A Multi-Institutional Cooperative Study of Osteosarcoma
Partial Report with Emphasis on Survival After Limb Salvage

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Summary. Malignant musculoskeletal tumors, notably osteosarcoma, continue to pose difficult problems in diagnosis and treatment. One medical institution is unlikely to see enough patients with osteosarcoma to provide material for an adequate study, hence, the attraction of cooperative multi-institutional studies.

Few clinical trials have been designed to compare treatments among randomly selected patients with osteosarcoma. The need for adequate controls or comparison groups is acknowledged, but having patients and physicians agree on randomization is extremely difficult, particularly in osteosarcoma. The question arises: How can we learn more about osteosarcoma, its management, and its survival prospects without randomization, utilizing only observational data?

These considerations led to the project “Exploratory Studies of Osteosarcoma Prognosis,” in which 13 comprehensive cancer centers in the United States participated. The study cohort consisted of patients with osteosarcoma who were seen and treated during the period July 1977 to December 1982. All of the patients had tumors that fulfilled Dahlin’s definition of osteosarcoma. The 13 centers provided 1005 patients, of whom 543 fulfilled all the study requirements.

Choosing variables carefully, we compared the expected outcome with the observed outcome. The observed and expected survival curves after amputation and after limb-salvage resection were essentially identical.

Key words: Osteosarcoma—Patient variables—Prediction of outcome

Introduction

Osteosarcoma has long presented major challenges that so far have been unresolved in spite of the efforts of knowledgeable persons. A retrospective study of osteosarcoma can be divided into the prechemotherapy and postchemotherapy periods and now, in addition, the emerging period of limb salvage.

At the base of the observation period were the early days, as when a destructive swelling was diagnosed as “sarcoma,” and amputation was performed. Few of these patients survived more than 2 or 3 years [1]. Survival to 3 years ranged from near 0% to the 20s.
During the late 1960s and early 1970s, the reports of Cortes et al. [2] and Jaffe [3] describing the use of doxorubicin and methotrexate, first for metastatic disease and later as ingredients of adjuvant treatment programs, made a turning point for the better. Much has been accomplished since then, but many questions about the effectiveness of treatment remain unanswered.

Two decades have passed, during which a great many reports have been published, detailing a wide variety of studies of osteosarcoma, many of which are of fundamental importance. Key items in this new knowledge include the following:

a) The recognition of a dozen or more different types of osteosarcoma, each having its own peculiar biological behavior [4]

b) The design and general acceptance of logical staging schemes and the effort at developing a reliable uniform record system to assure the validity of comparisons among studies [5]

c) The increasing availability and reliability of sophisticated imaging techniques

d) The development of medical and surgical oncology training programs

e) The formation of organizations, such as the Musculoskeletal Tumor Society, which foster free interchange of experience and ideas

f) The proliferation of cooperative multiinstitutional studies

Saving life has always been the principal goal. An increasing effort to save the affected limb also has evolved whenever there is reasonable promise that such “limb salvage” will not decrease the chances of saving life. In recent years, treatment directed at limb salvage has become popular at cancer centers all over the world, and evidence is emerging concerning its efficacy in saving life and limb [6, 7].

We studied a group of patients with osteosarcoma in an attempt to determine if survival after surgical resection for limb salvage was different from survival after amputation. The study did not evaluate morbidity or functional results.

Any study has a number of inherent problems, among which are: a comparison of treatment requires sizeable samples, direct comparison of two groups treated differently may be fallacious, patients selected for one treatment may be different from those selected for another, and observed differences in treatment response may merely reflect patient differences [8].

Material and Methods

We present our data and the patient characteristics found to be associated with recurrence and death from osteosarcoma. We applied a method for comparing groups of patients who may differ with respect to their characteristics and their prognosis for survival from osteosarcoma.

A group of 13 comprehensive cancer centers pooled their data (Table 1). All centers were members of the Centralized Cancer Patient Date System (CCPDS) and had a uniform cancer data system based on cooperation and quality control. The records of all patients with osteosarcoma treated at these institutions from 1 July 1977 to 31 December 1982 were collected. These records were complete