Beyond RECIST: Prognostic value of Soft-Tissue Volume Reduction in Ewing Sarcoma

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Significance & Hypothesis/Techniques:

Response Evaluation Criteria in Solid Tumors (RECIST) poorly predicts overall survival (OS) and relapse-free survival (RFS) in Ewing sarcoma following neoadjuvant chemotherapy (NAC). Although tumor volume has demonstrated prognostic value, prior studies have not separately evaluated soft-tissue and osseous tumor compartments. Histological response has also been found to be correlated with tumor size reduction in some analyses and predictive of OS and RFS. This study assessed whether post-chemotherapy changes in total tumor volume (TV), soft-tissue volume (SV), and bone volume (BV) in conjunction with histological response after neoadjuvant chemotherapy (NAC) are associated with OS and RFS. We hypothesize volume reduction will be correlated with histological response and that larger reductions in total volume and soft tissue volume will be associated with improved OS and RFS.

Innovation:

Evaluation of tumor change to NAC via volumetric osseous, total, and soft tissue compartments and RECIST one-dimensional measurements association with OS and RFS.

Approach (Materials and Methods):

We retrospectively reviewed patients with primary Ewing sarcoma treated at a single academic institution, identifying 61 eligible cases. Pre- and post-chemotherapy magnetic resonance imaging studies were analyzed. RECIST response categories of responders (CR and PR) and non-responders (SD and PD) were determined using maximal tumor dimensions. Three-dimensional volumetric measurements of TV, SV, and BV were obtained from axial T1-weighted and contrast-enhanced images using dedicated imaging software. Post-chemotherapy volume changes were correlated with OS and RFS using nonparametric testing and parametric survival regression. Failure probability curves were generated according to the degree of SV reduction.

Results:

The mean patient age was 17.7±8.8 years, and 41% were female. The pelvis (31%) and femur (18%) were the most common primary sites. Ten patients had metastasis at presentation, and 15 of the remaining patients developed local or distant failure. Thirty-five patients underwent surgery, and 26 underwent definitive radiation therapy after NAC.

RECIST responses included 13% CR, 50% PR, 31% SD, and 6% PD. RECIST response, TV reduction, and BV reduction were not significantly associated with OS. Greater SV reduction trended toward improved OS ($p=0.055$) and was significantly associated with improved RFS ($p=0.024$). In survival modeling, SV reduction predicted RFS ($p=0.0265$) and showed a trend for OS ($p=0.0704$). Failure probability analysis suggested improved OS and RFS with SV

reduction exceeding 90% (Figure 1 and Figure 2, respectively). Histological response and SV had a moderate relationship (r_s=*0.3511,* p=0.0387). Although, SV >90% was associated with improved overall RFS and trended to improved OS regardless of if a good (>95%) or poor (<95%) histological response to NAC was noted (Figure 1 and Figure 2).

Discussion and Impact:

Soft-tissue volume reduction after NAC may predict improved OS and RFS, particularly when reduction exceeds >90% regardless of histological response. Total tumor volume and bone volume were not associated with survival, likely reflecting the limited reduction observed in the osseous component. Consistent with prior studies, one-dimensional RECIST measurements and RECIST response categories were poor predictors of OS and RFS in Ewing sarcoma.

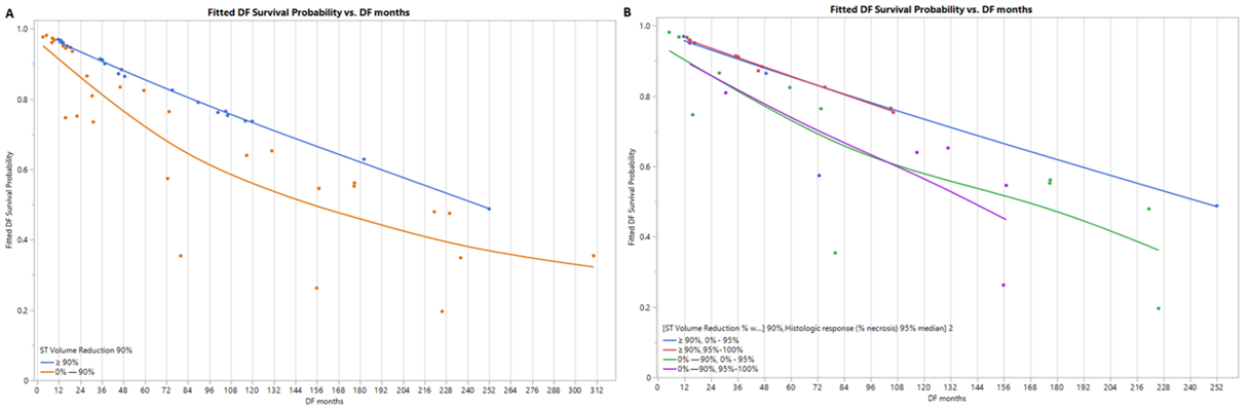

Figure 1: Relapse Free Survival: A): Fitted survivability curves of patients with >90% soft tissue volume reduction and those with less than 90% soft tissue volume reduction. B) Fitted survivability curve of patients with 90> soft tissue volume reduction and less than 90% volume reduction with stratification by histological response greater than 95% and less than 95%.

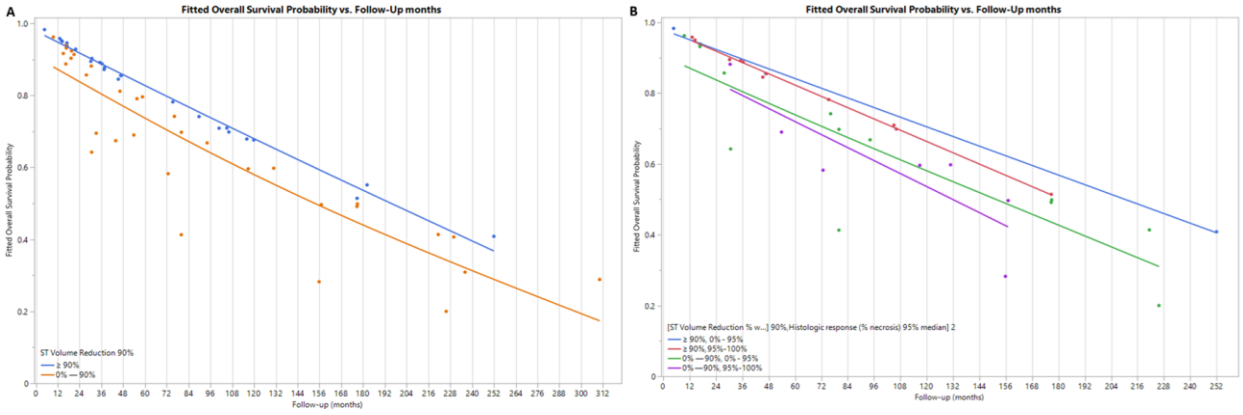

Figure 2: Overall Survival: A): Fitted overall survivability curves of patients with >90% soft tissue volume reduction and those with less than 90% soft tissue volume reduction. B) Fitted overall survivability curve of patients with 90> soft tissue volume reduction and less than 90% volume reduction with stratification by histological response greater than 95% and less than 95%.