Prognostic factors, treatment, and survival in cutaneous pleomorphic sarcoma

Maria A. Ibanez, BS,[a] Kyle Rismiller, MD,[a] and Thomas Knackstedt, MD[a,b]
Cleveland, Ohio

Background: Limited information exists on the influence of demographics, tumor characteristics, and treatment on survival in cutaneous pleomorphic sarcoma (CPS).

Objective: To describe incidence rates and prognostic factors affecting survival in CPS.

Methods: National Cancer Institute's Surveillance, Epidemiology, and End Results data (1972-2013) was analyzed for 2423 patients with CPS diagnoses.

Results: The age-adjusted incidence rate was 0.152 cases/100,000 person-years and was 4.5-fold higher in male than female patients. Male sex, white race, and increasing age >40 years were significantly associated with decreased overall survival. Head and neck tumors, tumors >15 mm, and tumors with grade III or IV histology were associated with significantly decreased survival. Surgical excision had a survival benefit compared with no treatment. Radiation therapy did not provide a survival benefit. Patients with localized disease had the greatest survival followed by regional and distant disease.

Limitations: Surveillance, Epidemiology, and End Results data might not be reflective of all CPS patients. Recurrences, restaging, or other nonmortality events over time were not tracked.

Conclusion: Tumor size, grade, sex, age at diagnosis, and race appear to influence survival as prognostic factors in CPS. Surgical tumor extirpation provides a survival benefit over no treatment whereas primary or adjuvant radiation does not provide a survival benefit. (J Am Acad Dermatol 2020;83:388-96.)

Key words: epidemiology; demographics; prognostic factors; treatment; undifferentiated pleomorphic sarcoma.

Cutaneous pleomorphic sarcoma (CPS), formerly known as malignant fibrous histiocytoma, and occasionally referenced as undifferentiated pleomorphic sarcoma or pleomorphic dermal sarcoma, is one of the most common adult sarcomas.[1] CPS is the cutaneous variant of undifferentiated pleomorphic sarcoma. Since O'Brien and Stout[2] first described this malignancy in 1964, there has been a debate on the exact histogenesis, with some investigators claiming a histiocytic[3,4] and others a mesenchymal origin.[5,6]

Abbreviations used:

CI:	confidence interval
DSS:	disease-specific survival
FNCLCC:	French Federation of Cancer Centers Sarcoma Group
HR:	hazard ratio
ICD-O:	International Classification of Disease for Oncology
MMS:	Mohs micrographic surgery
NCI:	National Cancer Institute
SEER:	Surveillance, Epidemiology, and End Results

From the School of Medicine, Case Western Reserve University, Cleveland[a]; and Metrohealth Hospital, Cleveland.[b]
Funding sources: None.
Conflicts of interest: None disclosed.
Accepted for publication August 29, 2018.

Reprint requests: Thomas Knackstedt, MD, Metrohealth Hospital, 2500 Metrohealth Drive, Cleveland, OH 44109. E-mail: thomas.j.knackstedt@gmail.com.
Published online November 8, 2018.
0190-9622/$36.00

https://doi.org/10.1016/j.jaad.2018.08.054

Atypical fibroxanthoma is considered to be the superficial variant of CPS, as they are histologically indistinguishable and have been shown to share cytogenetic markers.[7,8] However, although atypical fibroxanthoma is regarded as a locally aggressive neoplasm of intermediate malignancy,[8] a diagnosis of CPS can be the harbinger of more worrisome disease, morbidity, and mortality. Nevertheless, limited information regarding the prognosis of CPS exists. Tumor size, depth, and grade have been linked to CPS outcomes,[9,10] but few studies have been published.

The goal of CPS treatment is tumor extirpation with negative pathologic margins. Surgical excision has been fraught with high local recurrence rates due to inadequate margins[11] and the tumor's infiltrative growth pattern between fascial planes and even muscle fibers.[12] Mohs micrographic surgery (MMS) and wide local excision have been used successfully for CPS treatment.[6,10,13] Radiation therapy has been suggested as adjuvant therapy in high-risk cases.[11] With the overall impact of these therapies appearing unclear, our study aims to correlate the factors that influence the effects of treatment on overall survival. We furthermore seek to provide additional insight into variables of prognostic significance.

CAPSULE SUMMARY

- Cutaneous pleomorphic sarcoma is an aggressive tumor with local recurrence and potential for metastasis.
- In this Surveillance, Epidemiology, and End Results database study, male sex, white race, age >39 years, primary site in the head and neck, size >15 mm, and distant disease were identified as negative prognostic factors. This study demonstrated that surgical treatment of high-risk patients improves outcomes.

