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Original article

Clinicopathologic characteristics and survival for adult renal sarcoma: A population-based study

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Abstract

Introduction: To analyze the association of clinicopathologic characteristics and treatment modality with survival among adult patients with renal sarcoma.

Methods: We identified 489 adults diagnosed with renal sarcoma from the Surveillance, Epidemiology and End Results registry between 1973 and 2011. Cancer-specific survival was estimated using the Kaplan-Meier method and was compared between groups with log rank and Cox models.

Results: Median age at diagnosis was 61 years, while median tumor size was 11 cm. Tumor histology was leiomyosarcoma in 175, liposarcoma in 100, other subtypes in 129, and unknown in 85 cases. Tumor stage at diagnosis was nonmetastatic in 322 (67%) and metastatic in 167 (33%) cases. Treatment of nonmetastatic disease was surgical resection in 171 patients, radiation in 24, both in 35, neither in 18, and unknown in 74 cases. Treatment of metastatic disease was surgery in 39 patients, radiation in 27, both in 11, neither in 42, and unknown in 48. For nonmetastatic and metastatic disease, 5-year cancer-specific survival rates were 58% and 16%, respectively. On multivariable analysis, surgery was associated with decreased cancer-specific mortality among both patients with nonmetastatic disease (hazard ratio = 0.34; 95% CI: 0.14–0.85) and those with metastatic disease (hazard ratio = 0.38; 95% CI: 0.18–0.77). Age, race, tumor size, and tumor grade were independently associated with cancer death in nonmetastatic disease, whereas race and tumor histology remained associated with mortality in metastatic disease (all $P < 0.05$).

Conclusion: Although metastatic renal sarcoma has an ominous prognosis, durable survival may be achieved for localized tumors. Although we recognize the potential for selection bias, our results suggest an association between surgical resection and decreased mortality for both nonmetastatic and metastatic renal sarcoma.

Keywords: Cohort studies; Kidney neoplasm; Nephrectomy; Sarcoma; Survival rate

1. Introduction

Primary renal sarcoma constitutes only 1% of all kidney tumors [1]. Given its rarity, limited data exist regarding demographics, prognostic factors, and optimal treatment approaches [2–4]. Indeed, the management of adult renal sarcomas is largely based on extrapolation of outcomes from other renal tumor histologies as well as from sarcomas originating from other anatomic sites. Nevertheless, given the disparate natural history of sarcomas from other primary kidney tumors, in addition to the uncertain relative outcomes of renal sarcomas vs. sarcomas from other sites, data regarding prognosis and treatment of patients specifically with renal sarcoma are still needed [5,6]. Studies evaluating renal leimyosarcoma have indicated that larger tumor size, more advanced stage, and higher grade are associated with worse outcome [2–4]. However, the associations of other factors such as histological subtype with cancer outcomes have not been well delineated.

Previous studies have suggested that surgical resection for adult renal sarcomas may be associated with improved

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survival [2–4]. However, these series have included a limited number of patients. In addition, the role for surgery in the setting of metastatic renal sarcoma has not been determined. Indeed, metastatic sarcomas are traditionally treated with chemotherapy [3,7], although for patients with metastatic renal cell carcinoma, cytoreductive nephrectomy has been an established component of multimodal treatment [8–10]. Therefore, the objectives of the present study were to analyze the association of clinicopathologic characteristics and treatment modality with survival for patients with renal sarcoma using a large, population-based registry.

