Current Concepts Review

The Surgical Staging of Musculoskeletal Sarcoma*

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The concept of staging malignant tumors arose in response to the need for meaningful assessment of various methods of treatment in end-result studies. Its purpose was to ensure that lesions of comparable prognostic import were used to evaluate methods of management, so that one form of treatment was not inadvertently biased by inclusion of a preponderance of favorable lesions while another method was adversely weighted on the basis of lesions with unfavorable predictors. The first staging system was developed for carcinoma of the cervix. The predictors were local invasion, regional metastases to lymph nodes, and distant metastases to other organs. In the ensuing years the importance of the concept of staging has been widely recognized and adopted internationally. Staging systems based on the natural history of the tumor have been developed for almost all histogenic types of various malignant neoplasms. Conspicuous by its absence has been a staging system for sarcomas of connective-tissue derivation.

An adequate surgical procedure has been recognized as the effective means of treating the majority of primary musculoskeletal sarcomas. Historically, amputation has been employed liberally. The recent demonstration that certain chemotherapeutic agents are capable of suppressing or even eradicating microdisease[8,10] has encouraged an enthusiastic proliferation of innovative therapies for many of these highly malignant tumors[12,14,18]. Almost all of these therapies were designed to supplant or replace so-called standard surgical procedures, and have as their aim control of micrometastases and preservation of a functional extremity. The trend toward conservative, limb-saving surgery (usually performed under an umbrella of adjunctive chemotherapy, irradiation, or immunoactive agents) presents the surgeon and the patient with a seemingly attractive array of treatment options, the long-term effectiveness of which are unknown. Many of these extremity-preserving options include a surgical procedure that by itself is known to carry substantial risk of recurrence and hence an increased risk of metastasis. Although surgical intervention remains an important step in the management of musculoskeletal sarcoma, issues relating to the magnitude and timing of the surgical procedure are as unsettled as those relating to the most appropriate use of the adjuncts themselves.

The relative rarity of musculoskeletal neoplasms in a setting of splintering therapies suggests that if sufficient patient data are to be accumulated rapidly for the timely analysis of end results and the evaluation of clinical trials, inter-institutional cooperation will be essential. There is an urgent need for a standard and commonly accepted terminology defining surgical stages, surgical procedures, and management of data.

A surgical staging system for sarcoma should: (1) incorporate the most significant prognostic factors into a system that describes progressive degrees of *risk* to which a patient is subject; (2) define a series of progressive stages of the disease that has specific implications for surgical management; (3) furnish guidelines for the use of adjunctive therapies; and (4) facilitate inter-institutional as well as interdisciplinary communication, comparison of data, and cooperation.

The single attempt to develop a staging system for sarcomas of bone by the Task Force on Malignant Bone Tumors of the American Joint Committee for Cancer Staging and End-Results Reporting failed to yield a satisfactory system. They recommended that institutions with access to large numbers of patients, consistency in management, and long-term follow-up undertake the task[6]. The staging system for soft-tissue sarcomas proposed by the American Joint Committee in 1977[15], and the recent modification suggested by Hajdu, have been of limited value in the surgical management of soft-tissue lesions[18].

Specific histogenesis has little bearing on the definitive surgical management of a musculoskeletal sarcoma[4,6]. Rather, the usual determinant of selection of a procedure is whether the lesion is low grade with a propensity for local recurrence but with little risk of metastasis, or high grade and aggressive with a significant tendency to both local recurrence and metastasis[14,18,19]. How a specific procedure is accomplished is influenced by the anatomical setting of the lesion, and has to do with whether the lesion is confined within well defined anatomical compartments or is diffusely infiltrating through ill

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defined adventitial planes and spaces[2-4,7,13,16]. Although size is a factor in surgical planning, it is not the dominant one.

A common surgical staging system has been developed for both bone and soft-tissue sarcomas. It is clear-cut, straightforward, and clinically practical because it relates the stage of the disease to selection of surgical procedure and adjunctive measures[7].

The system has three stages: I — a low-grade lesion without metastases, II — a high-grade lesion without metastases, and III — a lesion of either grade with regional or distant metastases.

The low-risk Stage-I lesions may be of any histogenic type. They are reasonably well differentiated and have a low mitotic rate and moderate cytological atypia. The high-risk Stage-II lesions, also of any histogenic type, are poorly differentiated and have high mitotic rates, increased cellularity and cytological atypia, necrosis, and vascular invasion. In some tumors, the roentgenographic and clinical aggressiveness is also taken into account and contributes to the assessment of the surgical grade[16].

