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CORR Insights

CORR Insights®: Can Multistate Modeling of Local Recurrence, Distant Metastasis, and Death Improve the Prediction of Outcome in Patients With Soft Tissue Sarcomas?

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Where Are We Now?

When counseling with patients with soft-tissue sarcoma, clinicians are hindered by a lack of robust data on the outcome patients are most interested in: overall survival. Although a number of well-designed investigations have reported on survival and how it relates to baseline risk factors, many factors influence this key end point, and we lack effective tools to adjust our survival estimates to account for development of interval events such as local recurrence and oligometastases or the lack of interval events (ie, a disease free interval). Imagine otherwise identical 60-year-old patients presenting with the same localized 10-centimeter high-grade sarcoma of the thigh; we may counsel each of them that the 5-year overall survival rate is 60% to 70% [4, 6]. However, if one of the patients develops a local recurrence that is resected in the first year, and the other remains without signs of disease, should they still be counseled the same way? The intuitive answer is that they should not, but there is little evidence to inform these conversations.

In the current study, Posch and colleagues present an elegant statistical model to help the clinician understand the complex interplay among baseline risk factors, local recurrence, metastasis, and overall survival in patients with localized soft-tissue sarcoma. Most investigations [3–6] consider individual outcomes such as local recurrence, metastasis, and death as they relate to individual pretreatment prognostic factors (like tumor grade, histologic subtype, and size). But in the current study, the authors incorporated interval-time-dependent events such as the development of local recurrence and distant metastasis, time from treatment, and their effects on overall survival from disease. By considering patients to be occupying one of the five

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"states" (no evidence of disease, local recurrence, metastasis, local recurrence with metastasis, and death) the authors can quantify the probability of occupying or transitioning to another state based on known risk factors, time spent in a particular state, and competing risks such as death from other causes.

While some authors describe local recurrence as a risk factor for metastasis and death from disease [3, 5], we lack consensus on this [1]. The current study argues that recurrence indeed does increase the risk of distant metastasis and decrease overall survival. The authors of the current study show that sarcoma outcomes can be modeled and evaluated in a dynamic fashion through the incorporation of time-dependent surveillance events and competing risks.

Where Do We Need To Go?

The methodology in the current study, while statistically complex, fully analyzes the potential course of the sarcoma patient. I would argue that this model should become the standard by which large sarcoma series are analyzed and reported given the number of outcomes of interest, how the outcomes themselves interact with one another, and how they account for competing risks. The multistate model shows great promise and can impact overall survival by: (1) serving as an invaluable patient counseling tool, (2) guiding appropriate use of adjuvant treatments, and (3) determining the most effective use of local and distant surveillance strategies.

But before we get that far, large-scale investigations are still needed to develop the multistate model to the point where it can be employed as a predictive instrument for a specific patient.

How Do We Get There?

In order to develop the multistate model as a predictive tool for sarcoma outcomes, a large-scale investigation would need to include: (1) a larger number of patients, (2) an evaluation of more factors (such as diabetes or other immunocompromising diseases and adjuvant treatment regimens including chemotherapy and radiotherapy) that could relate to the outcomes of interest, and (3) prospective data. This effort, although daunting, is feasible and would seem ideally suited towards a large database analysis. No such database currently exists, although there is a mounting interest among members of the Musculoskeletal Tumor Society in its creation. Given the trouble with studying an extremely rare and heterogeneous disease such as soft-tissue sarcoma, organization within our specialty to develop this powerful research tool would allow for the ability to complete the answers to important questions such as the one offered by the exceptional effort put forth by these authors.

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