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Changing incidence and survival of desmoplastic small round cell tumor in the USA

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ABSTRACT

The incidence and prognosis of desmoplastic small round cell tumor (DSRCT) is inadequately understood. Survival analysis for DSRCT has not been investigated in a population-based study. We conducted a retrospective cohort study using the Surveillance, Epidemiology, and End Results (SEER) 9 Registry (1975–2018). Annual percent changes in incidence were estimated using SEER*Stat, and risk ratios were estimated using Poisson regression. Cox regression models were constructed to estimate the hazard ratio for survival at 5 years. The incidence rate of DSRCT has been rising in the last two decades. Men had a higher age-adjusted incidence rate, and nonmetropolitan counties had a higher incidence rate than metropolitan counties. Blacks had a higher risk of being diagnosed with DSRCT than whites. The observed survival at 12, 36, and 60 months was 81%, 39.9%, and 23.4%, respectively. Those >70 years had a poorer survival than those <60 years ($P < 0.001$). Compared to surgery with chemotherapy, surgery with chemoradiotherapy was linked to a 53% lower risk of mortality ($P < 0.001$). We conclude that the DSRCT incidence has been increasing since 2000 with a white male predominance. Gender doesn't affect survival in DSRCT, and surgery combined with chemoradiotherapy improves survival compared to surgical management with chemotherapy alone.

KEYWORDS Desmoplastic small round cell tumor; DSRCT; incidence; prognosis; SEER; survival

Desmoplastic small round cell tumor (DSRCT) is a highly uncommon and aggressive soft tissue sarcoma with a poor prognosis. First described in 1989 by Gerald and Rosai based on distinct clinicopathological features of small round blue cells intermixed in the desmoplastic stroma, DSRCT remains a reasonably new tumor with sparse incidence.[1] Limited cohort analyses, such as a Brazilian study by Campos et al, a UK study by Honore et al, and a Chinese study by Xiang et al, suggest a median age of diagnosis around 24 to 26 years with male predominance.[2–5] Current literature is extremely scarce regarding the incidence, racial disparities, and survival of patients with DSRCT, perhaps because of its rarity. We examined incidence, risk ratios, and survival, focusing on patient demographics and factors affecting survival, by utilizing the Surveillance, Epidemiology, and End Results (SEER) database, which provides information on patient demographics and survival. We intended to extend knowledge about DSRCT by examining factors associated with improved survival in these patients.

METHODS

Data were obtained from the SEER 9 cancer registry database for 1975 through 2018. SEER 9 reports all available cases diagnosed since 1975 through the current available data year and includes 28% of the US population as of the 2010 census.[6] Details regarding the SEER database can be found at http://seer.cancer.gov/data/. SEER 9 was selected as it offered the longest follow-up (1975–2018) for registered patients. The registries included in SEER 9 are San Francisco–Oakland, Connecticut, Detroit (Metropolitan), Hawaii, Iowa, New Mexico, Seattle (Puget Sound), Utah, Atlanta (Metropolitan, Greater Georgia, Rural Georgia).

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Table 1. Number of incident desmoplastic small round cell tumor cases and age-specific and age-adjusted incidence rates per 1 million persons[a]

Category	Variable	Cases	Incidence rate
Sex	Male	123	0.22
	Female	31	0.05
Counties	Metropolitan	133	0.14
	Nonmetropolitan	21	1.14
Race	White	94	0.11
	Black	40	0.29
	Other[b]	20	0.16
Age group (years)	<60	143	0.15
	60–69	5	0.05
	>70	6	0.07
Year	1975–2000	9	0.01
	2001–2018	145	0.31

[a]Standardized to the US standard population 2000, by age, gender, ethnicity, race, and year of diagnosis; data from Surveillance, Epidemiology, and End Results (SEER) 9 (1975–2018).
[b]American Indian/Native American and Asian/Pacific Islander.

Table 2. Specific incidence rate ratios for desmoplastic small round cell tumor by gender, location, race, age, and year of diagnosis[a]

Category	Variable	Rate ratio
Sex	Male	1
	Female	0.77 (0.75–0.81)*
Counties	Metropolitan	–
	Nonmetropolitan	0.98 (0.52–1.57)
Race	White	–
	Black	2.6 (1.75–3.89)*
	Other	1.5 (0.88–2.5)
Age group (years)	<60	–
	60–69	0.37 (0.12–0.90)*
	>70	0.45 (0.16–1.01)**
Year	1975–2000	–
	2001–2018	22.3 (11.31–50.2)*

[a]Estimated using Poisson regression. Data from Surveillance, Epidemiology, and End Results (SEER) 9 (1975–2018).
*Statistically significant ($P < 0.05$).
**Nearing significance ($P = 0.05$).