The two stages just described are further divided by the anatomical setting of the lesion — that is, whether it is intracompartmental or extracompartmental. Intracompartmental lesions are confined within the boundaries of well defined anatomical structures; that is, a bone, joint, or fascially defined compartment of a functional muscle group. Extracompartmental lesions either arise within or secondarily extend into extrafascial spaces or planes that have no natural anatomical barriers to extension. Both detailed pathological examination of specimens and surgical exploration have confirmed that the clinical distinctions between intracompartmental and extracompartmental lesions may reliably be made preoperatively by the relevant combinations of careful history, physical examination, roentgenograms, tomograms, angiograms, computerized tomography scans, radionuclide scans, and other specialized studies. The details of determining both the surgical grade and site of a tumor have been published elsewhere[7].

The staging system for tumors is summarized as follows: IA, low-grade intracompartmental; IB, low-grade extracompartmental; IIA, high-grade intracompartmental; IIB, high-grade extracompartmental; and III, any grade, anywhere, with any metastases. This system has correlated well with the incidence of local recurrence and metastases when applied to patients treated for primary bone and soft-tissue sarcoma[7]. Stage-I lesions had both a low incidence of local recurrence and a low rate of metastasis, while Stage-II lesions had a higher rate of local recurrence and substantially higher rate of metastasis. The system clearly separated patients into low and high-risk populations. The implications are obvious: (1) surgical management is different for the two groups; (2) the need for adjunctive therapy is different; and (3) the two groups should be analyzed separately for evaluation of results of treatment.

The system fulfills the need for a series of progressive stages of disease that have specific surgical implications. Previous work has shown that if the operative treatment is to be definitive, at least a wide margin is required for Stage-I lesions and a radical margin, for Stage-II lesions[7,17]. If, for whatever reason, a lesser margin is achieved, the rate of local recurrence increases substantially, and in this setting, adjunctive therapies to suppress local recurrence may be indicated. For intracompartmental (A) lesions in either stage, a wide or radical margin usually can be accomplished by a local procedure. Extracompartmental (B) lesions in either stage usually require an ablative procedure to secure either a wide or a radical margin[7].

In order to assess the facility with which the staging system might be used for group studies, a retrospective study involving thirteen extramural institutions was done. Participating members of the Musculoskeletal Tumor Society from these institutions (University of Texas System Cancer Center — M. D. Anderson Hospital, State University of New York at Buffalo, University of California at Los Angeles and at San Francisco, Case Western Reserve University, University of Chicago, University of Iowa, Massachusetts General Hospital, Mayo Clinic, Memorial Hospital for Cancer, University of Miami, University of Minnesota, and Rizzoli Institute of Orthopaedics, Bologna) contributed a total of 146 cases, all of which had a minimum two-year follow-up. Patients were included without regard for treatment. Three cases were eliminated because of insufficient data and four, by reasons of diagnosis. Problems in using the system were reported in 6 per cent of the lesions, and were mainly attributed to compartmentalization. Bookkeeping errors were noted and corrected in 2.5 per cent of the responses.

The 139 cases from the extramural institutions and the 258 from the University of Florida were analyzed separately and tables of the probability of survival at one, two, three, and five-year intervals were constructed by the method described by Cohen for censored data. The intramural and extramural sets of data had the same trend and were not different from intramural absolute survival rates using uncensored data; hence the two studies were combined.

The probability of survival for the combined group of 397 patients as a function of the stage of disease showed the validity of the proposed staging system. At intervals of one, two, three, and five years, patients with low-grade Stage-IA intracompartmental lesions had a probability of survival of 0.99, 0.99, 0.98, and 0.97, respectively; those with Stage-IB low-grade extracompartmental lesions, of 0.98, 0.95, 0.93, and 0.89; and those with high-grade Stage-IIA lesions, of 0.94, 0.88, 0.83, and 0.73; while those with extracompartmental Stage-IIB lesions had a probability of survival of 0.85, 0.73, 0.62, and 0.45. The group with Stage-III lesions had a correspondingly worse probability of survival: 0.61 at one year, 0.37 at two years, 0.22 at three years, and 0.08 at five years. The prob-

abilities of survival for the patients at the five-year interval were: Stage-IA lesions, 0.97; Stage-IB, 0.89; Stage-IIA, 0.73; Stage-IIB, 0.45; and Stage-III, 0.08.

There is a significant difference in the probability of survival between patients with lesions in each stage (I, II, and III) at each year after diagnosis ($p < 0.01$). Patients with Stage-I lesions are at low risk while patients with Stage-II lesions are at high risk ($p < 0.01$). Although the risk, in terms of patient survival, of Stage-IA and IB lesions is not statistically different, the difference in surgical management required for local control justifies their separation into different classifications. The difference in the probability of survival between patients with Stage-IIA and those with Stage-IIB lesions is significant ($p < 0.01$). The survival data for patients with bone and those with soft-tissue sarcoma were analyzed separately and indicated that the staging system works equally well for both.

