such as intravenous antibiotics, or persistent deep packing for 120 days or longer." By this definition, in clinic debridements or seroma/hematoma aspirations were considered major wound complications.

Survival curves and statistics were generated using the Kaplan-Meier method. Univariate analyses for categorical variables and continuous variables were performed with χ^2 tests and regression analyses, respectively. Multivariate analyses were performed using forward selection and considered only those variables with a *P* value of <.1 by univariate analyses. All *P* values are 2-tailed. Median follow-up was calculated using the method of Schemper and Smith (10).

Results

Seventy-three patients with STS of the extremities were identified who were preoperatively irradiated and underwent resection with curative intent at our institution between 1996 and 2010. Patient and tumor characteristics are listed in either Table 1 or as part of the univariate analysis in Table 2. Other pertinent data are as follows: median patient age was 56 years (range, 19-85 years). Average tumor size was 12.2 cm, 62% (n=45) of tumors were at least 10 cm in largest dimension, and 21% (n=15) were at least 20 cm in largest dimension.

Fifty-four patients (74%) received radiation at our institution, and 19 (26%) were irradiated elsewhere before undergoing resection at our institution. Median radiation dose was 5000 cGy and ranged from 4320 cGy-5400 cGy. Fraction size was 200 cGy for 19 patients, 180 cGy for 42 patients, and mixed or unknown for 12 patients. Six patients were treated with an external beam postoperative RT boost for positive margins (dose range, 2000-3000 cGy), 3 were treated with postoperative brachytherapy with catheters placed at the time of surgery (all received 1500 cGy at 0.5 cm from plane of the catheters), and 4 had intraoperative external-beam RT to 1000 cGy. Chemotherapy was administered to 18% of patients (n=13) (12 before RT and 1 after surgery); all received adriamycin and ifosfamide. At 3 years, local control was 94%, overall survival was 72%, and disease-free survival was 61% (Fig. 1). Median follow-up time was 3.5 years.

All patients underwent a gross total resection, and 18% (n=13) had positive margins. Plastic surgery closed the wound in 63%

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