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Survival Analysis of Patients with Osseous Malignant Vascular Tumors: Results of the Surveillance, Epidemiology, and End Results (SEER) Database from 1973 to 2015

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Background: Osseous malignant vascular tumors (OMVTs) are rare lesions. Moreover, the prognostic determinants of OMVTs have not been reported. This study aimed to present epidemiological data and analyze the prognostic factors of survival in OMVT patients.

Material/Methods: OMVT patients who were diagnosed between 1973 and 2015 were screened using the Surveillance, Epidemiology, and End Results (SEER) program database, with special attention paid to osseous hemangiosarcoma (OAS) and osseous hemangioendothelioma (OHE). We assessed the prognostic values of cancer-specific survival (CSS) and overall survival (OS) rates with a Cox proportional hazards regression model and univariate and multivariate analyses. OS and CSS curves were obtained using the Kaplan-Meier method.

Results: A total of 202 cases were selected from the SEER database. The specific histopathological diagnoses were osseous hemangiosarcoma (n=127) and osseous hemangioendothelioma (n=75). Among OMVT patients, histology was an important factor in determining survival. Using multivariate analysis, old age, distant tumor stage, surgery, and low tumor grade were predictors of OS for OAS patients. Old age, surgery, and low tumor grade were predictors of CSS. Using multivariate analysis, old age and surgery were predictors of OS and CSS for OHE patients.

Conclusions: This study is the largest population-based study to show the demographic characteristics and analyze the prognosis of OMVT patients. Independent predictors of OS for patients with AS included old age, distant tumor stage, low tumor grade, and surgery. Old age, surgery, and low tumor grade were also predictors of CSS for patients with OAS. Independent predictors of CSS and OS for patients with OHE included old age and surgery.

MeSH Keywords: Bone and Bones • Hemangioendothelioma • Hemangiosarcoma • Prognosis

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Background

Few cases of osseous malignant vascular tumors (OMVTs) are reported. Therefore, the prognostic factors of survival are not well established. OMVTs include osseous hemangiosarcoma (OAS) and osseous hemangioendotheliomas (OHEs).

Hemangiosarcoma (AS) accounts for one-third of malignant vascular tumors (MVT) and is commonly present in patients 50–70 years of age [1]. Osseous hemangiosarcoma is rare, as low as only 1% of all primary bone sarcomas, and is associated with a poor prognosis [2]. The most common locations of osseous AS are the long and short tubular bones, followed by the pelvis and trunk [1]. Histologically, OAS is composed of vascular channels lined by endothelial cells with enlarged prominent nucleoli, nuclei, and increased mitoses. Inflammatory cells may also be present [2,3]. A previous study of 821 angiosarcoma patients showed that age >70 years, black race, grade 3 tumor, and tumor size >3 cm were associated with the worst 5-year OS rates in a multivariable analysis model [4].

Primary hemangioendotheliomas (HE) of bones are less common and account for less than 1% of malignant bone tumors [5], affecting patients 40–50 years of age. It can occur in almost any location but is mainly reported in soft tissues [5]. The most common locations are long bones of the lower extremities [6–9]. OHE was previously known as angiolymphoid hyperplasia with eosinophilia or histiocytoid hemangioma, which is a rare vascular tumor with a biological behavior between hemangiosarcoma and hemangioma [10]. Few studies have reported on the risk factors of hemangioendotheliomas (HEs) in bones. A related study showed worse survival in patients with hemorrhagic symptoms, including hemoptysis and pleural effusion, in pulmonary epithelioid hemangioendothelioma patients [11].

OMVTs pose a challenge in achieving local disease control and improving patient survival. Few studies have reported on the significant morbidity and complications associated with surgical resection. Therefore, clinicians are still wondering whether a uniform treatment strategy should be applied to all patients regardless of histopathology or whether each disease should be treated as a separate entity. Furthermore, the prognostic factors that affect survival remain unclear.

Here, an epidemiologic analysis of OMVTs is presented using the Surveillance, Epidemiology, and End Results (SEER) database, the U.S. National Cancer Institute's surveillance program. No previous study has performed an in-depth analysis of OMVT patients using this database. A total of 171 cases of OMVTs were analyzed to represent the largest sample size of patients with OMVTs to date. We analyzed the clinicopathologic and demographic features of this rare tumor and its survival outcomes.

Material and Methods

We obtained frequency and survival data from the SEER dataset for diagnoses made between 1973 and 2015. OMVT cases were screened with the morphological codes for hemangiosarcoma (9120/1) and hemangioendothelioma (9130/1). OMVT cases were restricted to the long bones of the upper limb, scapula, and associated joints (C40.0) and the long bones of the lower limb and associated joints (C40.2); the short bones, namely, the short bones of the upper limb, scapula, and associated joints (C40.1) and the short bones of the lower limb and associated joints (C40.3); the overlap of bones, joints, and articular cartilage of the limbs (C40.8); the bones of the limbs (C40.9); bones of the skull and face and associated joints (C41.0); the mandible (C41.1); the vertebral column (C41.2); the ribs, sternum, clavicle and associated joints (C41.3); the pelvic bones, sacrum, coccyx, and associated joints (C41.4); the overlap of bones, joints, and articular cartilage (C41.8); and bone (C41.9). Frequency data were stratified by sex, age, race, tumor size, grade, SEER extent of disease, and treatment strategy. SEER extent of disease is classified into localized, regional, and distant disease as reported previously [12,13]. We calculated five-year survival rates with Kaplan-Meier analysis, and we calculated the cancer-specific survival rates and overall survival. We extracted SEER data with SEER*Stat 8.1.5 (National Cancer Institute, Bethesda, MD) software. Survival data were imported into Statistical Product and Service Solutions (SPSS) 24th edition to yield Kaplan-Meier curves and CSS rates. Probability values (p values) <0.05 were considered statistically significant for all tests.

Results

Patient demographics

The demographic characteristics of the 202 patients with OMVTs identified in the SEER database are displayed in Table 1. The specific histopathological diagnoses were hemangiosarcoma (n=127) and hemangioendothelioma (n=75).