METHODS

Patient population

Patients included in the study were identified as having CPS (World Health Organization's International Classification of Disease for Oncology [ICD-O], third edition, code 8830-3) during 1973-2013 through the National Cancer Institute (NCI)'s Surveillance, Epidemiology, and End Results (SEER) database. The SEER registry is a collection of 18 cancer registries covering 28% of the US population. Cases of a primary site other than skin (C44.0-C44.9) were excluded. This code has remained consistent across ICD-O systems and across the diseases entomologic evolution, facilitating this registry search over a 40-year timespan. Atypical fibroxanthoma, termed intermediate neoplasms, are not logged in SEER and were not included in the analysis. Follow-up data was collected on available patients until 2013. All patient diagnoses were biopsy proven and did not include patients who received clinical, radiographic, or posthumous diagnoses.

Study variables and definitions

Relevant demographic data included sex, race (SEER categories of black, white, Asian, other), and age at diagnosis. Anatomic location, tumor size, histologic grade, lymph node status, and treatment data were recorded. Treatments included local destruction (including laser and cryosurgery), surgical excision, and primary or adjuvant radiation therapy. Histologic grade of sarcomas is routinely interpreted according to the French Federation of Cancer Centers Sarcoma Group (FNCLCC), a 3-grade system. SEER acknowledges this cancer grading system but converts this grading system into a 4-grade system as follows: FNCLCC grade 1 (SEER grade 2), FNCLCC grade 2 (SEER grade 3), and FNCLCC grade 3 (SEER grade 4). This 4-grade system was used in the statistical analysis. Surgeries were categorized as nonwide excision (including tumor excision, excisional biopsy, and gross excision); wide excision (including wide local excision and amputation); or MMS. Surgical treatments and patients receiving surgery alone versus patients receiving surgery and radiation were compared. Vital status, cause of death, and follow-up were ascertained.

Disease stage

The standardized SEER historic stage variable under the heading of the SEER Localized, Regional, and Distant Staging System, which is applicable to all malignancies and spans across years otherwise subject to variable formal staging systems, was used for staging. The stage categories are local, regional, distant, and unstaged.[14,15] Local was defined as an invasive malignant neoplasm confined entirely to the organ of origin. Regional was defined as a malignant neoplasm that either a) extended beyond the limits of the organ of origin directly into surrounding organs or tissues or b) involved a regional lymph node by way of the lymphatic system. Distant was defined as a malignant neoplasm that had spread to body parts remote from the primary tumor by direct extension or by discontinuous metastasis to distant organs or tissues

Table I. Characteristics of the 2423 patients in the overall cutaneous pleomorphic sarcoma cohort included in analysis, after adjustment for exclusion criteria

Characteristic	Value
Sex, n (%)	
Male	1887 (77.9)
Female	536 (22.1)
Race, n (%)	
White	2205 (91.0)
Black	51 (2.1)
Other	41 (1.7)
Unknown	126 (5.2)
Age, y	
≤19	31 (1.3)
20-39	87 (3.6)
40-59	275 (11.3)
60-79	1144 (47.2)
≥80	886 (36.6)
Primary site, n (%)	
Head and neck	1788 (73.8)
Trunk	177 (7.3)
Extremities	436 (18.0)
Skin, NOS	22 (0.9)
Treatment, n (%)	
Local or incomplete	51 (2.1)
Nonwide excision/NOS	1367 (56.4)
Wide excision/definitive	510 (21.0)
Mohs	175 (7.2)
None	288 (11.9)
Unknown	32 (1.3)
Radiation sequence, n (%)	
Patients receiving radiation	212 (8.8)
Neoadjuvant, n (%)	28 (13.2)
Adjuvant, n (%)	166 (78.3)
Unknown sequence, n (%)	18 (8.5)
Radiation type, n (%)	
Patients receiving radiation	212 (8.8)
Beam, n (%)	209 (98.6)
Beam + implants or isotopes, n (%)	1 (0.5)
Radiation, NOS, n (%)	2 (0.9)
Refused	3 (0.1)
None	2182 (90.0)
Unknown	26 (1.1)
Grade, n (%)	
Well differentiated (I)	38 (1.6)
Moderately differentiated (II)	123 (5.1)
Poorly differentiated (III)	115 (4.7)
Anaplastic (IV)	87 (3.6)
Unknown	2060 (85.0)
SEER historic stage, n (%)	
Localized	1639 (67.6)
Regional	365 (15.1)
Distant	36 (1.5)
Unstaged	383 (15.8)
Vital status, n (%)	
Alive	1158 (47.8)
Dead	1265 (52.2)
Due to MFH	150 (11.9)
Tumor size, mm, mean (SD)	21.8 (21.3)
Follow-up, m, mean (SD)	76.8 (78.8)

MFH, Malignant fibrous histiocytoma; *NOS*, not otherwise specified (by SEER registrar); *SD*, standard deviation.

or via the lymphatic system to a distant lymph node. For unstaged tumors, information was not sufficient to assign staging.