Within the SEER database, *International Classification of Diseases for Oncology* (ICD-O-3) 8806/3 was used via SEER*Stat software to select cases of DSRCT only. Only cases that had a microscopically confirmed diagnosis were included.

The year of diagnosis was categorized into two groups for incidence: 1975 to 2000 and 2001 to 2018. Age was categorized into <60 years, 60 to 69 years, and ≥70 years for incidence and survival analysis. Race and ethnicity were examined separately due to the denominator imprecision. Race was classified as white, black, and other (Asian/Pacific Islander, American Indian/Alaskan Native). County attributes were available as metropolitan and nonmetropolitan counties in SEER 9. Data regarding cancer location on diagnosis were grouped accordingly. We classified patient characteristics like age, race, and gender as incidence without any change.

SEER*Stat was utilized to calculate the incidence and age-adjusted rates, grouped by age, gender, ethnicity, and year. The SEER 9 registry was used to analyze trends from 1975 to 2000 using yearly diagnosis. The period-specific rates were plotted utilizing temporal trend figures and portrayed as rate per 1 million. We used annual rates for temporal trends to quantify the annual percent changes with 95% confidence intervals (CIs). Incidence rate ratios for gender and ethnicity/race were calculated. An age-stratified Poisson model was used to report 95% CIs for the age-adjusted incidence rate ratios. Gender, race, year group, age group, and treatment-based survival were calculated using the Kaplan-Meier method. Cox regression models were constructed using Stata Corp (2017) Stata Statistical Software to estimate the hazard ratio for survival at 5 years after adjusting for age, gender, and race.

RESULTS

As shown in *Table 1*, there were 154 cases of DSRCT from 1975 to 2018 in the SEER 9 database. The study population was 79.8% men and 20.2% women; 86% of cases were from nonmetropolitan counties, while 14% were from metropolitan counties. In terms of race, 61% of cases were white, 26% were black, and 13% were other minorities. Most cases (92.8%) were in those <60 years, and most (94%) were reported after the year 2000. The male and female age-adjusted DSRCT incidence rates were 0.22 and 0.05 per million, respectively *(Table 1)*. Nonmetropolitan counties had a higher incidence rate than metropolitan counties (1.14 vs. 0.14 per million). The DSRCT age-adjusted incidence rates increased from 1975–2000 to 2001–2018 (0.01 vs. 0.31 per million, respectively). Incidence rates were highest in those <60 years. The location of reported cases is shown in the Supplementary Material.

Modeled rate ratios were adjusted for gender and age. Adjusted risks ratios showed that women had a reduced DSRCT risk compared to men *(Table 2)*. Blacks had a significantly increased risk of being diagnosed with DSRCT relative to whites. Compared to the 1975–2000 time period, the risk of being diagnosed with DSRCT increased more than 100% in 2001–2018. Compared to ages <60 years,

Table 3. Incidence rate ratios for desmoplastic small round cell tumor by year and age group

Category	Variable	Rate ratio (confidence interval)	
		Females (relative to males)	Blacks (relative to whites)
Year	1975–2000	0.15 (0.003–1.15)	0.89 (0.02–9.4)
	2001–2018	0.26 (0.17–0.39)*	2.52 (1.7–3.7)*
Age group (years)	<60	0.22 (0.14–0.33)*	3.04 (2.05–4.4)*
	60–69	0.44 (0.03–3.1)	3.2 (0.1–39.8)
	>70	3.39 (0.37–158.7)	–

[a]Estimated using Poisson regression. Data from Surveillance, Epidemiology, and End Results (SEER) 9 (1975–2018).
*Statistically significant ($P < 0.05$).

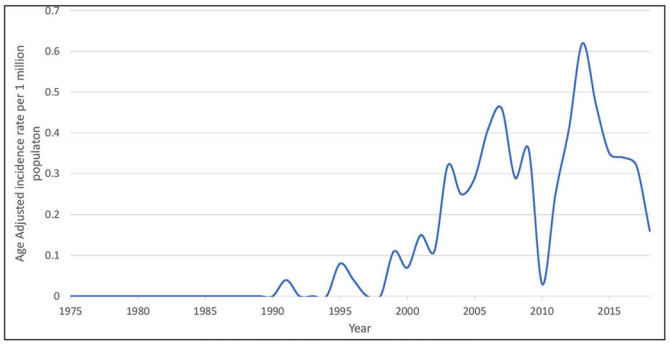

Figure 1. Trends in desmoplastic small round cell tumor incidence rates, using SEER 1975 to 2018.