Osseous hemangiosarcoma (OAS) patients

Patients with OAS had a mode age of >60 years (56.7%). Most patients with OAS were male (70.1%) and white (85.8%). Most (78%) patients were diagnosed after 1 Jan 2000. A total of 35.4% patients had high-grade tumors, 16.5% had low-grade tumors, and 48% had a histologically unknown tumor grade. Twenty-six percent of cases were at a localized stage, 20.5% were at a regional stage, 41.7% were at a distant tumor stage, and 11.8% of cases were at an unknown stage. More than half of the lesions were located in the limbs (55.1%). Most tumor sequences were the first (81.9%). A total of 23.6% of the cases had a tumor size >5 cm, 16.5% had a tumor size ≤5 cm, and

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Table 1. Clinical characteristics of patients with osseous malignant vascular tumors (OMVT).

Variables		Number (%)					
		Hemangiosarcoma (N=127)		Hemangioendothelioma (N=75)		Total	
	Mean (years)	62		50		57	
Age	≤40	16	(12.6%)	27	(36%)	43	(21.3%)
	41–60	39	(30.7%)	22	(29.3%)	61	(30.2%)
	>60	72	(56.7%)	26	(34.7%)	98	(48.5%)
Sex	Female	38	(29.9%)	37	(49.3%)	75	(37.1%)
	Male	89	(70.1%)	38	(50.7%)	127	(62.9%)
Race recode (W, B, Other)	Black	14	(11%)	7	(9.3%)	21	(10.4%)
	Other	4	(3.1%)	7	(9.3%)	11	(5.4%)
	White	109	(85.8%)	61	(81.3%)	170	(84.2%)
Grade	Low	21	(16.5%)	17	(22.7%)	38	(18.8%)
	High	45	(35.4%)	8	(10.7%)	53	(26.2%)
	Unknown	61	(48%)	50	(66.7%)	111	(55%)
Location	Limb	70	(55.1%)	41	(54.7%)	111	(55%)
	Unknown	6	(4.7%)	9	(12%)	15	(7.4%)
	Axial bone	51	(40.2%)	25	(33.3%)	76	(37.6%)
Tumor sequence	First	104	(81.9%)	63	(84%)	167	(82.7%)
	≥Second	23	(18.1%)	12	(16%)	35	(17.3%)
Surgery	No	49	(38.6%)	30	(40%)	79	(39.1%)
	Yes	70	(55.1%)	42	(56%)	112	(55.4%)
	Unknown	8	(6.3%)	3	(4%)	11	(5.4%)
Radiotherapy	No/Unknown	73	(57.5%)	42	(56%)	115	(56.9%)
	Yes	54	(42.5%)	33	(44%)	87	(43.1%)
Chemotherapy	No/Unknown	96	(75.6%)	59	(78.7%)	155	(76.7%)
	Yes	31	(24.4%)	16	(21.3%)	47	(23.3%)
Stage	Localized	33	(26%)	27	(36%)	60	(29.7%)
	Regional	26	(20.5%)	14	(18.7%)	40	(19.8%)
	Distant	53	(41.7%)	27	(36%)	80	(39.6%)
	Unknown	15	(11.8%)	7	(9.3%)	22	(10.9%)
Tumor size	≤5 cm	21	(16.5%)	18	(24%)	39	(19.3%)
	>5 cm	30	(23.6%)	9	(12%)	39	(19.3%)
	Unknown	76	(59.8%)	48	(64%)	124	(61.4%)
Decades	<2000 s	28	(22%)	23	(30.7%)	51	(25.2%)
	≥2000s	99	(78%)	52	(69.3%)	151	(74.8%)
1y-os	0	55	(43.3%)	58	(77.3%)	113	(55.9%)
5y-os	0	34	(26.8%)	45	(60%)	79	(39.1%)
1y-css	0	79	(62.2%)	63	(84%)	142	(70.3%)
5y-css	0	65	(51.2%)	54	(72%)	119	(58.9%)

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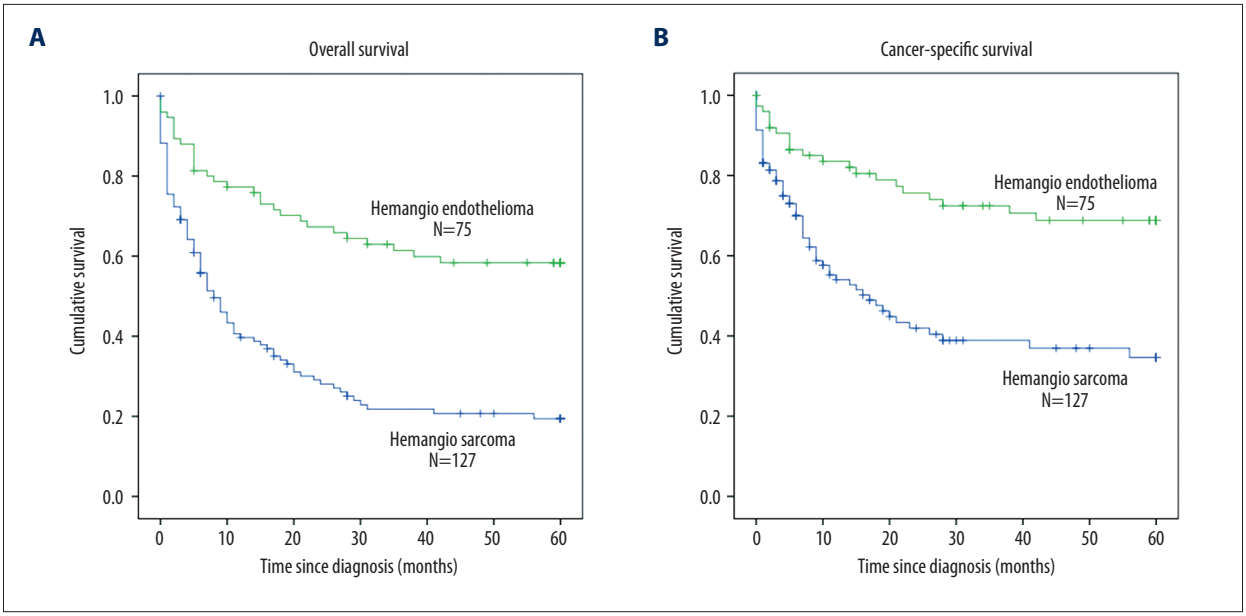

Figure 1. Overall survival (**A**) and cancer-specific survival (CSS) (**B**) estimates for 202 patients with osseous malignant vascular tumors (OMVTs) using data from the Surveillance, Epidemiology, and End Results (SEER) program database, 1973–2015.