Statistical analysis

Data were retrieved using SEER*Stat 8.3.4 (NCI) and analyzed with SPSS for Windows version 22 (IBM Corp, Armonk, NY) and SEER*Stat 8.3.4 (NCI). Continuous variables were analyzed by using the *t* test and analysis of variance, as appropriate, with application of the Welch, Brown-Forsythe, and Mann-Whitney U methods when indicated. Categorical variables were analyzed by using the chi-square tests, transitioning to logistic regression for polynomial variables. Race-specific and age-specific rate ratios, incidence, and mortality were calculated on the basis of on the year 2000 US standard population. The Kaplan-Meier method in conjunction with the log-rank test and Cox proportional hazards model was used for survival analyses. A $P < .05$ value was considered significant.

RESULTS

Population characteristics and incidence

In the 40-year study time span, 2423 patients were given CPS diagnoses. Table I provides a summary of the demographic, clinical, and pathologic characteristics of the CPS cohort. The age-adjusted incidence was 0.288 (95% confidence interval [CI] 0.271-0.306) tumors/100,000 person-years in men ($P < .001$) and 0.064 (95% CI 0.057-0.071) tumors/100,000 person-years in women ($P < .001$). The incidence was 4.5-fold higher in male than in female patients, and white persons were disproportionately affected by CPS in age-adjusted incidence analysis with 1.67 cases/1 million population. The overall incidence of CPS increased at an annual change of 3.0% (95% CI 2.282%-3.730%; $P < .001$). Men experienced a greater increase in incidence at an average of 4.1% (95% CI 3.211%-5.072%; $P < .001$) annually.

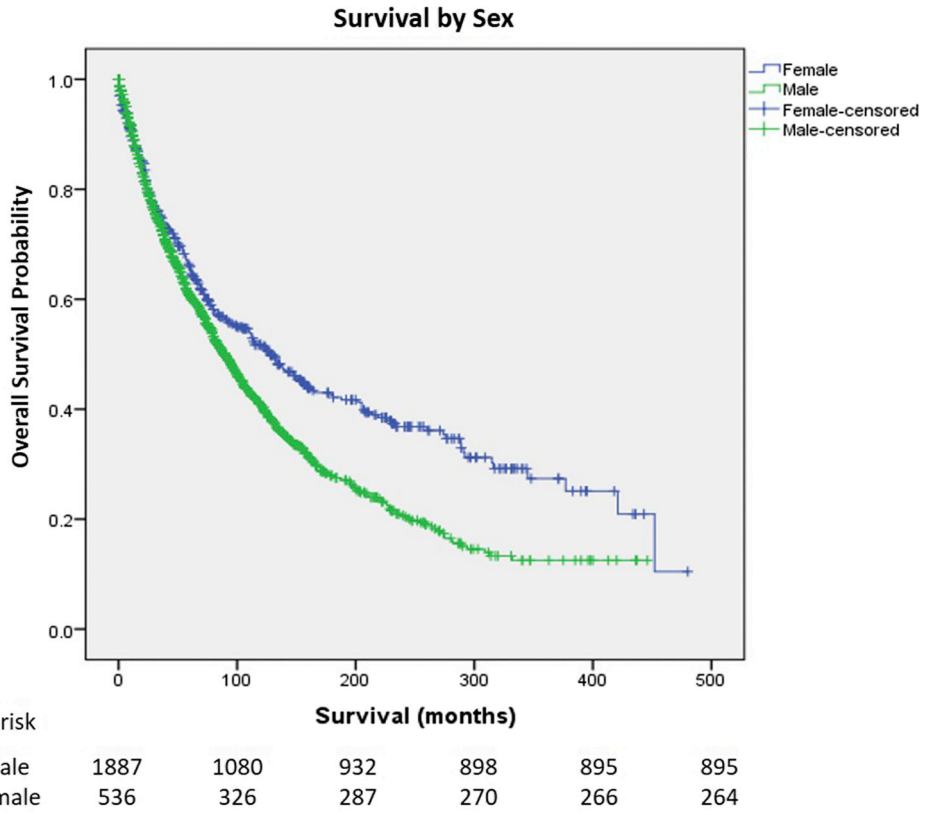

Fig 1. Kaplan-Meier curves of sex as a prognostic factor in patients with cutaneous pleomorphic sarcoma. Female patients had a significantly better survival than male patients. A controlled multivariable analysis demonstrated that men had a higher rate of death (hazard ratio 0.74, 95% confidence interval 0.65-0.85; $P < .001$).

