Assessing Performance of Sarcoma Prediction Tools in an Upper Extremity Soft Tissue Sarcoma Cohort

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INTRODUCTION: Soft tissue sarcomas (STS) of the upper extremity (UE) are rare but can lead to devastating outcomes. The Memorial Sloan Kettering Cancer Center (MSKCC) nomogram, Sarculator, and PERSARC predict local recurrence (LR), distant metastases (DM), and overall survival (OS) in STS patients. Due to unique presenting characteristics and surgical considerations of UE tumors, these existing prognostic tools may lack generalizability. This study aims to assess the performance of sarcoma prediction tools in an UE STS surveillance cohort. We hypothesized UE-specific tumor characteristics and surgical considerations would negatively impact the performance of currently available sarcoma prediction tools.

METHODS:

Retrospective review of UE STS patients treated at a single sarcoma center between January 1, 2012 to December 31, 2022 was performed. Demographics, tumor characteristics, treatment information, and outcomes including LR, DM, and OS were recorded. External validation was performed by calculating the concordance index (C-index) for the MSKCC and Sarculator nomograms and PERSARC calculator; C=0.5 indicates random prediction and C=1 indicates perfect prediction. Total point count and event probability were calculated from MSKCC and Sarculator digitized nomograms. Data was processed according to PERSARC's variable encoding. Days to LR or last follow-up were calculated. Two-sided 95% confidence intervals were calculated through bootstrap resampling. RESULTS:

A total of 211 patients with UE STS were identified with average clinical follow-up of 4.9 years. Ninety-three patients (44%) presented after undergoing unplanned excision. Cohort characteristics are shown in Table 1. One hundred sixtyeight patients (80%) received neoadjuvant or adjuvant treatment. Forty-nine patients (23%) experienced LR while 47 patients (22%) developed DM. Thirty-five patients expired (17%) at an average of 41.0 months after presentation. External validation cohort details, C-index values, and event rates are shown in Table 2. On the surveillance validation cohort, Cindices for MSKCC nomograms were 0.54 [0.40, 0.66] and 0.50 [0.38, 0.62] for 3- and 5-year LR. C-indices for Sarculator were 0.63 [0.56, 0.69] and 0.62 [0.56, 0.67] for 5- and 10-year DM and 0.39 [0.33, 0.45] and 0.40 [0.34, 0.45] for 5- and 10-year OS. C-indices for PERSARC were 0.55 [0.47, 0.63] for 5-year LR and 0.44 [0.35, 0.54] for 5-year OS. Sarculator had the strongest overall performance in predicting 5- and 10-year DM (C=0.63; C=0.62) and the weakest overall performance in predicting 5- and 10-year OS (C=0.41; C=0.41).

DISCUSSION AND CONCLUSION:

Currently available STS prediction tools performed poorly on a contemporary UE-specific cohort, raising concerns on their generalizability and widespread use. Nuances in tumor presentation, frequency of unplanned excisions, and unique surgical considerations in UE STS may contribute to poor performance in models developed from anatomically heterogenous STS cohorts, explaining the lack of generalizability in existing tools. Prognostic tools derived from historical cohorts may perform poorly on contemporary cohorts due to demographics differences, variable event distribution, and evolving treatment paradigms including adjuvant radiation. Future efforts to develop a clinical risk stratification tool specifically for UE STS may be strengthened by incorporating pathology and imaging features given significant heterogeneity in the strengtheneon in the strengtheneon of the strengtheneo

Patient Demographics Age at presentation, median (years)	56 (IQR: 38-69)
Sex, n (%)	
Male	119 (56)
Female	92 (44)
Bace, n (%)	
White	122 (58)
Other	30 (14)
Asian/Pacific Islander	27 (13)
N/A*	20 (9)
Black	12(6)
Ethnicity, n (%)	
Non-Hispanic	157 (74)
Hispanic	45 (21)
N/A*	9 (4)
Marital status, n (%)	
Married	117 (55)
Single	64 (30)
Widowed	18 (9)
Divorced	12 (6)
Presenting Tumor Characteristics	
Unplanned excision, n (%)	
Yes	93 (44)
No	118 (56)
Location, n (%)	62 (29)
Arm	59 (28)
Forearm	51 (24)
Shoulder	20 (9)
Hand	10 (8)
Elbow	3 (1)
Wrist	
FNCLCC grade, n (%)	0.0 (18)
Grade 1	36 (17)
Grade 2	19 (9)
Grade 3	164 (73)
N/A	2 (1)
Histologic subtype, n (%)	07 (10.0)
Undifferentiated pleomorphic sarcoma	30 (10.0)
Myxofibrosarcoma	32 (15.2)
Other	24 (11.4)
Synovial sarcoma	10 (0.2)
Leiomyosarcoma	18 (8.5)
Undifferentiated sarcoma	16 (7.6)
Sarcoma not otherwise specified	15 (7.1)
Epithelioid sarcoma	13(6.2)
Undifferentiated spindle cell sarroma	10 (4.7)
Dermatofibrosarcoma protuberans	7 (3.3)
Linosarcoma	21 (10.0)
Size*	
<5 cm n (%)	69 (33)
5-10 cm n (%)	84 (40)
>10 cm n (%)	55 (26)
Modian (cm)	6.45 ± 5.65
Depth n (%)	
Superficial	34 (16)
Deen	177 (84)

Model and Development Cohort	Surveillance Cohort, n	Derivative Concordance Index, C and Event Rate, n (%)	Surveillance Validation Concordance Index, C and Event Rate, n (%)
MSKCC n=684 with eSTS, treated with surgery only from 1982- 2006 at single contra	41	3-year LR: 0.74 5-year LR: 0.73 92/684 (13)	3-year LR: 0.54 [0.40, 0.66] 5-year LR: 0.50 [0.38, 0.62] 10/41 (24)
Sarculator n=1452 with eSTS, treated with surgery and adjuvant therapy from 1994-2013 at single center	157	DM: 0.759 376/1452 (26) OS: 0.767	5-year DM: 0.63 [0.56, 0.69] 10-year DM: 0.62 [0.56, 0.67] 33/157 (33) 5-year OS: 0.41 [0.32, 0.49] 10-year OS: 0.41 [0.23, 0.58] 135/157 (86)
PERSARC n=766 with eSTS, treated with surgery and adjuvant therapy from 2000-2014 at five European centure	100	CILR: 0.696 OS: 0.677	5-year OS: 0.44 [0.35, 0.54] 84/100 (84) 5-year LR: 0.55 [0.47, 0.63] 17/100 (17)

*<u>eSTS</u>= extremity soft tissue sarcoma