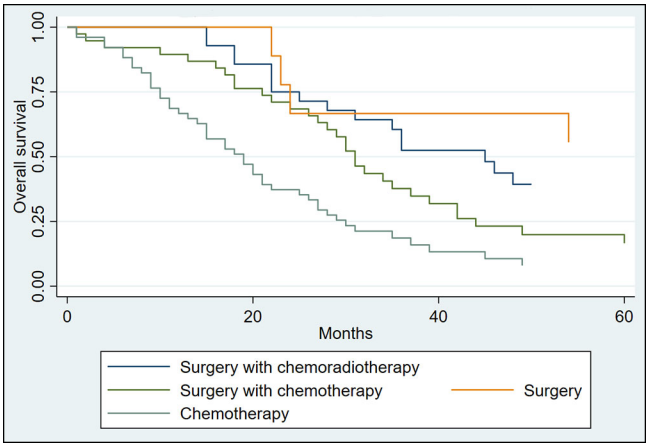

Figure 2. Kaplan-Meier curves of survival for desmoplastic small round cell tumor: surgery with chemoradiotherapy compared with surgery with chemoradiotherapy, surgery alone, and chemotherapy alone ($P < 0.001$ via log-rank test).

ages 60–69 had a 63% lower risk of DSRCT diagnosis, and ages >70 years had a 55% lower risk of being diagnosed with DSRCT, results that approached statistical significance ($P = 0.05$) *(Table 2)*. Interactions between year and age groups were assessed by race and gender. The DSRCT risk was significantly lower among women than men in 2001 to 2018 *(Table 3)*. Women <60 years were 78% less likely to be diagnosed with DSRCT than men. Women aged 60 to 69 and >70 had no difference in risk of being diagnosed with DSRCT than men. DSRCT risk was significantly lower among blacks relative to whites in 2001 to 2018. On age group analysis, only blacks with age <60 years had a significantly higher risk than whites (relative risk, 3.04).

The annual percent change for the DSRCT incidence rate from 1975 to 2018 could not be calculated due to the latest 1 year without any case. The annual percent change from 2000 to 2018 was 0.87% for all cases; however, this was not statistically significant *(Figure 1)*. The percent change was 376% from 1975 to 2018 for all cases. Trends for gender, year, and age groups were inconsistent for multiple years without any reported cases (Supplementary Figure 1).

The observed survival at 12, 36, and 60 months was 81%, 39.9%, and 23.4%, respectively. The median survival time for all cases was 27 months. The median survival time for men was 27 months, while it was 25 months for women. The median survival time for the white race was 25 months vs. 31 months for the black race. Cases diagnosed before the year 2000 had a median survival time of 35 months, while cases diagnosed after 2000 had a survival time of 27 months. Those <60 years had a median survival time of 28 months; between 61 and 70, 22 months; and >70, only 4 months. Patients who underwent chemotherapy alone had a median survival time of 19 months. There were no cases with radiotherapy alone. Those who underwent surgery with chemoradiotherapy had a median survival time of 45 months, while patients who underwent surgery with chemotherapy had survival of 31 months. Patients undergoing surgery with radiotherapy but no chemotherapy had a median survival time of 48 months; however, the sample size was only two patients.

After adjusting for age, gender, and race, there was no difference in survival in women compared to men (adjusted hazard ratio [HRadj] 0.85, 95% CI 0.52–1.4, $P = 0.5$). Those >70 years had poor survival compared to those <60 years (HRadj 29.4, 95% CI 7.02–123.1, $P < 0.001$). There was no difference in survival in blacks compared to

whiles (HRadj 0.99, 95% CI 0.6–1.5, $P = 0.9$). Cases diagnosed after the year 2000 did not have any significant difference in survival compared to cases diagnosed before the year 2000 (HRadj 1.48, 95% CI 0.76–2.8, $P = 0.2$). Compared to surgery with chemotherapy, surgery alone had no change in survival (HRadj 0.37, 95% CI 0.14–1.01, $P = 0.06$); however, surgery combined with chemoradiotherapy was linked to a 53% lower risk of mortality (HRadj 0.47, 95% CI 0.25–0.90, $P < 0.01$). Chemotherapy alone compared to surgery with chemotherapy was linked to a 79% increased risk of mortality (HRadj 1.79, 95% CI 1.10–2.9, $P < 0.01$). Kaplan-Meier curves for survival based on therapeutic interventions are shown in *Figure 2* ($P < 0.001$ via log-rank test).