Survival

Demographics. In total, 150 individuals died from CPS, resulting in a CPS-specific mortality rate of 6.19 persons/year. The 5-year absolute survival rate was 61.9%. Women experienced better disease-specific survival (DSS) than men (hazard ratio [HR] 0.74; 95% CI 0.65-0.85; $P < .001$) (Fig 1, Table II). White persons had worse DSS than black persons (HR 0.49, 95% CI 0.33-0.75; $P = .001$) and others (American Indian and Alaska Native, Asian and Pacific Islander, HR 0.46, 95% CI 0.29-0.73; $P = .001$) (Fig 2, Table II). After age 40 years, as age increased, DSS worsened: 40-59 years (HR 27.29, 95% CI 3.78-197.20; $P = .001$), 60-79 years (HR 76.86, 95% CI 10.66-554.06; $P < .001$), and ≥80 years (HR 212.92, 95% CI 29.49-1537.17; $P < .001$) (Table II).

Tumor characteristics. Grade III and IV CPS tumors were associated with worse DSS than grade I tumors. Patients with anaplastic or undifferentiated (grade IV) tumors had a 227% higher chance of death per additional year lived (HR 2.27, 95% CI 1.30-3.97; $P = .004$) (Table II). Survival was worse in patients with grade IV tumors than those with poorly differentiated (grade III) tumors (HR 1.85, 95% CI 1.08-3.15; $P = .024$). The difference in survival of persons with moderately differentiated (grade II) tumors was not significantly different from those with grade I tumors (HR 1.17, 95% CI 0.69-2; $P = .564$).

Patients with tumors on the head and neck had worse DSS than those with tumors on the trunk (HR 0.62, 95% CI 0.50-0.78; $P < .001$) and extremities (HR 0.61, 95% CI 0.52-0.71; $P < .001$) (Fig 3, Table II). Patients with tumors of >15-mm diameter had a higher rate of death (HR 1.31, 95% CI 1.09-1.56; $P = .004$) (Table II). Patients with localized disease had the greatest DSS, followed by those with regional disease (HR 1.23, 95% CI 1.06-1.43; $P = .005$) and distant disease (HR 7.49, 95% CI 5.24-10.70; $P < .001$) (Table II).

Treatment. Patients undergoing a definitive surgical treatment, such as nonwide excisions (HR 0.81, 95% CI 0.67-0.97; $P = .019$) and wide excisions (HR 0.74, 95% CI 0.61-0.91; $P = .004$), had a survival benefit compared with those who did not receive treatment (Table II).

Table II. Multivariable survival analysis of cutaneous pleomorphic sarcoma cohort

Characteristic	HR	95% Confidence limits		*P* value
		Lower	Upper	
Race				
White	Referent	—	—	—
Black	0.49	0.33	0.75	.001
Other	0.46	0.29	0.73	.001
Sex				
Male	Referent	—	—	—
Female	0.74	0.65	0.85	<.001
Age group, y				
≤19	Referent	—	—	—
20-39	3.20	0.38	26.73	.283
40-59	27.29	3.78	197.20	.001
60-79	76.86	10.66	554.06	<.001
≥80	212.92	29.49	1537.17	<.001
Primary site				
Head and neck	Referent	—	—	—
Trunk	0.62	0.50	0.78	<.001
Extremities	0.61	0.52	0.71	<.001
Tumor grade				
Well-differentiated (I)	Referent	—	—	—
Moderately differentiated (II)	1.17	0.69	2.00	.564
Poorly differentiated (III)	1.85	1.08	3.15	.024
Anaplastic (IV)	2.27	1.30	3.97	.004
Tumor size	1.01	1.00	1.01	<.001
Tumor size >15 mm				
No	Referent	—	—	—
Yes	1.31	1.09	1.56	.004
SEER historic stage				
Localized	Referent	—	—	—
Regional	1.23	1.06	1.43	.005
Distant	7.49	5.24	10.70	<.001
Treatment				
None	Referent	—	—	—
Local or incomplete	0.80	0.54	1.19	.270
Nonwide excision or NOS	0.81	0.67	0.97	.019
Wide excision or definitive	0.74	0.61	0.91	.004
Mohs	0.79	0.58	1.06	.116
Radiation				
No	Referent	—	—	—
Yes	1.13	0.94	1.35	.201
Year of diagnosis	1.02	1.01	1.02	<.001

NOS, Not otherwise specified (by SEER registrar); *SEER*, Surveillance, Epidemiology, and End Results.

Patients undergoing local destruction as treatment (HR 0.80, 95% CI 0.54-1.19; $P = .270$) did not have a survival benefit over those receiving no treatment. Patients undergoing MMS (HR 0.79, 95% CI 0.58-1.06; $P = .116$) also did not have a survival benefit compared with those receiving no treatment. Radiation of any type (HR 1.13, 95% CI 0.94-1.35; $P = .201$) yielded no overall survival benefit (Table II).

DISCUSSION

CPS is an aggressive tumor with a propensity for local recurrence and potential for metastasis. There is a limited scope of literature on the prognostic factors for CPS. Our study encompasses a comprehensive multivariable survival analysis for different prognostic factors of patients with CPS by using SEER registry data.