59.8% had an unknown tumor size. After diagnosis, 55.1% of patients underwent surgical treatment, 24.4% of the patients underwent chemotherapy, and 42.5% of the patients underwent radiotherapy. The OS rates of the AS patients 1 and 5 years after diagnosis were 43.3% and 26.8%, respectively. The CSS rates 1 and 5 years after diagnosis were 62.2% and 51.5%, respectively (Table 1, Figure 1).

Osseous hemangioendothelioma (OHE) patients

Patients with OHEs had a mode age of ≤40 years (36%). Most patients with OHE were male (50.7%) and white (81.3%). Most (69.3%) patients were diagnosed after 1 Jan 2000. A total of 10.7% of patients had high-grade tumors, 22.7% had low-grade tumors, and 66.7% had a histologically unknown tumor grade. Thirty-six percent of cases were at a localized stage, 18.7% were at a regional stage, 36% were at a distant tumor stage, and 9.3% cases were at an unknown stage. More than half of the lesions were located in the limbs (54.7%). Most tumor sequences were the first (84%). Twelve percent of cases had a tumor size >5 cm, 24% had a tumor size ≤5 cm, and 64% had an unknown tumor size. Fifty-six percent of patients accepted surgical treatment, 21.3% of the patients underwent chemotherapy, and 44% of the patients underwent radiotherapy after diagnosis. The OS rates of OHE patients 1 and 5 years after diagnosis were 77.3% and 60%, respectively. The CSS rates 1 and 5 years after diagnosis were 84% and 72%, respectively (Table 1, Figure 1).

Univariate and multivariate analyses of factors influencing cancer-specific survival (CSS) and overall survival (OS) rates are shown in Tables 2 and 3.

Osseous hemangiosarcoma (OAS) patients

For both the CSS and OS analysis, race, sex, decade of diagnosis, radiotherapy, and chemotherapy showed no significant differences in survival (p>0.05; Tables 2 and 3). Univariate survival analysis demonstrated that older age was associated with significantly worse OS rates (≤40 years *vs.* >60 years, p<0.001; 41–60 years *vs.* >60 years, p=0.001; Table 2; Figure 2A) and CSS rates (≤40 years *vs.* >60 years, p=0.019; Table 2; Figure 3A) for OAS. Tumor grade was associated with significantly worse OS (p<0.001; Table 2; Figure 2D) and CSS (p<0.001; Table 2; Figure 3C). Surgery was significantly associated with better OS (p<0.001; Table 2; Figure 2B) and CSS (p<0.001; Table 2; Figure 3B). Tumor stage was associated with significantly worse OS (Localized *vs.* Distant, p=0.008; Regional *vs.* Distant, p=0.006; Table 2; Figure 2C), and CSS (Localized *vs.* Distant, p=0.019; Regional *vs.* Distant, p=0.033; Table 2; Figure 3D). Tumor size was significantly associated with a worse CSS rate (≤5 cm *vs.* >5 cm, p=0.016; Table 2; Figure 2E) but not with OS (≤5 cm *vs.* >5 cm, p=0.059; Table 2). Tumor sequence was significantly associated with a worse CSS rate (p<0.001; Table 2) but not with OS (p=0.458; Table 2).

In the multivariate analysis of OAS patients (Table 3), old age (>60 years, HR=6.439; 95% CI, 2.435–17.028; p<0.001), distant tumor stage (HR=2.007, 95% CI, 1.132–3.558, p=0.017), low tumor grade (HR=4.4; 95% CI, 1.727–11.206; p=0.002), and surgery (HR=0.484; 95% CI, 0.218–0.835; p=0.009) were predictors of OS. Old age (>60 years, HR=4.926; 95% CI, 1.608–15.089; p=0.005), low tumor grade (HR=14.654; 95% CI, 1.901–112.943; p=0.01), and surgery (HR=0.335; 95% CI, 0.169–0.665; p=0.002) were predictors of CSS.

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Table 2. Univariate analyses for OS and CSS for patients with osseous hemangiosarcoma and hemangioendothelioma identified in the SEER Program database from 1973 to 2015.

	Hemangiosarcoma(N=127)		Hemangioendothelioma(N=75)	
	OS	CSS	OS	CSS
Age				
≤40 *vs.* 41–60	0.055	0.066	0.154	0.138
≤40 *vs.* >60	<0.001*	0.019*	<0.001*	0.001*
41–60 *vs.* >60	0.001*	0.24	0.007*	0.099
Sex				
Female *vs.* Male	0.349	0.342	0.61	0.927
Race recode				
Black *vs.* White	0.846	0.09	0.848	0.953
Black *vs.* other	0.247	0.189	0.464	0.458
White *vs.* other	0.196	0.059	0.443	0.361
Grade				
High *vs.* low	<0.001*	<0.001*	0.062	0.963
High *vs.* unknown	<0.001*	<0.001*	0.043*	0.158
Low *vs.* unknown	0.547	0.423	0.688	0.375
Location				
Limb *vs.* axial	0.902	0.9	0.102	0.571
Limb *vs.* unknown	0.224	0.022	0.002	0.001
Axial *vs.* unknown	0.242	0.041	0.081	<0.001
Tumor sequence				
First *vs.* ≥second	0.458	<0.001	0.494	0.049
Surgery				
Yes *vs.* no	<0.001*	<0.001*	<0.001*	0.001*
Yes *vs.* unknown	0.886	0.905	0.001*	<0.001*
No *vs.* unknown	0.137	0.139	0.417	0.164
Radiotherapy				
Yes *vs.* no/unknown	0.82	0.803	0.162	0.734
Chemotherapy				
Yes *vs.* no/unknown	0.667	0.741	0.576	0.295
Tumor size				
≤5 cm *vs.* >5 cm	0.059	0.016*	0.986	0.911
>5 cm *vs.* unknown	0.157	0.05	0.142	0.134
≤5 cm *vs.* unknown	0.675	0.692	0.32	0.259
Decade				
<2000s *vs.* ≥2000s	0.114	0.288	0.733	0.451

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Table 2 continued. Univariate analyses for OS and CSS for patients with osseous hemangiosarcoma and hemangioendothelioma identified in the SEER Program database from 1973 to 2015.

