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# The New American Joint Commission on Cancer Staging System for Soft Tissue Sarcomas: Splitting versus Lumping

**Sam S. Yoon, M.D.**[1,*]

[1]Gastric and Mixed Tumor Service, Department of Surgery, Memorial Sloan Kettering Cancer Center, New York, NY

The staging of soft tissue sarcomas (STS) with the traditional TNM methodology used by the American Joint Commission on Cancer (AJCC) has been problematic for several reasons. First, there are over 50 different histologic subtypes of STST, all of which have quite varying epidemiology, clinical features, biology, responses to therapy, and prognoses. The primary reason for lumping these heterogeneous histologies together is that they are generally thought to arise from mesenchymal tissues, but that is akin to lumping all adenocarcinomas together. Second, STS arise throughout the body, and biological behavior, local recurrence, and distant metastasis are often site-dependent. Finally, STS rarely metastasize to lymph nodes (except for a few subtypes such as epithelioid and clear cell sarcomas), and thus the N category of TNM staging is not particularly useful.

Prior editions of the AJCC staging system for STS have compensated for these issues by incorporating histologic grade as part of the T category (1, 2). Low grade STS rarely metastasize and thus are considered stage I regardless of the size. The risk of metastasis for intermediate and high grade tumors increases as tumor size increases, so these tumors are stages II to IIIB depending on size. The most recent 8$^{th}$ edition of the AJCC staging system for STS corrects one major issue in that it now splits the staging of STS into anatomic sites, with the trunk and extremity now staged separately from other sites such as the head and neck or retroperitoneum (3). Other changes include the following:

1. T categories have increased from two (T1 ≤5 cm; T2 >5 cm) to four (T1 ≤5 cm; T2 >5 cm, ≤10 cm; T3 >10cm, ≤15cm; T4 >15cm
2. AJCC prognostic stage groups have changed, including classifying node positive disease as stage IV rather than stage III.

In this issue of Annals of Surgical Oncology, Fisher *et al.* use the National Cancer Database (NCDB) to analyze over 26,000 patients with trunk and extremity STS and compare the 7$^{th}$ and 8$^{th}$ editions of the AJCC staging systems (4). They determine that separation of the T categories into four groups and the modification of the AJCC prognostic groups increases the number of patients now classified as stage III and that the overall stage groupings have better discrimination in terms of overall survival. However, dividing tumors ≥10cm in size into two T stages (T3 and T4) does not divide those patients into groups with different

[*]Corresponding author: Dr. Sam S. Yoon, Gastric and Mixed Tumor Service, Memorial Sloan Kettering Cancer Center, 1275 York Ave, H1209, New York, NY 10065, Phone: 212-639-7436, Fax: 212-639-7460, yoons@mskcc.org.

overall survivals. Classifying node positive disease as stage IV rather than stage III increases the percent of patients classified as stage IV in less than 1% of patients (from 9.8% to 10.6%). They also determine that node positive patients without metastases (N1M0) have an overall survival of 33.1%, which was intermediate between stage III patients and stage IV patients.

Fisher *et al.* should be commended for putting together a large cohort of STS patients and performing a thorough comparison of the 7th and 8th editions of the AJCC staging systems, especially given that the 8th edition has just been published. One primary advantage of this study is the use of the large NCDB, which captures about 70% of the newly diagnosed cancer cases in the United States. The staging modifications in the 8th AJCC staging system were based on single institution databases and require validation. However as with most studies of this nature, there are several potential problems. First, the extent and quality of radiologic staging likely varied between institutions. For most trunk and extremity sarcomas the most common site of distant metastasis is the lungs, and we do not know if all patients received high resolution chest CTs. In addition, some sarcoma subtypes such as myxoid/round cell liposarcomas preferentially metastasize to extra-pulmonary sites (5), and these patients generally need CT scans of the chest, abdomen, and pelvis and possibly even total spine MRIs (6) for complete radiologic staging. Inadequate radiologic staging may have missed some patients who had synchronous metastatic disease. Second the extent of surgery, use of neoadjuvant/adjuvant radiation and systemic therapy varies widely among institutions and may have impacted on pathological staging and survival. We are not told what percent of patients received neoadjuvant therapy, and this therapy can significantly alter the surgical pathology. Finally, the only requirement for followup in these patients was that they have at least 90 days of follow-up. Thus patients with poor follow-up or patients lost to follow-up after 90 days may skew the overall survival results.

There are a two additional important points that should be made regarding the staging of patients with STS. While the AJCC 8th edition staging system for STS represents a significant advance in terms of now grouping tumors by location, it continues to disregard histologic subtype. Given there are over 50 different histologic subtypes, it is impractical to account for them all in one staging system. In addition, the including of tumor grade in T categories does partially make up for the varying biology of histologic subtypes. Various nomograms have accounted for the more common histologic subtype in making predications regarding local and distant recurrence, and it is possible that future editions of the AJCC staging system will include such nomograms following validation (7, 8). Also, the stage of patients with lymph node metastasis and no distant metastasis (N1M0) continues to change. In the AJCC 6th edition these patients were stage IV, in the AJCC 7th edition these patients were stage III, and in the current edition these patients are now stage IV again. In the Fisher study, N1M0 patients only represented 0.8% of patients, and the overall survival of these patients suggests these patients should be stage IIIB.

Niels Bohr, who received the 1922 Nobel Prize in Physics for his work on atomic structures, stated “Prediction is very difficult, especially if it’s about the future.” Yogi Berra, the often quoted New York Yankee player and manager, made a similar statement decades later. Overall, the article by Fisher *et al.* suggests that the 8th edition of the AJCC staging system

for STS improves on prior editions. However there are issues not addressed in the current AJCC staging system that future revisions may need to consider including consideration of neoadjuvant therapy and biomarkers.

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