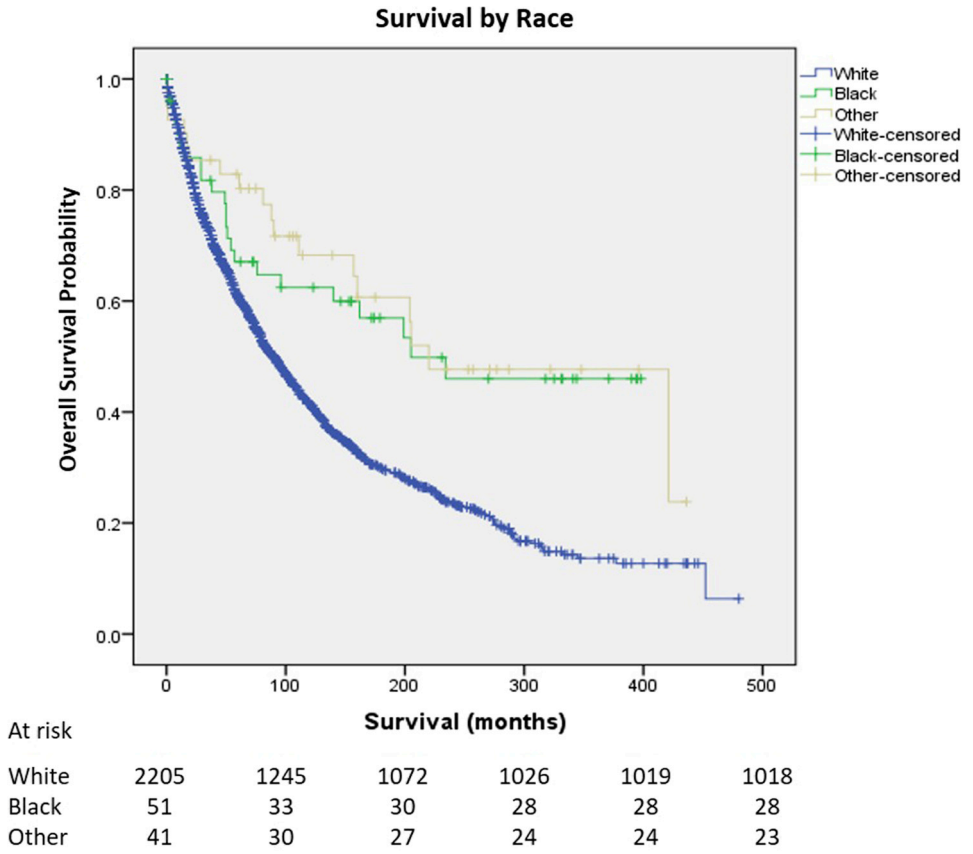

Fig 2. Kaplan-Meier curves of race as a prognostic factor in patients with cutaneous pleomorphic sarcoma. White persons had worse survival than black or other persons (American Indian or Alaska Native, Asian or Pacific Islander). A controlled multivariable analysis demonstrated that blacks and other races experienced a better disease-specific survival than white persons (hazard ratio 0.46, 95% confidence interval 0.29-0.73; P = .001).

The survival analysis identified male sex, white race, and increasing age as negative predictors of DSS. Male sex had been previously associated with worse prognosis among soft tissue sarcomas and CPS.[16] In the current work, there was no significant difference in the overall survival between black race and other race/ethnicities (American Indian and Alaska Native, Asian and Pacific Islander). To our knowledge, race has not been previously identified as a prognostic factor of CPS. Worse survival in whites occurs in contrast to improved survival of whites in other sarcoma studies.[17,18] Survival declines as age increases above the age of 39 years; no significant relationship was found below this threshold. These results complement previous reports showing increased risk for local recurrence in patients >50 years of age.[13]

Tumor location has been implicated as an important prognostic factor of CPS, with tumors presenting mostly on the trunk and extremities and less frequently on the head and neck.[19] Our data show that tumors of the head and neck were associated with worse overall survival when compared with tumors of the trunk and extremities. Patients with head and neck tumors were 1.6 times more likely to die than those with extremity or truncal tumors. Several other studies support our findings,[5,20] although Boroucki et al demonstrated increased survival of persons with CPS tumors on the head and neck compared with persons with CPS tumors on the extremities.[21] Similar to other malignancies (melanoma and nonmelanoma skin cancer), the worse survival in head and neck locations might be due to more narrow excision margins given the proximity to vital anatomic structures, a rich vascular supply, and dense underlying lymphatic network.