	Hemangiosarcoma(N=127)		Hemangioendothelioma(N=75)	
	OS	CSS	OS	CSS
Stage				
Localized *vs.* regional	0.776	0.851	0.607	0.156
Localized *vs.* distant	0.008*	0.019*	0.001*	0.006*
Localized *vs.* unknown	0.371	0.857	0.015	0.003*
Regional *vs.* distant	0.006*	0.033*	0.005*	0.004*
Regional *vs.* unknown	0.292	0.694	0.019*	0.001*
Unknown *vs.* distant	0.256	0.059	0.763	0.686

Table 3. Multivariate analyses for OS and CSS for patients with osseous hemangiosarcoma and hemangioendothelioma identified in the SEER Program database from 1973 to 2015.

		Hemangiosarcoma				Hemangioendothelioma			
		OS		CSS		OS		CSS	
		p	HR (95% CI)	p	HR (95% CI)	p	HR (95% CI)	p	HR (95% CI)
Grade	Low	/	1	/	1	/	1	/	1
	High	0.002*	4.4 (1.727, 11.206)	0.01*	14.654 (1.901, 112.943)	0.306	2.411 (0.448, 12.98)	0.93	0.897 (0.078, 10.333)
	Unknown	0.002*	4.145 (1.658, 10.365)	0.013*	13.086 (1.715, 99.882)	0.586	1.481 (0.36, 6.092)	0.629	1.481 (0.3, 7.302)
Tumor size	≤5 cm	/	1	/	1	/	1	/	1
	>5 cm	0.287	1.508 (0.708, 3.215)	0.072	2.631 (0.918, 7.535)	0.624	1.618 (0.236, 11.085)	0.429	2.88 (0.21, 39.562)
	Unknown	0.582	1.198 (0.63, 2.279)	0.134	2.018 (0.805, 5.057)	0.705	0.811 (0.275, 2.397)	0.92	0.932 (0.236, 3.686)
Surgery	No	/	1	/	1	/	1	/	1
	Yes	0.009*	0.484 (0.281, 0.835)	0.002*	0.335 (0.169, 0.665)	0.006*	0.236 (0.085, 0.655)	0.016*	0.204 (0.056, 0.741)
	Unknown	0.964	1.021 (0.407, 2.565)	0.733	0.821 (0.265, 2.542)	0.515	1.54 (0.42, 5.648)	0.346	1.918 (0.495, 7.437)
Stage	Localized	/	1	/	1	/	1	/	1
	Regional	0.882	1.053 (0.533, 2.081)	0.834	1.092 (0.481, 2.48)	0.139	0.244 (0.038, 1.578)	0.959	N/A
	Distant	0.017*	2.007 (1.132, 3.558)	0.133	1.749 (0.843, 3.63)	0.153	2.254 (0.739, 6.879)	0.121	2.893 (0.757, 11.058)
	Unknown	0.383	0.695 (0.307, 1.574)	0.091	0.37 (0.117, 1.17)	0.645	1.403 (0.332, 5.936)	0.337	2.222 (0.436, 11.328)
Age	≤40	/	1	/	1	/	1	/	1
	41–60	0.068	2.491 (0.935, 6.641)	0.106	2.48 (0.826, 7.45)	0.016*	5.121 (1.352, 19.401)	0.011*	7.631 (1.599, 36.411)
	>60	<0.001*	6.439 (2.435, 17.028)	0.005*	4.926 (1.608, 15.089)	<0.001*	9.719 (2.997, 31.516)	0.002*	9.116 (2.213, 37.557)

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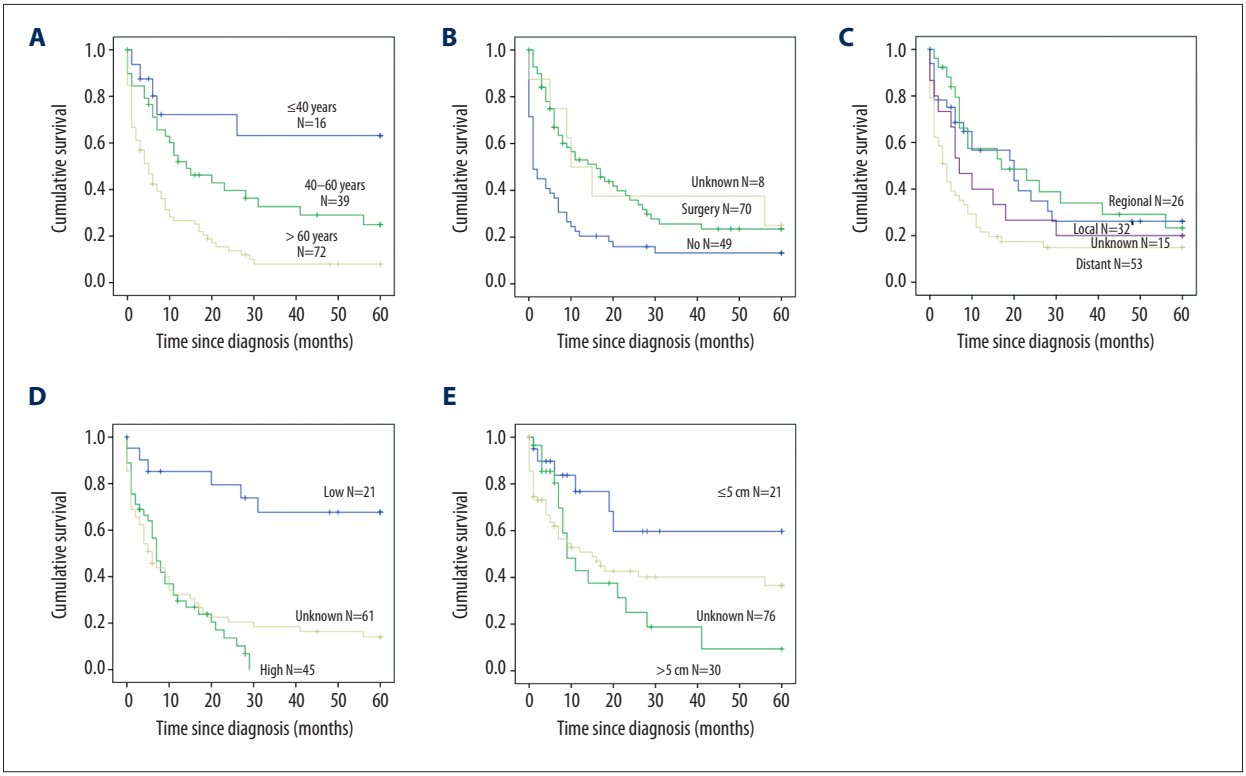

Figure 2. The Kaplan-Meier method was used to calculate the OS rate for patients with osseous hemangiosarcoma, classified by (**A**) age at diagnosis (years), (**B**) surgery or not, (**C**) tumor stage, (**D**) tumor grade, and (**E**) tumor size. OS – overall survival.

