EDITORIAL

Managing Elderly Soft Tissue Sarcoma Patients—Should Age Drive Treatment?

Dina Lev, MD^{1,2} and Raphael E. Pollock, MD^{2,3}

¹Department of Cancer Biology, University of Texas M. D. Anderson Cancer Center, Houston, TX; ²Sarcoma Research Center, University of Texas M. D. Anderson Cancer Center, Houston, TX; ³Department of Surgical Oncology, University of Texas M. D. Anderson Cancer Center, Houston, TX

As the mean age of the US population increases because of the maturation of the “Baby Boomer” generation, several important demographic sequellae emerge. The overall incidence of new cancer cases is increasing, there is a concomitant generally increased incidence of cancer cases within specific disease sites, and there is an associated increased incidence of disease site-specific lesions within older age groups as a percentage of those burdened by certain malignancies. In light of these trends, it is both appropriate and timely that we consider how cancer care is given to older populations within the confines of specific disease entities.

Within this context, age-denominated patterns of care in some diseases such as soft tissue sarcoma offer particular challenges because of its relative rarity, the comparative paucity of sarcoma-focused high-volume treatment centers that are associated with a higher quality of sarcoma care, and the reality that this is a disease that has a bimodal distribution that preponderantly afflicts both the young as well as a generally older adult population compared with most other solid tumor processes.¹ In light of these considerations, it is appropriate to consider whether or not we are overtreating or undertreating soft tissue sarcoma patients; manifestly, if treatments offered are inappropriate as a function of age, should we consider altering our patterns of care for this and other rare diseases that occur more frequently in older populations?

The *Annals of Surgical Oncology* has provided a bona fide service to soft tissue sarcoma practitioners by publishing 2 seminal studies in 2009 and 2010 that materially

contribute to this debate. Lahat and colleagues at The University of Texas MD Anderson Cancer Center analyzed a large cluster of soft tissue sarcoma patients ($n = 325$) who underwent R0/R1 resection at that institution over a recent 10-year interval.² In the current issue the *Annals* published an additional report; this one authored by Al-Refaie and collaborators from the University of Minnesota, who based their study on a carefully considered analysis of Surveillance Epidemiology and End Results (SEER) registries of extremity soft tissue sarcoma patients ($n = 2,586$) treated between 1991 and 2006.³ While not exactly comparable, within the constraints of an individual institutional experience versus a population-based study it is intriguing to consider both the similarities and differences of these analyses because they are informative and pertinent to the questions posed above.

The MD Anderson series patient median age of 72 years was in keeping with the reality that approximately 55% of these patients had significant comorbidities, resulting in a preoperative ASA score of 3 or greater. The site of the soft tissue sarcoma was most commonly extremity, with high-grade undifferentiated pleomorphic sarcoma (formerly known as malignant fibrous histiocytoma) greater than 5 cm maximum diameter as the most common presentation. Postoperative mortality (30 day) was less than 1%, whereas approximately 30% of patients experienced at least 1 complication. Patients 75 years or older received chemotherapy less often and had a shorter median disease-specific survival rate (70 vs. 113 months; $P = .05$); use of radiotherapy did not differ as a function of age. In a multivariable Cox proportional hazards model for soft tissue sarcoma-specific survival, age greater than or equal to 75 years, larger tumor size, and high tumor grade were the only factors significantly related to sarcoma-specific survival of the more than 20 patient, tumor, and treatment-

related variables analyzed. It is interesting that no treatment-related parameters contributed directly and significantly to sarcoma-specific survival as a function of age in this analysis, although the possibility could be suggested that the relative lack of chemotherapy administration in the older patient cohort might have influenced the shorter sarcoma-specific survival rate.

The SEER population-based data analysis likewise is informative in a manner complementary to the above single institution experience. This latter report was limited to extremity soft tissue sarcoma, 30% of which were diagnosed in patients 65 years or older. There was a significantly decreased use of both sarcoma-directed surgery and preoperative or postoperative radiotherapy as a function of age, especially in patients 85 years or older. Likewise, older age was also associated with decreased sarcoma-specific survival, as observed in patients 75 years or older.

It is intriguing that both studies suggest that increased sarcoma-specific mortality as a function of age may be the result in part of less aggressive or comprehensive sarcoma-targeted treatments offered to patients in these age brackets. While it is tempting to conclude that elderly sarcoma patients cared for in the more general treatment arena outside of comprehensive cancer center sarcoma programs trended toward being undertreated, it is also possible that older patients treated at some sarcoma centers may be overtreated, at least regarding exposure to aggressive systemic therapies whose modest efficacy could be outweighed by their toxicities, thereby negatively affecting sarcoma-

specific survival in elderly recipients. If nothing else, these two studies point to age-related differing patterns of sarcoma care as exists in both sarcoma centers as well as the more general oncology therapeutic milieu.

Future studies might profitably focus on developing more precise predictors of treatment tolerance for our aging populations whose cancer burden will increase over the next interval. Clinical trials focusing on treatment intensity as a function of age may likewise prove to be very informative in this debate. Finally, to improve disease-specific survival in elderly patients burdened by rare diseases such as soft tissue sarcoma, involvement of physicians and affiliated caregivers equipped to evaluate and apply multidisciplinary treatment programs tailored to preexisting comorbidities rather than age per se may hold the best promise for improved prognosis in this challenging clinical circumstance.

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