Patients with tumors >15 mm in diameter and those with distant disease had worse prognoses, validating previous studies.[16,19] This relationship between tumor size and survival has previously been described and holds true in other cutaneous malignancies as well. Pezzi et al[9] found patients with intermediate-grade tumors >10 cm had a worse

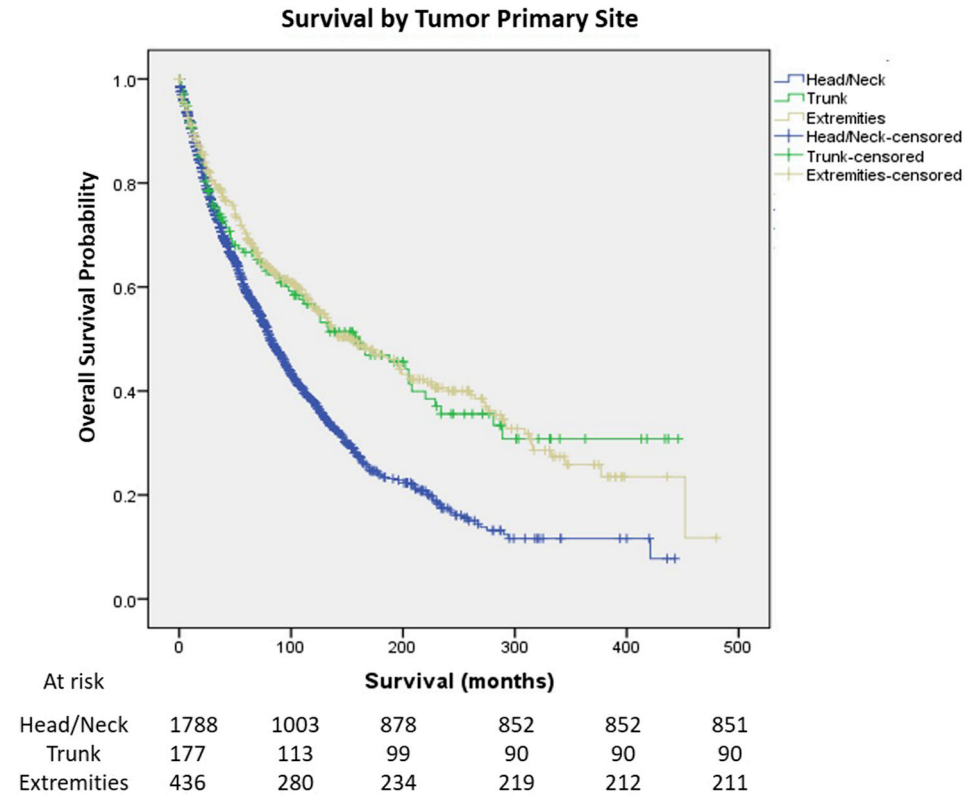

Fig 3. Kaplan-Meier curves of anatomic location as a prognostic factor in patients with cutaneous pleomorphic sarcoma. Patients with tumors of the head and neck had worse survival than those with tumors in the trunk or extremities. A controlled multivariable analysis demonstrated that patients with tumors on the trunk (hazard ratio 0.62; 95% confidence interval 0.50-0.78; $P < .001$) and extremities (hazard ratio 0.61; 95% confidence interval 0.52-0.71; $P < .001$) had the greatest disease-specific survival compared with those with tumors of the head and neck.

survival rate compared with patients with smaller tumors or tumors of equal size with better differentiation, but this study was not limited to cutaneous tumors. Although past studies have demonstrated that higher tumor grades are associated with worse survival, tumor size as a confounder is often present.[9,16] We confirm that higher tumor grade (grades III and IV) is associated with worse survival than lower tumor grades (grade I and II) and serves as an independent prognostic variable on multivariate analysis.

Distant metastasis in soft tissue sarcomas is a significant cause of death, though data on CPS explicitly is limited.[9] Distant disease had a worse prognosis than localized or regional disease in our series. Patients who received nonwide and wide excisions had a survival benefit over patients who did not receive treatment. Evidence-based margin recommendations for CPS do not exist. Henderson et al[11] reported local recurrence rates of 25%-75% and attributed the recurrence to insufficient primary tumor clearance. This is not surprising, given the infiltrative nature and frequently subclinical growth pattern. Half of patients might have positive margins after the initial tumor resection.[22] Indeed, Sabesan et al[5] suggested that the initial operation of soft tissue sarcoma, including CPS, be as radical as possible to lower recurrence rates. Local recurrence was nevertheless noted in 66% of wide (>3 cm) and 85% of marginal (<3 cm) head and neck resections. Local recurrence was noted in 71% of wide and 75% of marginal trunk and extremity CPS resections.[5] Shinozaki et al[23] found similar recurrence rates for marginal resections (72%) but notes only a 17% recurrence for wide resection margins (not further specified). In an evaluation of soft tissue head and neck sarcoma, 72% of patients with negative margins showed local control whereas only 34% of patients with borderline or positive margins had local disease control.[24]