Osseous hemangioendothelioma (OHE) patients

For both CSS and OS, race, sex, decade of diagnosis, radiotherapy, chemotherapy, and tumor size showed no significant differences in survival rates (p>0.05; Table 2). Univariate survival analysis demonstrated that older age was associated with a significantly worse OS rate (≤40 years *vs.* >60 years, p<0.001; 41–60 years *vs.* >60 years, p=0.007; Table 2; Figure 4A) and CSS rate (≤40 years *vs.* >60 years, p=0.001; Table 2; Figure 5A) for OHE patients. Surgery was significantly associated with better OS (p<0.001; Table 2; Figure 4B) and CSS (p<0.001; Table 2; Figure 5B). Tumor stage was significantly associated with worse OS (Localized *vs.* Distant, p=0.001; Regional *vs.* Distant, p=0.005; Table 2; Figure 4D) and CSS (Localized *vs.* Distant, p=0.006; Regional *vs.* Distant, p=0.004; Table 2; Figure 5D). Tumor sequence was significantly associated with worse CSS (p=0.049; Table 2) but not with OS (p=0.494; Table 2). However, tumor grade was not significantly associated with OS (Figure 4C) or CSS (Figure 5C) of OHE patients.

Multivariate analysis of HE patients (Table 3) indicated that old age (>60 years, HR=9.719; 95% CI, 2.997–31.516; p<0.001; 41–60 years, HR=5.121; 95% CI, 1.352–19.401; p=0.016) and surgery (HR=0.236; 95% CI, 0.085–0.655; p=0.006) were predictors of OS. Old age (>60 years, HR=9.116; 95% CI, 2.213–37.557; p=0.001; 41–60 years, HR=7.631; 95% CI, 1.599–36.411; p=0.011) and surgery (HR=0.204; 95% CI, 0.056–0.741; p=0.016) were also predictors of CSS.

Discussion

Due to the rarity of osseous malignant vascular tumors (OMVT), there are few studies that describe the survival of these patients. To the best of our knowledge, this report is the first such study and has largest sample size of patients with OMVTs. The data were obtained from the SEER database of the U.S. National Cancer Institute, the largest registry of cancer survival and incidence. The SEER data are high quality and collected in a standard manner, leading to a low rate of errors in the SEER cancer registry. Furthermore, multivariate regression analysis was used in this study to identify independent prognostic factors of survival.

In this study, we extracted data from 202 OMVT cases from the SEER database that were diagnosed from 1973 to 2015. The 1- and 5-year OS rates of OMVTs were 55.9% and 39.1%, respectively, in this study. The 1- and 5-year CSS rates of OMVTs were 70.3% and 58.9%, respectively. We found that histology was an important factor in determining survival for patients with OMVTs. Independent predictors of OS for patients with OAS included old age, distant tumor stage, low tumor grade, and surgery. Old age, surgery, and low tumor grade were also

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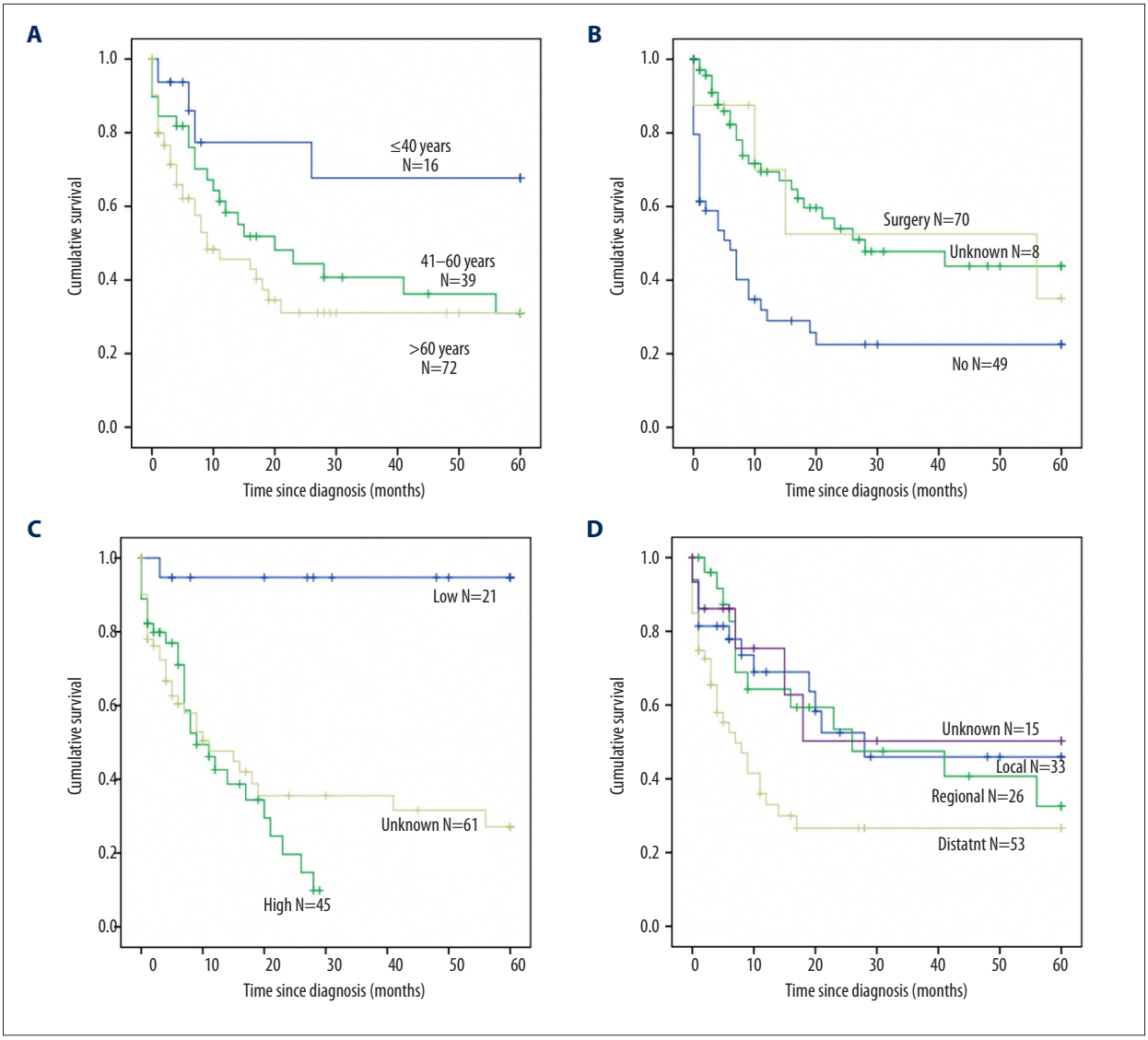

