Four-Decade Epidemiological Trends of Synovial Sarcoma: An Analysis of the Surveillance, Epidemiology, and End Results Program
Marc El Beaino, MD, MS(1,2,3), Westley T. Hayes, MS(2,3), Tai L. Li, BS(2,3), Katherine M. Connors, MD(2), Michael A. Joseph, PhD, MPH(1), Patrick P. Lin, MD(4)

1Department of Orthopaedic Oncology, University of Texas MD Anderson Cancer Center, Houston, TX, USA
2Department of Orthopaedic Surgery and Rehabilitation Medicine, State University of New York Downstate Medical Center, Brooklyn, NY, USA
3School of Public Health, State University of New York Downstate Medical Center, Brooklyn, NY, USA

BACKGROUND

- Synovial sarcoma is a rare soft-tissue malignancy that can arise at any age and anatomic area.
- Currently available epidemiological estimates of the disease lack comprehensive translation into clinical practice due to being derived from small-scale short-term databases.
- Understanding the demographic patterns and burden characteristics of synovial sarcoma through analysis of a large population-based registry is essential to thoroughly assess the severity and successfully implement therapeutic modalities for the disease.
- As of yet, no study has delineated the incidence, prevalence, mortality, and overall survival trends of the disease, as well as its case-fatality ratio.

QUESTIONS/PURPOSES

- What are the incidence and prevalence of synovial sarcoma in the United States in the last 40 years?
- What are the mortality and case fatality of synovial sarcoma in the United States over the past 40 years?
- What is the overall survival and the risk factors that may influence synovial sarcoma patient prognosis?

METHODS

- The Surveillance, Epidemiology, and End Results (SEER) program was used to retrospectively identify patients with synovial sarcoma (ICD-O-3 codes 9040/3, 9041/3, 9042/3, and 9043/3) between 1975 and 2017.
- Extracted demographic variables included patient age, sex, race, and vital status at last follow-up, whereas disease characteristics encompassed tumor site, size, grade, and stage at the time of diagnosis.
- Population-based extracted data included:
  - Age-adjusted incidence
  - 20-year limited-duration prevalence
  - Incidence-based mortality
  - Case-fatality
  - Overall survival
- Descriptive analysis quantified patient demographics and tumor-specific variables.
- Epidemiological metrics, including incidence, prevalence, and mortality, were computed in SEER*Stat version 8.3.6.
- Patient survivorship and case-fatality were assessed using a log-rank with Kaplan-Meier estimates and Fisher’s exact test, respectively.
- Independent predictors of worse prognosis were determined by a multivariable Cox proportional hazard model analysis, using patient sex and age, as well as tumor size, grade, and stage as covariates.
- Univariate and multivariate analyses were conducted using SPSS v27 (IBM Corp., Armonk, USA) with a p-value of <0.05 as threshold for statistical significance.

RESULTS

- A total of 3397 patients were identified, of whom 1789 (52.7%) and 1608 (47.3%) were males and females, respectively.
- The disease predominantly affected middle aged adults (1219 (35.9%)), arising in their soft tissues as a localized tumor (1880 (55.3%)).
- Of 3396 subjects with known vital status at last follow-up, 1294 (38.1%) died as a result of their disease.
- The annual age-adjusted incidence of synovial sarcoma increased significantly from 0.92 (95%CI 0.55 – 1.46) per million persons in 1975 to 1.80 (95%CI 1.53 – 2.10) per million persons in 2017 (p=0.047), the highest rates being detected in G3/G4 and distant diseases (Figure 1).

![Figure 1. Annual grade and stage-specific incidence increased from 0.04 (95%CI 0.01 – 0.25) to 0.73 (95%CI 0.55 – 0.94) per million persons for G3/G4 tumors and from 0.03 (95%CI 0.01 – 0.25) to 0.33 (95%CI 0.22 – 0.48) per million persons for metastatic diseases (both p<0.001).](image)

- The 20-year limited-duration prevalence of synovial sarcoma almost doubled between 1995 and 2017, growing from 9.8% (95%CI 8.6 – 11.1) to 18.1% (95%CI 16.9 – 19.4), respectively (p<0.001).
- Except for children and patients with well-differentiated (G1) diseases, significant surges were detected in all individuals, the highest of which (3-fold) occurring in middle adults and G3/G4 tumors (Figure 2).

![Figure 2. Over the study period, the 20-year limited-duration prevalence of synovial sarcoma increased significantly in almost all individuals with a 4.6-fold increment in poorly differentiated (G3/G4) tumors (1.6‰ [95%CI 1.2 – 2.2]) in 1995 and 7.3‰ [95%CI 6.8 – 7.8]) in 2017 (p<0.001).](image)

- The incidence-based mortality of synovial sarcoma increased substantially from 0.16 (95%CI 0.03 – 0.48) per million persons in 1975 to 1.17 (95%CI 0.95 – 1.41) per million persons in 2017 (p<0.001).
- In 1975, 9 (31.0%) of 29 patients died of synovial sarcoma, whereas in 2016, 24 (14.3%) of 168 patients died as a result of their disease (p=0.033).
- The median overall survival was 21.7 years in the entire cohort, dropped to 1.3 years in subjects with metastatic disease at diagnosis, and could not be reached in patients with localized-stage disease and primary tumors <5 cm (Figure 3).

![Figure 3. Kaplan-Meier estimates of size and stage-specific overall survival of synovial sarcoma between 1975 and 2017.](image)

- On multivariable analysis, male sex, older age, as well as tumor size, grade, and stage, were all found to independently predict worse patient survival (Table 1).

![Table 1. Multivariable Cox regression analysis evaluating the effect of patient demographics and tumor characteristics on overall survival.](image)

CONCLUSIONS

- Improvements have been attained in the early detection and management of synovial sarcoma.
- Although advances in treatment have led to higher survival rates, improvements are still needed in the metastatic setting.
- Long-term follow-up of synovial sarcoma patients is warranted for adequate tumor relapse monitoring.

REFERENCES