The lack of a survival benefit with MMS is surprising, given the past positive reports of MMS utilization.[8,10,25] Love et al, in a review of cases treated with MMS, reported an 82% clearance rate in 28 cases followed for 2.4 years.[26] A single-center study of CPS of the head and neck showed that patients who received MMS did not have lower recurrence rates than those treated with wide local excision or wide local excision plus radiation therapy.[27] Intuitively, if nonwide and wide local excision provide a survival benefit, MMS should convey a similar advantage, since a comprehensive peripheral and deep margin assessment should decrease frequency of local recurrence. The lack of a survival benefit with MMS can be interpreted as a type II error—incorrectly retaining a false null hypothesis. Although this observation might have been caused by a lack of power to detect a survival benefit with MMS, it is more likely that other variables confound poor survival in MMS patients. Indeed, MMS patients were more likely to be male, older, and with head and neck tumors than the overall SEER CPS cohort. We report all 3 of these characteristics to be associated with worse survival, and this trend appears to mask any benefit obtained from MMS. By virtue of the SEER database, survival is the only available chronistic endpoint, and additional studies evaluating the effect of MMS on disease recurrence are necessary.

The use of adjuvant therapy has been controversial for soft tissue sarcomas.[8,11,16] Our analysis revealed that there was no survival advantage for patients who received radiation therapy, contradicting previous studies that showed a survival advantage when CPS and other soft tissue sarcomas received radiation therapy.[28,29] However, other papers suggest that radiation therapy could be used when clear surgical margins cannot be obtained, making it a decision on the basis of individual scenarios.[11,19,30] In the absence of strong evidence highlighting the benefit of adjuvant radiation, this should be determined on a case by case basis, given the potential morbidity and risk for radiation-induced angiosarcoma 6-10 years after treatment.[31]

Limitations

Our patient population is limited to the SEER database and is therefore not reflective of all CPS patients and provides limited case-specific detail. However, this registry provides one of the largest cohorts of CPS patients to be studied and allows for a comprehensive evaluation of prognostic factors. Our results might be limited by the reclassification of CPS, considering it was first described in 1964. Our study did not analyze tumor depth, which has been associated with a higher risk for metastasis and a worse overall prognosis.[10,19] We also did not address the impact of local recurrence, which can be a significant source of morbidity. SEER data is logged in the immediate diagnostic and treatment period and does not track information on recurrences, restaging, or additional nonmortality events over time.

Conclusion

This study represents a retrospective analysis of prognostic factors and characteristics of CPS. Factors of prognostic significance that appear to influence overall survival in CPS include age at diagnosis, sex, race, and tumor size, grade, and location. It is noteworthy that while the SEER database might not be sufficient to draw conclusions regarding appropriate margin selection, surgical tumor extirpation provides a survival benefit over no treatment, whereas primary or adjuvant radiation does not provide a survival benefit.

REFERENCES

1. Nishio J, Iwasaki H, Nabeshima K, Ishiguro M, Isayama T, Naito M. Establishment of a new human pleomorphic malignant fibrous histiocytoma cell line, FU-MFH-2: molecular cytogenetic characterization by multicolor fluorescence in situ hybridization and comparative genomic hybridization. *J Exp Clin Cancer Res*. 2010;29(1):153.
2. O'Brien JE, Stout AP. Malignant fibrous xanthomas. *Cancer*. 1964;17(11):1445-1456.
3. Weiss SW, Enzinger FM. Malignant fibrous histiocytoma. An analysis of 200 cases. *Cancer*. 1978;41(6):2250-2266.
4. Ozzello L, Stout AP, Murray MR. Cultural characteristics of malignant histiocytomas and fibrous xanthomas. *Cancer*. 1963;16(3):331-344.
5. Sabesan T, Xuexi W, Yongfa Q, Pingzhang T, Ilankovan V. Malignant fibrous histiocytoma: outcome of tumours in the head and neck compared with those in the trunk and extremities. *Br J Oral Maxillofac Surg*. 2006;44(3):209-212.
6. Barnes L, Kanbour A. Malignant fibrous histiocytoma of the head and neck. *Arch Otolaryngol Head Neck Surg*. 1988;144(10):1149-1156.
7. Sakamoto A, Oda Y, Itakura E, et al. Immunoexpression of ultraviolet photoproducts and p53 mutation analysis in atypical fibroxanthoma and superficial malignant fibrous histiocytoma. *Mod Pathol*. 2001;14(6):581.
8. Soleymani T, Tyler Hollmig S. Conception and Management of a poorly understood spectrum of dermatologic neoplasms: atypical fibroxanthoma, pleomorphic dermal sarcoma, and undifferentiated pleomorphic sarcoma. *Curr Treat Options Oncol*. 2017;18(8).
9. Pezzi CM, Rawlings MS, Esgro JJ, Pollock RE, Romsdahl MM. Prognostic factors in 227 patients with malignant fibrous histiocytoma. *Cancer*. 1992;69:2098-2103.
10. Brown MD, Swanson NA. Treatment of malignant fibrous histiocytoma and atypical fibrous xanthomas with micrographic surgery. *J Dermatol Surg Oncol*. 1989;15:1287-1292.
11. Henderson MT, Hollmig ST. Malignant fibrous histiocytoma: changing perceptions and management challenges. *J Am Acad Dermatol*. 2012;67(6):1335-1341.