Figure 3. The Kaplan-Meier method was used to calculate the CSS rate for patients with osseous hemangiosarcoma, classified by (**A**) age at diagnosis (years), (**B**) surgery or not, (**C**) tumor grade, and (**D**) tumor stage. CSS – cancer-specific survival.

predictors of CSS for patients with OAS. The CSS and OS rate predictors for patients with OHE included old age and surgery. The results were useful for providing a basis for constructing a predictive model of OMVT patients.

A previous analysis of 60 AS patients revealed that the 5-year overall survival (OS) rate was 20% [14]. Complete surgical resection is essential for positive outcomes [15]. Unfortunately, the sample size of that cohort was still small. Our population-based study found that surgery was an independent predictor of OS (HR=0.484; 95% CI, 0.218–0.835; p=0.009) and CSS (HR=0.335; 95% CI, 0.169–0.665; p=0.002) rates for patients with AS. Old age, distant tumor stage, and low tumor grade were also prognostic factors for CSS and OS. In an analysis of cutaneous hemangiosarcoma [16], age (<50 years), tumor stage (localized), and anatomical site (trunk) were associated with favorable prognoses, which was consistent with our results. Tumor size was not a reliable factor for predicting AS because of variable growth patterns [17].

Currently, a combination of radiation and surgery is the preferred treatment for AS [18]. The median radiotherapy dose after surgery was 60 Gy (range, 60.0–70.0 Gy) [19]. Considering the surgical types, histopathologically clear surgical margins are of value and are associated with better outcomes [20], which was consistent with our study. In this study, the radiotherapy and chemotherapy dosage data were not available. Therefore, an in-depth analysis of radiotherapy and chemotherapy was not performed.

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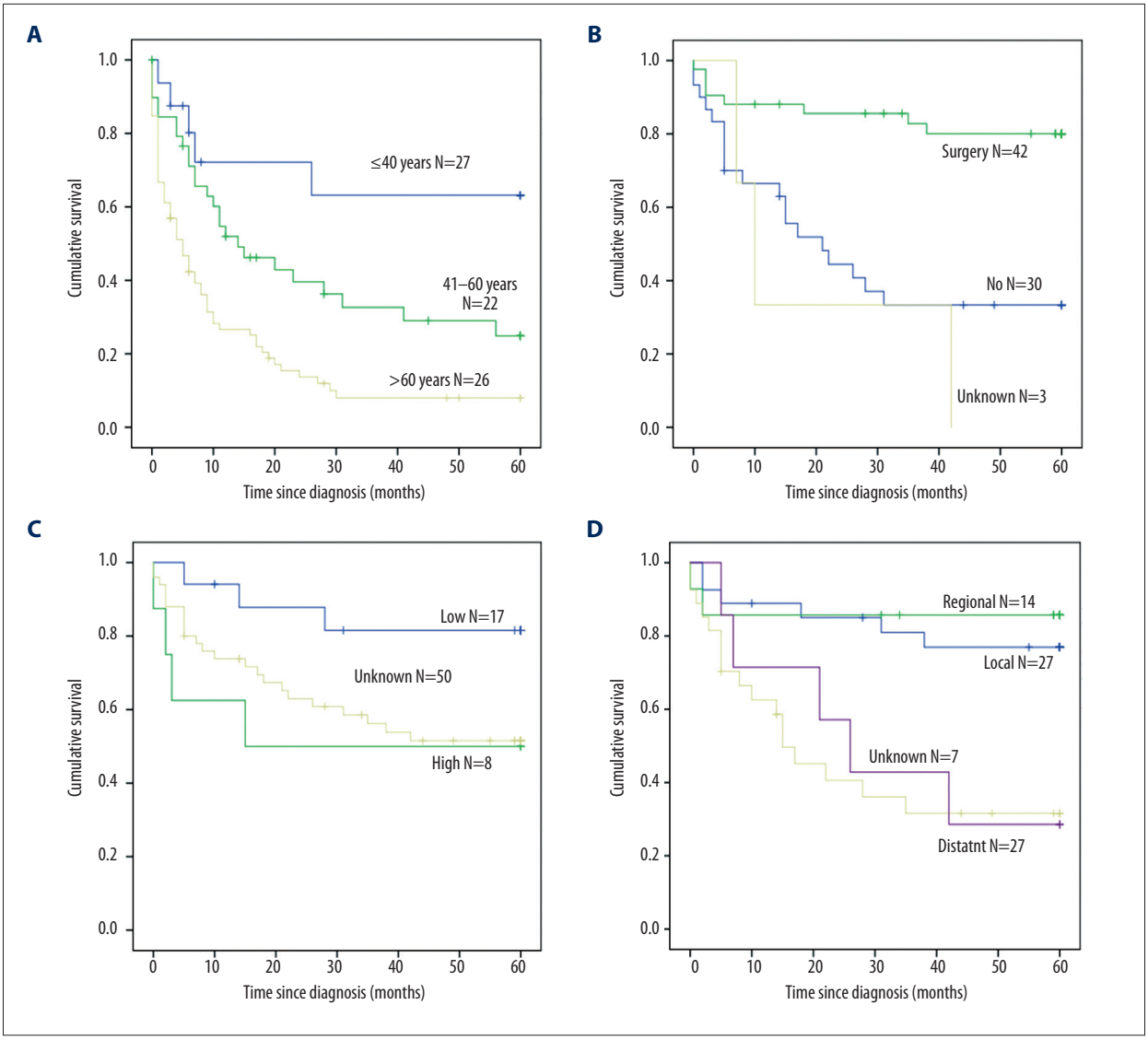

Figure 4. The Kaplan-Meier method was used to calculate the OS rate for patients with osseous hemangioendothelioma, classified by (**A**) age at diagnosis (years), (**B**) surgery or not, (**C**) tumor grade, and (**D**) tumor stage. OS – overall survival.

