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Chest wall Ewing sarcoma: a population-based analysis

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ABSTRACT

Background: The globally low incidence of pediatric chest wall Ewing sarcoma (CWES) has limited prior studies of this disease to mostly small, single-institution reviews. Our objective was to assess incidence, demographics, treatment patterns, and long-term survival of this disease through a population-based analysis.

Materials and methods: The Surveillance, Epidemiology, and End Results database was used to identify patients aged 0-21 y diagnosed with CWES from 1973 to 2011. Patients were grouped by decade to assess changes in treatment patterns and outcomes. The effects of clinical, demographic, and treatment variables on overall survival (OS) were assessed by the computation of Kaplan–Meier curves and the log-rank test, with Cox proportional hazard regression used for multivariable analysis.

Results: A total of 193 pediatric patients with histologically confirmed CWES were identified. The disease was more common in men (61%), whites (92%), and 11- to 17-y olds (49%). It was metastatic at presentation in 37% of patients. When grouped approximately by decade, 10-y OS improved progressively from 38% in 1973-1979 to 65% in 2000-2011 ($P = 0.033$). The use of radiation decreased from 84% in the earliest period to 40% in the most recent, whereas the proportion of patients receiving surgery increased from 75% to 85%. When controlling for covariates in multivariable analysis, male patients were found to have a higher mortality than female patients (hazard ratio: 2.4; confidence interval: 1.4, 4.4; $P = 0.0028$).

Conclusions: This population-based analysis of CWES demonstrated an impressive trend of improving OS, with increasing use of surgery and decreasing use of radiation therapy. Our study demonstrated a gender difference in survival of CWES, with females having a better prognosis. The presence of metastatic disease is a very important prognostic factor for this illness.

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Introduction

Ewing sarcoma (ES) is a rare aggressive malignant tumor of bone and/or soft tissue, most commonly found in adolescents and young adults. It was first described by the pathologist, James Ewing, in 1921 and is one of the classic childhood "small round blue cell tumors". Ewing family of tumors comprise Ewing's sarcoma of the bone (ES), extraosseous ES, primitive neuroectodermal tumor, Askin's tumor (ES of chest wall),[1] and atypical ES.[2] These tumors are felt to be of a single neoplastic process now that its molecular characteristics have been elucidated. Most ESs have a consistent chromosomal translocation, which usually involves the *EWS* gene on chromosome 22 and results in a chimeric fusion oncogene that has been studied extensively.[3]

In the pediatric and adolescent population, ES is the second most common bone tumor after osteosarcoma, and its highest incidence occurs between 10 and 15 y of age.[4] There are only about 200 new ES cases diagnosed per year in the United States.[5] Chest wall Ewing sarcoma (CWES) makes up only about 15%-20% of those,[6] thus making CWES a very rare malignancy.

Clinical trials involving national and international collaborative groups have resulted in treatment advances and led to the current therapeutic approaches. The treatment of CWES is multimodal and has involved chemotherapy, radiation therapy, and surgery. Chemotherapy is standard and given to all patients as this is felt to eradicate micrometastatic disease at diagnosis even if metastases are not detectable. The appropriate therapy regarding local control for ES and CWES has been the subject of many studies.[7-10] In the early 2000s, Shamberger and Grier[11] reported that for CWES, neoadjuvant chemotherapy was able to increase the rate of complete resections and thus increase the avoidance of radiation usage. Currently, in most North American centers, radiation therapy is used mainly in those cases where positive margins are present after surgical resection, if surgical resection is not possible and for local control of metastatic disease.

The sensitive anatomic location of these tumors complicates both surgical and radiologic management of CWES. It is unclear from the available literature whether survival of CWES differs from the survival of generalized ES. The goal of this study was to use a population-based database to assess the incidence, demographics, treatment trends, and long-term survival of CWES in the United States over the last 40 y.

Materials and methods

Study population

The NCI-Surveillance, Epidemiology, and End Results (SEER) public-use database was queried for patients with CWES using SEER*Stat version 8.1.5 (NCI, Bethesda, MD) in this institutional review board–exempt study.[12] Inclusion criteria were first primary tumors of the chest wall (ribs, sternum, clavicle) with a histologic diagnosis of ES and/or primitive neuroectodermal tumor, diagnosed from 1973 to 2011, in patients aged 0-21 y. Data collected included age, gender, year of diagnosis, ethnicity, race, tumor size, presence of metastatic disease, and treatment modality. Exclusions were made for patients with no survival data available. This yielded a study population of 193 patients. For the purpose of examining changes in survival over time, patients were grouped, on average, by decade of diagnosis. Stage was assessed using SEER historic stage A, with local and/or regional considered nonmetastatic, and distant considered metastatic. The SEER database did not include data regarding radiation dose, chemotherapy regimen, and site of metastatic disease.

Comparative survival analysis

For the purpose of comparing the survival rate of CWES with the survival rate for all cases of ES, a second group was needed. The SEER database was queried for all patients aged 0-21 y diagnosed with ES from 1973 to 2011.

Statistical analysis

Statistical analysis included both a calculation of comparative statistics, as well as univariate and multivariate survival analysis, performed using SAS version 9.3 (SAS Institute, Cary, NC). Factors assessed in univariate survival analysis using the Kaplan–Meier product-limit method were: patient age group, gender, ethnicity, race, decade of diagnosis, tumor size, stage, use of radiation therapy, and surgical treatment status. Those factors appearing to be significant on univariate analysis were considered in the Cox proportional hazard regression multivariable model.

Results

Of 1904 pediatric patients identified with ES in SEER, 193 had primary tumors of the chest wall. This represents a CWES incidence of less than 0.1 per million in the United States. This was predominantly a white, non-Hispanic patient population with a slight male predominance. Most patients were between the ages of 11 and 17 y, and over 60% of patients were between 11 and 21 y old. An approximately equal number of patients had tumors above or below 8 cm in size. However, this data set included a large number of cases in which tumor size was not recorded. Most patients had nonmetastatic disease at presentation (Table 1). The rate of patients presenting with metastatic disease did not change significantly over the study period ($P = 0.675$).

We compared local treatment modalities over various periods and found a decrease in the proportion of patients receiving radiation therapy from 84% to 40%, along with an increase in the proportion of patients receiving surgery (Fig. 1).

Overall survival (OS) for the study population was 60% at 5 y and 55% at 10 y (Fig. 2). This was equivalent to the 10-y OS rate for all pediatric cases of ES in SEER (55%) over the same period. The 10-y overall CWES survival was compared over various periods, and it was found to improve progressively from 38% in 1973-1979 to 65% in 2000-2011 (Fig. 3). Patients with metastatic disease at the time of diagnosis had a significantly poorer 10-y OS (39%) compared with 65% for those with