DISCUSSION

This study reports incidence and survival across a comprehensive age continuum for DSRCT. Our analysis suggests periods of increased mortality and the incident risk of DSRCT in the USA since 1975. This is also the first study examining risk interactions by year groups, age groups, gender, and race. Examination of DSRCT by gender revealed that men have a higher age-adjusted incidence rate than women. Moreover, the incidence rate is increased in blacks. There was no significant difference in 5-year survival between women and men. The incidence was 0.22 and 0.05 per million for men and women, respectively. This incidence has been higher in nonmetropolitan counties compared to metropolitan counties. While those >70 years had a 55% lower risk of being diagnosed with DSRCT, their median survival was only 4 months, the lowest among all age groups.

Arising from the serosal surfaces, DSRCT is characterized by a peculiar translocation between Ewing sarcoma RNA binding protein 1 gene (*EWSR1*) and Wilms tumor suppressor gene (*WT1*) at t(11;22)(p13;q12), which leads to downstream activation of biological pathways including growth factors, not limited to platelet-derived growth factor, insulin growth factor, transforming growth factor–beta, and vascular endothelial growth factor via a chimeric transcription regulatory protein. This leads to the diagnosis of most patients at an advanced stage with multifocal disease, which makes treatment yet more challenging.[7,8] Other targets and molecular pathways have been recently described and are underway.[6,9]

Our survival analysis revealed that surgery combined with chemoradiotherapy was superior in prolonging survival compared to surgery with chemotherapy alone (HRadj 0.47, 95% CI 0.25–0.90, $P < 0.01$). The optimal treatment for DSRCT is poorly described in the literature with no designated guidelines. Cytoreductive surgery compounded by radiotherapy and multiagent chemotherapy remains the multimodal approach that has improved survival, which is consistent with our report.[4,10–13] Chemotherapy with the famous Lai's P6 protocol (cyclophosphamide, vincristine, ifosfamide, etoposide) or Scheer's VAIA regimen (ifosfamide, vincristine, Adriamycin, and actinomycin D) has been used in cases of DSRCT with no comparative differences.[5,14,15] DSRCT is modestly chemosensitive, although recurrence is widespread on these regimens despite the multimodal approach, showing an urgent need for targeted strategies.[5,6,13–15] Several trials involving hyperthermic intraperitoneal chemotherapy, immunotherapy, and radioimmunotherapy are underway.[16–18] Since there were no cases of treatment with surgery and radiotherapy, Cox regression was not conducted to avoid confounding. According to the Kaplan-Meier curves, surgery alone showed more prolonged survival than surgery with adjuvant therapy; a possible hypothesis is the aggressive presentation of those cases.

Our study has limitations, some of which are inherent to observational studies. The SEER 9 database does not report individual comorbidities and risk factors, which can influence these trends. There is a concern of migrating patients in and out of areas registered in the SEER database and selection bias. Cancer registries like SEER report only the month and year and number of whole months of survival in efforts to deidentify patients and ensure their privacy. Therefore, limitations exist since survival dates and times in SEER data are not exact. As data are deidentified by SEER, the potential for sample bias cannot be intervened. Specific treatment details, such as chemotherapy regimen or type of surgical interventions, are not available in the SEER 9 database.