12. Wang J, Zhong W, Xu Y, Feng L, Li Y, Dong B. A primary malignant fibrous histiocytoma of the scalp and intracranial tumor bleeding: a case report. *J Med Case Rep*. 2014;8(1):1-4.
13. Salo JC, Lewis JJ, Woodruff JM, Leung DH, Brennan MF. Malignant fibrous histiocytoma of the extremity. *Cancer*. 1999; 85(8):1765-1772.
14. Seiffert J, ed. *SEER Program Comparative Staging Guide for Cancer, Version 1.1*. Bethesda, MD: National Cancer Institute; 1993. NIH pub 93-3640.
15. Young Jr JL, Roffers SD, Ries LAG, Fritz AG, Hurlbut AA, eds. *SEER Summary Staging Manual-2000: Codes and Coding Instructions*. Bethesda, MD: National Cancer Institute, NIH Pub. No. 01-4969; 2001.
16. Peng KA, Grogan T, Wang MB. Head and neck sarcomas: analysis of the SEER database. *Otolaryngol Head Neck Surg*. 2014;15(4):627-633.
17. Alamanda VK, Song Y, Schwartz HS, Holt GE. Racial disparities in extremity soft-tissue sarcoma outcomes: a nationwide analysis. *Am J Clin Oncol*. 2015;38(6):595-599.
18. Lazarides AL, Visgauss JD, Nussbaum DP, et al. Race is an independent predictor of survival in patients with soft tissue sarcoma of the extremities. *BMC Cancer*. 2018;18(1):488.
19. Peiper M, Zurakowski D, Wolfram TK, Izbicki J. Malignant fibrous histiocytoma of the extremities and trunk: an institutional review. *Surgery*. 2004;135(1):59-66.
20. Clark DW, Moore BA, Patel SR, Guadagnolo BA, Roberts DB, Sturgis EM. Malignant fibrous histiocytoma of the head and neck region. *J Sci Spec Head Neck*. 2011;33(3):303-308.
21. Borucki RB, Neskey DM, Lentsch EJ. Malignant fibrous histiocytoma: database review suggests a favorable prognosis in the head and neck. *Laryngoscope*. 2017;128:3-6.
22. Fanburg-Smith JC, Spiro IJ, Katapuram SV, Mankin HJ, Rosenberg AE. Infiltrative subcutaneous malignant fibrous histiocytoma: a comparative study with deep malignant fibrous histiocytoma and an observation of biologic behavior. *Ann Diagn Pathol*. 1999;3(1):1-10.
23. Shinozaki T, Kato K, Watanabe H, Yanagawa T, Ahmed AR, Takagishi K. Discriminant analysis of prognostic factors for malignant fibrous histiocytoma in soft tissue. *J Orthop Sci*. 2001;6(4):339-342.
24. Barker JJ, Paulino A, Feeny S, McCulloch T, Hoffman H. Locoregional treatment for adult soft tissue sarcomas of the head and neck: an institutional review. *Cancer*. 2003;9(1):49-57.
25. Huether MJ, Zitelli JA, Brodland DG. Mohs micrographic surgery for the treatment of spindle cell tumors of the skin. *J Am Acad Dermatol*. 2001;44(4):656-659.
26. Love WE, Schmitt AR, Bordeaux JS. Management of unusual cutaneous malignancies: atypical fibroxanthoma, malignant fibrous histiocytoma, sebaceous carcinoma, extramammary paget disease. *Dermatol Clin*. 2011;29(2):201-216.
27. Hollmig ST, Kirkland EB, Henderson MT, Tang JY, Gladstone HB. The evolving conception and management challenges of malignant fibrous histiocytoma. *Dermatol Surg*. 2012;38(12):1922-1929.
28. Peiper M, Zurakowski D, Schwarz R, Zornig C. Survival in patients with primary soft-tissue sarcomas treated within 6 years. *J Cancer Res Clin Oncol*. 1998;124:199-206.
29. Rosenberg SA, Tepper J, Glatstein E, et al. Prospective randomized evaluation of adjuvant chemotherapy in adults with soft tissue sarcomas of the extremities. *Cancer*. 1983; 52(3):424-434.
30. Hardison SA, Davis PL 3rd, Browne JD. Malignant fibrous histiocytoma of the head and neck: a case series. *Am J Otolaryngol*. 2013;34(1):10-15.
31. Anzalone CL, Cohen PR, Diwan AH, Prieto VG. Radiation-induced angiosarcoma. *Dermatol Online J*. 2013;19(1):2.