2. Material and methods

2.1. Study population

After the study was approved by the Institutional Review Board, we queried the Surveillance, Epidemiology, and End Results (SEER) registry to identify adult (age $\geq$ 18 y) patients with the diagnosis of primary renal sarcoma (International Classification of Diseases 10 code "C64" and International Classification of Diseases-Oncology-3 histology codes 8800−8939) diagnosed between 1973 and 2011. The SEER program collects data of cancer cases from various locations and sources throughout the United States, currently covering approximately 28% of the population [11]. Of the 528 patients in the SEER registry who met the inclusion criteria, 39 (7%) were excluded owing to missing staging data. Data on patient's age at diagnosis (in years), race, sex (male or female), tumor size (in cm), laterality (left, right, or bilateral), grade, stage, histology, and primary treatment as well as overall survival (OS) and cancer-specific survival (CSS) in years were abstracted. Race was coded as white or nonwhite. Tumor grade was categorized as low (SEER grade I−II and well/moderately differentiated), high (SEER grades III−IV and poorly differentiated/undifferentiated), or unknown. Histological subtypes were divided into leiomyosarcoma, liposarcoma, other subtypes, and unknown. Tumor stage was based on the American Joint Committee on Cancer (AJCC) cancer staging —seventh edition—and coded as nonmetastatic (localized [AJCC stage T1-2N0M0] and locally advanced [AJCC stages T3-4N0M0 and TxN1M0]) or metastatic (AJCC stage TxNxM1). Primary treatment was categorized as nephrectomy alone (including partial and radical nephrectomy), radiotherapy alone, combination of nephrectomy and radiotherapy, neither surgery nor radiation (any treatment other than nephrectomy or radiotherapy, including no active treatment), and unknown. Notably, data regarding chemotherapy, targeted therapy, and secondary treatments are not available in the SEER registry.

2.2. Statistical analysis

Descriptive data are presented as median and interquartile range (IQR) or count and percentage. Univariable comparisons of baseline patient and disease characteristics, stratified by tumor stage (nonmetastatic and metastatic), were performed using the Fisher exact test for categorical data and the Wilcoxon signed rank test for continuous variables. Survival was estimated using the Kaplan-Meier method and was compared between groups using the log-rank test. Multivariable analyses of the association of clinicopathologic characteristics and treatment modalities with cancer-specific mortality, stratified by stage (nonmetastatic or metastatic), were performed using the Cox proportional hazard models. The models were adjusted for patient age, race, sex, tumor size, grade, histological subtype, laterality, and treatment modality. P values were estimated using analysis of deviance. All variables were kept in the model regardless of their P values. Missing data were combined into a separated category (named unknown) for all categorical variables with missing values and then included in the multivariable models. Hazard ratios are presented with 95% CIs. All statistical tests were 2 tailed and performed using R version 3.1.1 (R Foundation for Statistical Computing, Vienna, Austria). A $P < 0.05$ was considered statistically significant.

3. Results

A total of 489 patients met the inclusion criteria. Table 1 presents demographics and clinicopathologic characteristics, stratified by metastatic status. The median age at diagnosis was 61 years (IQR: 51−71), while the median tumor size was 11 cm (IQR: 6.9−16.0). Tumor stage at diagnosis was nonmetastatic in 322 (66%) cases, including 161 (33%) localized and 161 (33%) locally advanced tumors, and was metastatic in 167 (34%) cases. The most common histology was leiomyosarcoma, found in 175 (43%) patients, followed by liposarcoma in 100 (25%) and other subtypes in 129 (32%) cases. Among the 129 other subtypes, 32 (25%) were spindle cell sarcomas, 27 (21%) were malignant fibrous histiocytomas (undifferentiated pleomorphic sarcoma), 17 (13%) were fibrosarcomas, and 53 (41%) were other sarcomas. Notably, liposarcomas were less likely to be metastatic at diagnosis, as liposarcomas were localized or locally advanced at diagnosis in 86% of the cases, compared with 66% and 62% for leiomiosarcoma and other subtypes, respectively ($P < 0.001$). Similarly, high-grade tumors were found in 77% of patients with metastatic disease, compared with 62% among patients with nonmetastatic disease ($P = 0.03$).

The primary treatment modality was available in 367 (75%) patients, and consisted of surgery alone in 210 (57%), radiation alone in 51 (14%), surgery and radiation in 46 (13%), and neither surgery nor radiation in 60 (16%) cases. Patients with nonmetastatic disease were more likely to undergo nephrectomy, either alone or in combination with radiotherapy, than patients with metastatic disease (79% vs. 56%, respectively; $P < 0.001$). Meanwhile, patients with metastatic disease were more likely to receive