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Perioperative chemotherapy is not associated with improved survival in high-grade truncal sarcoma

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ABSTRACT

Background: The treatment benefit of perioperative chemotherapy (CTX) for truncal soft tissue sarcoma (STS) is not well established. This study evaluates the association of CTX with survival for patients with resected primary high-grade truncal STS.

Materials and methods: Adult patients with high-grade truncal STS who had curative-intent resection from 2000 to 2016 at seven U.S. institutions were evaluated retrospectively. Patients were stratified by receipt of CTX. Kaplan–Meier curves with log-rank tests were used to compare overall survival (OS) and recurrence-free survival. Logistic regression models were used to evaluate characteristics associated with OS.

Results: Of patients with primary high-grade truncal STS, 235 underwent curative-intent resections. The most common histology was undifferentiated pleomorphic sarcoma and mean tumor size was 7.8 cm. Thirty percent of the patients received CTX ($n = 70$). Among patients receiving CTX, 34% ($n = 24$) had neoadjuvant CTX, 44% ($n = 31$) adjuvant CTX, and 21% ($n = 15$) had neoadjuvant and adjuvant CTX. Patients receiving CTX were more likely to receive radiation (51% *versus* 34%, $P = 0.01$), have deep tumors (86% *versus* 73%, $P = 0.037$) and solid organ invasion (14% *versus* 3%, $P = 0.001$). On univariate analysis, patients who

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received CTX had worse OS ($P < 0.01$) and a trend toward worse recurrence-free survival ($P = 0.08$). Margin status was the only variable associated with improved OS on multivariate analysis (odds ratio 4.36, 95% confidence interval 1.56, 12.13, $P < 0.01$).
Conclusions: In this multi-institutional retrospective analysis of resected high-grade truncal STS, receipt of perioperative CTX was not associated with improved OS, which may be related to selection bias. Microscopically negative margin status was the only independent factor associated with OS.

Introduction

The anatomic location of primary soft tissue sarcomas (STSs) impacts prognosis and should be a factor in planning clinical care for patients.[1] When STS limited to a specific anatomic location is studied, the rarity of this disease as well as the heterogeneous biology among tumors limits the ability to arrive at clear treatment conclusions.[2,3] Truncal sarcomas account for approximately 10%-20% of STSs but the treatment generally follows algorithms based on randomized trials examining treatment of extremity lesions.[4-7] This is problematic as truncal STS presents unique clinical challenges specific to this tumor location.[8] Disease frequently affects the abdominal and chest wall resulting in major functional defects and complex reconstructions necessitating a multidisciplinary approach[9] (Fig. 1). Advanced disease may also penetrate these cavities and invade underlying organs further complicating treatment and reconstruction.

Although the role of surgery for treating STS and specifically truncal sarcomas is well established,[8,10-12] the role of perioperative chemotherapy (CTX) is controversial.[2,13] For truncal sarcoma, high-grade histology is associated with an eightfold increased risk of death compared with low-grade histology.[1] Neoadjuvant and adjuvant CTX has been used for high-grade STS in an effort to improve outcomes.[14] A meta-analysis of randomized controlled trials found a small overall survival (OS) benefit for adjuvant doxorubicin plus ifosfamide in resected STS but does not address the association of anatomic location to outcome.[15] The individual trials in this meta-analysis are conflicting with the largest trials pointing to a lack of benefit for perioperative CTX thus undermining the conclusions of the study.[2]

The impact of CTX on survival for truncal sarcoma has not been examined in multi-institutional studies. A large series of truncal high-grade STS from the United States Sarcoma Collaborative was evaluated to examine whether perioperative CTX is associated survival for patients with surgically resected, high-grade truncal STS.

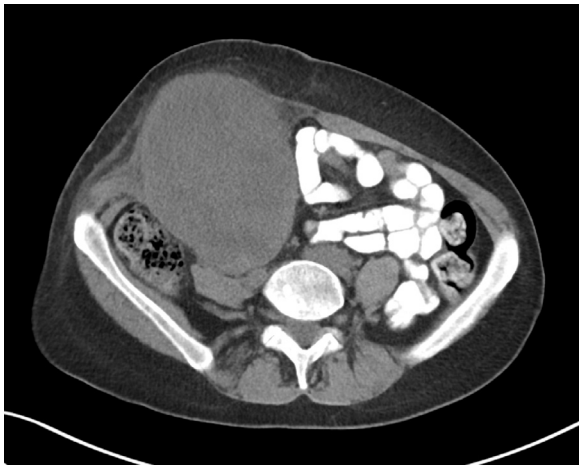

Fig. 1 – Computed tomography image of a high-grade truncal soft tissue sarcoma originating from the abdominal wall requiring complex reconstruction after resection.

Materials and methods

Selection of patients

The United States Sarcoma Collaborative is a retrospective multi-institutional database of soft tissue and retroperitoneal sarcoma patients treated at the following eight U.S. academic medical centers with high sarcoma volumes: The Ohio State University, Emory University, Stanford University, Wake Forest University, Medical College of Wisconsin, The University of Chicago Medicine, Washington University School of Medicine, and University of Wisconsin. All institutions obtained Institutional Review Board approval before beginning any research efforts. Seven of these institutions submitted STS patients and were included in this study. Clinicopathological data was collected on patients between 2000 and 2016 presenting with primary high-grade STS of the truncal region treated with complete surgical resection for curative intent. Truncal sarcomas were defined as originating from the soft tissue of the chest or abdominal wall, inguinal region, or shoulder. Before definitive treatment, all patients had a histological diagnosis established by fine needle aspiration, core needle biopsy, or planned incisional/excisional biopsy. Pathology reports were based on histology classification at the time of diagnosis and treatment. Slides were not re-reviewed at the time of this review. Patients having re-excisions for previous unplanned marginal resections were identified and excluded. Patients with synchronous metastatic disease, recurrent disease, sarcoma metastases to the trunk, low-grade tumors, tumors without metastatic potential (well-differentiated liposarcoma, dermatofibromasarcoma protuberans, desmoid tumor) and palliative resections were also excluded. Additional exclusion criteria were sarcomas of the spermatic cord and retroperitoneal sarcomas invading the chest/abdominal wall. Patients were compared according to whether or not they received perioperative CTX. Perioperative CTX was defined as CTX that was received either before or after surgery or both.