1. Gerald WL, Rosai J. Case 2. Desmoplastic small cell tumor with divergent differentiation. *Pediatr Pathol*. 1989;9(2):177–183. doi:10.3109/15513818909022347.
2. Xiang T, Zhang SY, Wang SS, Fei RS, Li H. A nationwide analysis of desmoplastic small round cell tumor. *Medicine (Baltimore)*. 2020;99(30):e21337. doi:10.1097/MD.0000000000021337.
3. Campos F, Coutinho DL, Silva MLG, et al. Clinical characteristics, management, and outcomes of 19 nonpediatric patients with desmoplastic small round cell tumor: a cohort of Brazilian patients. *Sarcoma*. 2020;2020:8713165. doi:10.1155/2020/8713165.
4. Honoré C, Amroun K, Vilcot L, et al. Abdominal desmoplastic small round cell tumor: multimodal treatment combining chemotherapy, surgery, and radiotherapy is the best option. *Ann Surg Oncol*. 2015;22(4):1073–1079. doi:10.1245/s10434-014-4123-6.
5. Honoré C, Delhorme JB, Nassif E, et al. Can we cure patients with abdominal desmoplastic small round cell tumor? Results of a retrospective multicentric study on 100 patients. *Surg Oncol*. 2019;29:107–112. doi:10.1016/j.suronc.2019.04.002.
6. Ferreira EN, Barros BD, de Souza JE, et al. A genomic case study of desmoplastic small round cell tumor: comprehensive analysis reveals insights into potential therapeutic targets and development of a monitoring tool for a rare and aggressive disease. *Hum Genomics*. 2016;10(1):36. doi:10.1186/s40246-016-0092-0.
7. Bexelius TS, Wasti A, Chisholm JC. Mini-review on targeted treatment of desmoplastic small round cell tumor. *Front Oncol*. 2020;10:518. doi:10.3389/fonc.2020.00518.
8. Thway K, Noujaim J, Zaidi S, et al. Desmoplastic small round cell tumor: pathology, genetics, and potential therapeutic strategies. *Int J Surg Pathol*. 2016;24(8):672–684. doi:10.1177/1066896916668637.
9. Ogura K, Somwar R, Hmeljak J, et al. Therapeutic potential of ntrk3 inhibition in desmoplastic small round cell tumor. *Clin Cancer Res*. 2021;27(4):1184–1194. doi:10.1158/1078-0432.CCR-20-2585.
10. Schwarz RE, Gerald WL, Kushner BH, Coit DG, Brennan MF, La Quaglia MP. Desmoplastic small round cell tumors: prognostic

indicators and results of surgical management. *Ann Surg Oncol*. 1998; 5(5):416–422. doi:10.1007/BF02303860.
11. Osborne EM, Briere TM, Hayes-Jordan A, et al. Survival and toxicity following sequential multimodality treatment including whole abdominopelvic radiotherapy for patients with desmoplastic small round cell tumor. *Radiother Oncol*. 2016;119(1):40–44. doi:10.1016/j.radonc.2015.10.016.
12. Kushner BH, LaQuaglia MP, Wollner N, et al. Desmoplastic small round-cell tumor: prolonged progression-free survival with aggressive multimodality therapy. *J Clin Oncol*. 1996;14(5):1526–1531. doi:10.1200/JCO.1996.14.5.1526.
13. Gani F, Goel U, Canner JK, Meyer CF, Johnston FM. A national analysis of patterns of care and outcomes for adults diagnosed with desmoplastic small round cell tumors in the United States. *J Surg Oncol*. 2019;119(7):880–886. doi:10.1002/jso.25426.
14. Scheer M, Vokuhl C, Blank B, et al; Cooperative Weichteilsarkom Studiengruppe. Desmoplastic small round cell tumors: multimodality treatment and new risk factors. *Cancer Med*. 2019;8(2):527–542. doi:10.1002/cam4.1940.
15. Lal DR, Su WT, Wolden SL, Loh KC, Modak S, La Quaglia MP. Results of multimodal treatment for desmoplastic small round cell tumors. *J Pediatr Surg*. 2005;40(1):251–255. doi:10.1016/j.jpedsurg.2004.09.046.
16. Espinosa-Cotton M, Cheung NKV. Immunotherapy and radioimmunotherapy for desmoplastic small round cell tumor. *Front Oncol*. 2021;11:772862. doi:10.3389/fonc.2021.772862.
17. Modak S, Zanzonico P, Grkovski M, et al. B7h3-directed intraperitoneal radioimmunotherapy with radioiodinated omburtamab for desmoplastic small round cell tumor and other peritoneal tumors: results of a phase I study. *JCO*. 2020;38(36):4283–4291. doi:10.1200/JCO.20.01974.
18. Garnier H, Murawski M, Jastrzebski T, et al. Case report: cytoreductive surgery and hyperthermic intraperitoneal chemotherapy application in intraperitoneally disseminated inflammatory myofibroblastic tumor and in the youngest patient in the world: new indication and modification of technique. *Front Surg*. 2021;8:746700. doi:10.3389/fsurg.2021.746700.