HE of bone is rare. It was first described by Weiss and Enzinger in 1982 and was considered to have variable outcomes depending on its histological characteristics and location [21]. Previous studies have described 6 patients with HE of bone [22–26]. The patients' prognoses were poor. Only 2 of the 6 patients survived 5 years postdiagnosis [26]. To the best of our knowledge, the present report has the largest sample size used to calculate the survival outcomes of patients with OHEs. A recent study showed that there was no sex predominance in adult patients with epithelioid hemangioendothelioma [27], which was consistent with our results. The effects of RT were related to the dose and the nonmetastatic state of the hemangioendothelioma [28]. A more detailed study was needed to analyze the effectiveness of RT on OHEs [29].

A recent study showed that histology was an important factor in determining survival for patients with MVT of the liver [30]. Patients with HE of the liver have the longest OS, whereas patients with AS of the liver have shorter survival but may still benefit from surgery. In our study, patients with OHE also showed better OS and CSS than patients with OAS. Patients with OAS and OHE all benefit from surgery, which agrees with a previous report [30].

Strengths and limitations

In this study, data collected from multiple centers provide satisfying statistical power for the study and allow for the research of rare tumors such as OMVTs. However, the study still has a few limitations. First, node status and extent of surgical types were lacking. Second, data on the radiotherapy dosage

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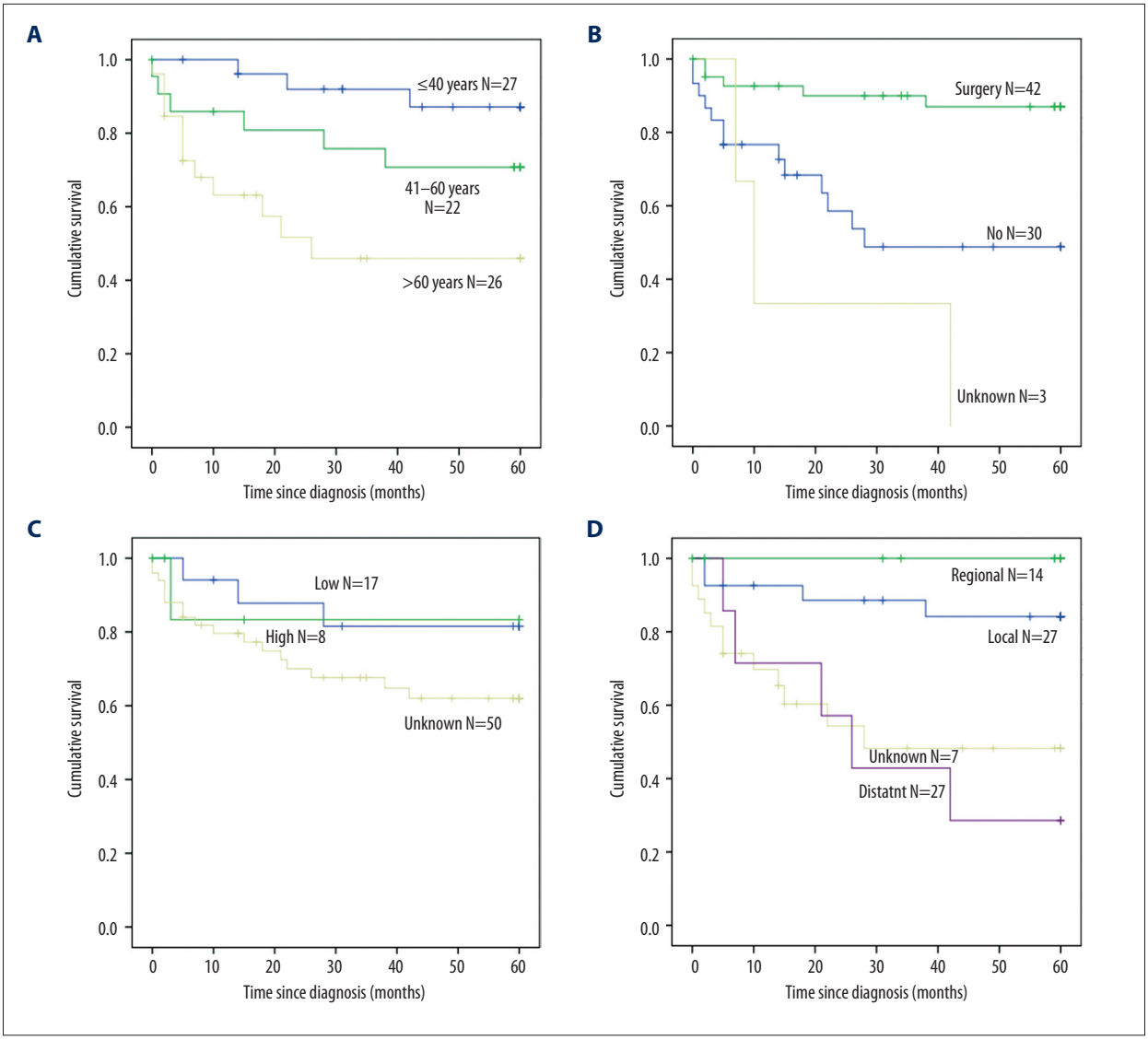

Figure 5. The Kaplan-Meier method was used to calculate the CSS rate for patients with osseous hemangioendothelioma, classified by (**A**) age at diagnosis (years), (**B**) surgery or not, (**C**) tumor grade, and (**D**) tumor stage. CSS – cancer-specific survival.

and specific regimen of chemotherapy were not available. Therefore, an in-depth analysis of radiotherapy and chemotherapy was not performed. Finally, the SEER data were qualitative or semiquantitative but not quantitative, which compromises the statistical confidence.