Since its organization in 1959, the American Joint Committee for Cancer Staging and End-Results Reporting has been responsible for the development of clinically useful staging systems for many types of cancer. The intended purpose was to designate the state of a cancer at various points in time and its relation to the natural course of a particular type of cancer[1]. The avowed interest was to provide a way of communicating information, to assist in decisions regarding treatment, to be a factor in judgment as to prognosis, and to provide a mechanism for comparing like or unlike groups of cases, particularly in regard to the results of different therapeutic procedures[1]. The philosophy embraced the view that "for most types of cancer, the extent to which the disease has spread is probably the most important factor determining prognosis and must be given prime consideration in evaluating and comparing different therapeutic regimens"[1]. To this end the Committee rather consistently employed the TNM system, with occasional appropriate modifications. *T* designates the local extent of disease (often translated into size) of the primary tumor; *N* designates nodal extent; and *M*, extent of metastasis. They acknowledged that staging classifications based on descriptions of the extent of disease require a thorough knowledge of the natural history of the particular cancers to be staged[1]. In addition to anatomical extent, the histopathological analysis and grade of the tumor are other recognized prime determinants of stage[1,15,16].

In 1977, an American Joint Committee-sponsored staging system for soft-tissue sarcomas was proposed[15]. Although this system has the merit of taking histological grade into account as a prime factor in the assessment of risk in soft-tissue sarcoma, the proposed system incorporates a number of conceptual premises that make its clinical use awkward.

1. Forty-seven per cent of the 1215 lesions on which the proposal was based were located in the head, neck, retroperitoneum, or other surgically inaccessible site. These lesions present such a different problem clinically, biologically, and surgically that they should not be grouped with lesions of the extremity for analysis.

2. The division of sarcomas into three histological grades is a histological nicety. Although it is likely to have great appeal to the pathologist, it has little to offer the surgeon in terms of surgical guidance because there is no "middle" surgical procedure.

3. The *T* designation (local extent) represents the size of the lesion. It is believed that size has prognostic significance that is a complex composite of anatomical setting, rate of growth, and time to physician intervention. Since neither growth rate nor time to diagnosis can be quantitated, this variable in the system of the American Joint Committee would have more relevance if it reflected the extent defined by anatomical setting — that is, compartmentalization (or compartmental escape). This designation is more consistent with the natural histological behavior of the sarcomas, and has meaning for the surgeon.

4. Appended to Stage III as IIIC are lesions with regional lymph-node metastases. Lymph-node involvement is so uncommon in the natural history of these lesions at the time of diagnosis as to not be worth a separate factor[4,13,20]. When this relatively rare phenomenon does occur, the prognosis is poor. If lymph-node metastases are given equal weight with other metastases, the surgeon knows that a contemplated procedure is likely to be palliative or must be supplemented with other treatment modalities to be curative.

5. A "tumor that grossly invades bone, major vessel, or major nerve"[15] (T_3) is a poorly defined criterion, and the methods by which these judgments are to be made are not defined. Lesions with such involvement are assigned to a higher stage without regard for grade. Analysis of our data on soft-tissue sarcoma by this method results in Stage-IVA lesions having a prognosis similar to American Joint Committee Stage-IIIA and IIIB lesions. Such involvement is a proper function of the anatomical setting (extent of the primary lesion) and as such does not require a separate category.

6. Lesions of certain histogenesis (synovial sarcoma or angiosarcoma) are assigned at least to Stage III because of their usually poor prognosis. This is a function of grade and should be treated as such. Occasional lower grades of these lesions do occur, and should be staged accordingly.

Although there is a substantial body of evidence indicating that the initial surgical procedure is a key factor in the survival of patients with soft-tissue sarcoma[2-4,19], the American Joint Committee system takes no account of, and is not designed to facilitate, surgical planning. Although the system proposed by Hajdu takes the site of the lesion into account, the division into superficial and deep categories does not substantially contribute to surgical planning.

The biological behavior and principles of surgical management of bone and soft-tissue sarcoma are essentially the same. Therefore, it is logical to use a common staging system that also would allow comparison of histogenic types.

The system proposed here clearly stages lesions according to risk to the patients, facilitates surgical planning, and is relevant to analysis of end results. It currently forms the basis of ongoing inter-institutional investigations that are being conducted by the Musculoskeletal Tumor Society.

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