Four-Decade Epidemiological Trends of Synovial Sarcoma: An Analysis of the Surveillance, Epidemiology, and End Results Program

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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 them being derived from small-scale short-term databases.
- Understanding the **demographical 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**).

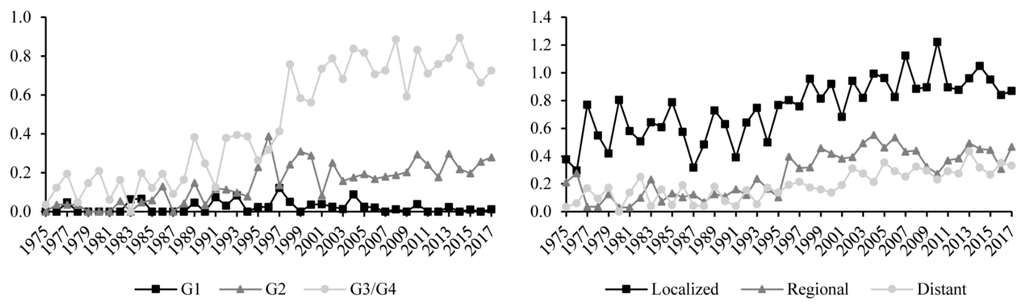


Figure 1. Annual grade and stage-specific incidence increased from 0.04 (95%CI 0.0 – 0.25) to 0.73 (95%CI 0.55 – 0.94) per million persons for G3/4 tumors and from 0.03 (95%CI 0.0 – 0.25) to 0.33 (95%CI 0.22 – 0.48) per million persons for metastatic diseases (both, p<0.001).

- 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 **G3/4 tumors** (**Figure 2**).

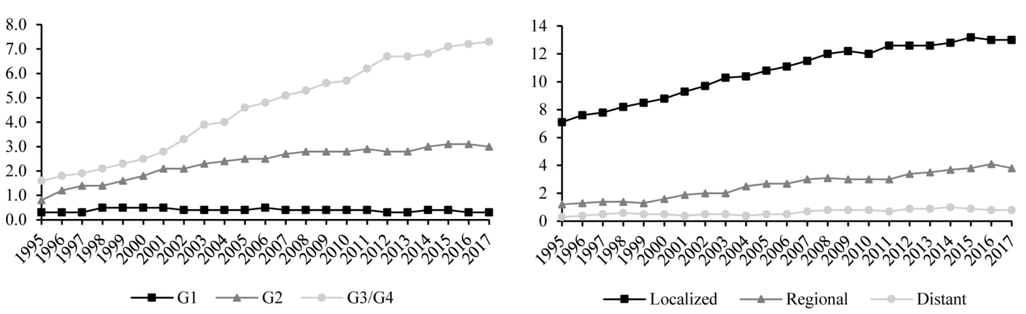


Figure 2. Over the study period, the 20-year limited-duration prevalence of synovial sarcoma increased significantly in almost all individuals with a 4.6-fold increment in poorly differentiated (G3/4) tumors (1.6‰ [95%CI 1.2 – 2.2] in 1995 and 7.3‰ [95%CI 6.8 – 7.8] in 2017) (p<0.001).

- 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**).

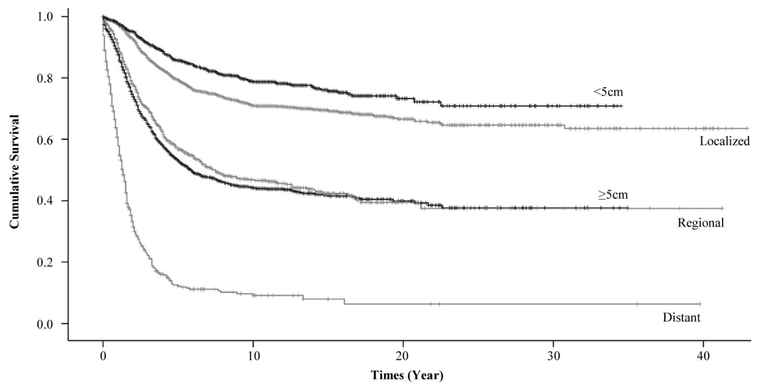


Figure 3. Kaplan-Meier estimates of size and stage-specific overall survival of synovial sarcoma between 1975 and 2017.

RESULTS

- 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**).

	Hazard Ratio (95% CI)
Age Groups	
Childhood	0.2 (95%CI 0.0 – 0.7)
Early Adolescence	0.3 (95%CI 0.2 – 0.6)
Middle Adolescence	0.4 (95%CI 0.2 – 0.6)
Late Adolescence	0.7 (95%CI 0.5 – 1.0)
Early Adulthood	0.8 (95%CI 0.6 – 0.9)
Middle Adulthood	Reference
Late Adulthood	1.9 (95%CI 1.4 – 2.6)
Sex	
Male	Reference
Female	0.8 (95%CI 0.7 – 1.0)
Tumor Size	
<5cm	Reference
≥5cm	2.4 (95%CI 1.9 – 3.1)
Tumor Grade	
G2	Reference
G3/G4	1.8 (95%CI 1.4 – 2.3)
Tumor Stage	
Localized	Reference
Regional	1.6 (95%CI 1.3 – 2.0)
Distant	5.6 (95%CI 4.5 – 7.1)

Table 1. Multivariable Cox regression analysis evaluating the effect of patient demographics and tumor characteristics on overall survival.

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**.

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