Conclusions

This study is the largest population-based study to show the demographic characteristics and analyze the prognosis of OMVT patients. Histology was found to be an important factor in determining survival for patients with OMVTs. Independent predictors of OS for patients with OAS included old age, distant tumor stage, low tumor grade, and surgery. Old age, surgery, and low tumor grade were also predictors of CSS rates for patients with OAS. Independent predictors of OS and CSS for patients with OHE included old age and surgery. The results of this study may improve doctors' understanding of the features and outcomes of OMVTs. The results may also be useful for patient health education and to provide a foundation for future research.

Conflict of interests

None.

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References:

1. Verbeke SL, Bertoni F, Bacchini P et al: Distinct histological features characterize primary angiosarcoma of bone. Histopathology, 2011; 58(2): 254–64
2. Wenger DE, Wold LE: Malignant vascular lesions of bone: Radiologic and pathologic features. Skeletal Radiol, 2000; 29(11): 619–31
3. Hozo I, Miric D, Bojic L et al: Liver angiosarcoma and hemangiopericytoma after occupational exposure to vinyl chloride monomer. Environ Health Perspect, 2000; 108(8): 793–95
4. Sinnamon AJ, Neuwirth MG, McMillan MT et al: A prognostic model for resectable soft tissue and cutaneous angiosarcoma. J Surg Oncol, 2016; 114(5): 557–63
5. Matamalas A, Gargallo A, Porcel JA et al: Cervical spine epithelioid hemangioendothelioma: Case report. Eur Rev Med Pharmacol Sci, 2014; 18(1 Suppl.): 72–75
6. Neves N, Lima-Rodrigues F, Ribeiro-Silva M et al: Epithelioid hemangioendothelioma presenting as a vertebral fracture. Acta Reumatol Port, 2010; 35(3): 370–74
7. McNamara D, Beauregard GC, Lemieux RJ: Scintigraphic "doughnut sign" on skeletal imaging due to a hemangioendothelioma of bone. J Nucl Med, 1993; 34(2): 297–300
8. Kopniczky Z, Tsimpas A, Lawson DD et al: Epithelioid hemangioendothelioma of the spine: report of two cases and review of the literature. Br J Neurosurg, 2008; 22(6): 793–97
9. Kerry G, Marx O, Kraus D, et al. Multifocal epithelioid hemangioendothelioma derived from the Spine region: case report and literature review. Case Rep Oncol. 2012;5(1): 91-98.
10. Verbeke SL, Bovee JV: Primary vascular tumors of bone: A spectrum of entities? Int J Clin Exp Pathol, 2011; 4(6): 541–51
11. Bagan P, Hassan M, Le Pimpec BF et al: Prognostic factors and surgical indications of pulmonary epithelioid hemangioendothelioma: A review of the literature. Ann Thorac Surg, 2006; 82(6): 2010–13
12. Niu Q, Lu Y, Xu S et al: Clinicopathological characteristics and survival outcomes of bladder neuroendocrine carcinomas: A population-based study. Cancer Manag Res, 2018; 10: 4479–89
13. Ge LP, Liu XY, Xiao Y et al: Clinicopathological characteristics and treatment outcomes of occult breast cancer: A SEER population-based study. Cancer Manag Res, 2018; 10: 4381–91
14. Palmerini E, Maki RG, Staals EL et al: Primary angiosarcoma of bone: A retrospective analysis of 60 patients from 2 institutions. Am J Clin Oncol, 2014; 37(6): 528–34
15. Sasaki R, Soejima T, Kishi K et al: Angiosarcoma treated with radiotherapy: Impact of tumor type and size on outcome. Int J Radiat Oncol Biol Phys, 2002; 52(4): 1032–40
16. Albores-Saavedra J, Schwartz AM, Henson DE et al: Cutaneous angiosarcoma. Analysis of 434 cases from the Surveillance, Epidemiology, and End Results Program, 1973–2007. Ann Diagn Pathol, 2011; 15(2): 93–97
17. Holden CA, Spittle MF, Jones EW: Angiosarcoma of the face and scalp, prognosis and treatment. Cancer, 1987; 59(5): 1046–57
18. Shustef E, Kazlouskaya V, Prieto VG et al: Cutaneous angiosarcoma: A current update. J Clin Pathol, 2017; 70(11): 917–25
19. Guadagnolo BA, Zagars GK, Araujo D et al: Outcomes after definitive treatment for cutaneous angiosarcoma of the face and scalp. Head Neck, 2011; 33(5): 661–67
20. Kleer CG, Unni KK, McLeod RA: Epithelioid hemangioendothelioma of bone. Am J Surg Pathol, 1996; 20(11): 1301–11
21. Walther C, Tayebwa J, Lilljebjorn H et al: A novel SERPINE1-FOSB fusion gene results in transcriptional up-regulation of FOSB in pseudomyogenic haemangioendothelioma. J Pathol, 2014; 232(5): 534–40
22. Iyoob VA: Postoperative pharyngocutaneous fistula: Treated by sternocleidomastoid flap repair and cricopharyngeus myotomy. Eur Spine J, 2013; 22(1): 107–12
23. Inyang A, Mertens F, Puls F et al: Primary pseudomyogenic hemangioendothelioma of bone. Am J Surg Pathol, 2016; 40(5): 587–98
24. Righi A, Gambarotti M, Picci P et al: Primary pseudomyogenic haemangioendothelioma of bone: Report of two cases. Skeletal Radiol, 2015; 44(5): 727–31
25. Larsson SE, Lorentzon R, Boquist L: Malignant hemangioendothelioma of bone. J Bone Joint Surg Am, 1975; 57(1): 84–89
26. Zheng J, Liu L, Wang J et al: Primary intracranial epithelioid hemangioendothelioma: A low-proliferation tumor exhibiting clinically malignant behavior. J Neurooncol, 2012; 110(1): 119–27
27. Scott MT, Indelicato DJ, Morris CG et al: Radiation therapy for hemangioendothelioma: the university of Florida experience. Am J Clin Oncol, 2014; 37(4): 360–63
28. Unni KK, Ivins JC, Beabout JW et al: Hemangioma, hemangiopericytoma, and hemangioendothelioma (angiosarcoma) of bone. Cancer, 1971; 27(6): 1403–14
29. Groeschl RT, Miura JT, Oshima K et al: Does histology predict outcome for malignant vascular tumors of the liver? J Surg Oncol, 2014; 109(5): 483–86

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