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Predictors of residual disease after unplanned excision of soft tissue sarcomas

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ABSTRACT

Background: Unplanned excision of soft tissue sarcomas (STS) is an important quality of care issue given the morbidity related to tumor bed excision. Since not all patients harbor residual disease at the time of reexcision, we sought to determine predictors of residual STS following unplanned excision.

Methods: We identified 76 patients from a prospective database (January 1, 2008-September 30, 2014) who received a diagnosis of primary STS following unplanned excision on the trunk or extremities. We used univariable and multivariable analyses to evaluate predictors of residual STS as the primary endpoint. We calculated the sensitivity, specificity, and accuracy of interval magnetic resonance imaging (MRI) to predict residual sarcoma at reexcision.

Results: Mean age was 52 y, and 63.2% were male. 50% had fragmented unplanned excision. Among patients undergoing reexcision, residual STS was identified in 70%. On univariable analysis, MRI showing gross disease and fragmented excision were significant predictors of residual STS (odds ratio, 10.59; 95% CI, 2.14-52.49; $P = 0.004$ and odds ratio, 3.61; 95% CI, 1.09-11.94; $P = 0.035$, respectively). On multivariable analysis, tumor size predicted distant recurrence and overall survival. When we combined equivocal and positive MRI, the sensitivity and specificity of MRI for predicting residual STS were 86.7% (95% CI, 73.2%-95.0%) and 57.9% (95% CI, 33.5%-79.8%), with an overall accuracy of 78.1% (95% CI, 66.0%-87.5%).

Conclusions: About 70% of patients undergoing repeat excision after unplanned excision of STS harbor residual sarcoma. Although interval MRI and fragmented excision appear to be the most significant predictors of residual STS, the accuracy of MRI remains modest, especially given the incidence of equivocal MRI.

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Introduction

Because soft tissue sarcomas (STS) are rare, it is not uncommon for physicians to excise a soft tissue mass without further work up, assuming it is a lipoma, lymph node, or hematoma. If the soft tissue mass proves to be an unsuspected STS, this approach is referred to as an "unplanned excision."[1-4]

From a quality of care perspective, unplanned excisions are problematic, as STS extends beyond its pseudocapsule, leading to an increased risk of residual disease and local recurrence. Furthermore, long-term control of disease may be compromised following an unplanned excision.[2,5-7]

When an unplanned excision occurs, there is no attention to the pursuit of tumor-free margins, and the oncologic nature of the unplanned excision is considered marginal at best. Repeat excision allows for a properly planned total resection. As a result, the standard recommendation following unplanned excision of STS is reexcision of the tumor bed to optimize oncologic outcome.[1,5,8]

Despite the oncologic benefits of repeat resection after unplanned excision, this approach is clearly associated with greater morbidity.[5] Furthermore, although studies have demonstrated improved local control and survival with wide margin reexcision after unplanned excision,[9] other studies have shown no oncologic benefit to reexcision.[2] Studies attempting to explain this discrepancy have suggested that microscopic residual disease remaining after reexcision may be a marker of clinical aggressiveness.[3,10]

Given the association of residual sarcoma after unplanned excision with worse survival as well as the significant potential surgical and functional morbidity, the ability to predict residual disease before repeat excision could permit a more tailored approach to repeat resection and combined modality therapy. This information may translate to improved patient risk stratification and limit additional surgical morbidity in patients unlikely to harbor residual disease.[11,12] Since not all patients harbor residual sarcoma following unplanned excision, we sought to analyze predictors of residual sarcoma following unplanned excision of STS, hypothesizing that these data may serve as baseline information for future prospective evaluation of a selective, algorithmic approach to tumor bed management following unplanned excision.

Materials and methods

From January 2008 to September 2014, 76 patients underwent unplanned excision of STS located on the trunk or extremity and presented to our sarcoma referral center for further evaluation and management recommendations. These patients were identified from a prospectively maintained cancer center database, and all patients were reviewed in a multidisciplinary Sarcoma Tumor Board. Patients with fibromatosis ($n = 17$) and gynecological sarcomas ($n = 22$) were excluded from this analysis. We also excluded patients who underwent an incisional biopsy.

This study was approved by the Institutional Review Board. Since it was considered no more than minimal risk, a waiver of consent was obtained. We then abstracted clinical, pathologic, and treatment data, including age, gender, tumor location, stage at presentation, histologic type, maximal tumor diameter, histologic grade, tumor depth, margin status, presence of fragmented excision, presence of repeat excision, interval between unplanned excision and reexcision, results of interval magnetic resonance imaging (MRI), presence of residual STS following resection, and local and distant recurrence. Pathology reports were used to determine fragmented excision, as the description of the gross specimen was very specific for one piece or fragments. Local recurrence–free survival, distant recurrence–free survival, disease-specific survival, and overall survival (OS) were calculated as described previously.[13,14]

Tumor size was analyzed as a continuous variable using maximal tumor dimension from initial pathological evaluation. Tumor sites included extremity (upper at or distal to the shoulder and axilla and lower at or distal to the buttock and groin) and trunk. Retroperitoneal and visceral tumors were excluded. Histologic grade was classified using a three-tiered system (grade I through III) according to established criteria.[15]

Histologic diagnosis was assigned by the published criteria of the World Health Organization Classification of Tumors of Soft Tissue and Bone.[15] For purposes of statistical analysis, we limited our analysis to six histology categories, including "other" which represented a composite of synovial sarcoma, extraskeletal myxoid chondrosarcoma, solitary fibrous tumor, angiosarcoma, fibromyxoid sarcoma, clear cell sarcoma, epithelioid sarcoma, primitive neuroectodermal tumor, and sarcoma, not otherwise specified.

Tumor bed reexcision included an *en bloc* resection of the entire tumor bed with a 2 cm margin while avoiding entry into the tumor bed and seroma cavity. Final margin status was determined either clinically (R2 for gross residual tumor left behind) or as part of the histopathologic assessment (R1 for microscopically positive margins and R0 for microscopically negative margins). Given the low rate of R2 disease ($n = 1$), data were analyzed in two groups: margin negative (R0) or margin positive (R1 and R2).

The date of recurrent disease was defined either by biopsy or by the radiologic detection of suspicious lesions when no biopsy was performed. Follow-up was counted from the date of diagnosis until the date of death or date of last follow-up. Freedom from local recurrence was counted from the date of resection. Patients who were free from recurrence or death were censored according to the date of their last follow-up.

Interval MRIs were considered positive if reported as consistent with gross residual disease (focal or discrete enhancing mass). MRIs interpreted as no evidence of residual disease were considered negative. There was a subset of MRIs showing "nonspecific tumor bed enhancement," and these were classified as equivocal. All MRIs were reviewed by the multidisciplinary tumor board.

Summary statistics were reported as mean ± standard deviation with median (range) where appropriate. Logistic