Journal of Cancer Research and Clinical Oncology (2019) 145:2793–2802
https://doi.org/10.1007/s00432-019-03009-8

ORIGINAL ARTICLE – CLINICAL ONCOLOGY

Therapeutic outcome and prognostic factors in sinonasal rhabdomyosarcoma: a single-institution case series

Wanpeng Li[1] · Hanyu Lu[1] · Dehui Wang[1]

Received: 3 June 2019 / Accepted: 19 August 2019 / Published online: 23 August 2019

Abstract

Background The purpose of this study was to explore the demographics, multimodality therapeutic outcomes*** and prognostic factors in sinonasal rhabdomyosarcoma (SNRMS).

Methods We conducted a retrospective analysis of 40 patients who underwent treatment of SNRMS from March 2007 to March 2018. The Kaplan–Meier method and the log-rank test were used to assess survival rates. The Cox regression model was used for multivariate survival analysis.

Results In total, 25 males and 15 females were included in the study; the median age was 33 years (range, 2–67 years). All patients underwent surgical resection, and surgery prior to or after adjuvant therapy (chemotherapy and radiotherapy) was performed in 91.4% of the patients. The overall 1-, 3- and 5-year survival rates were 77.0%, 46.5% and 46.5%, respectively, during a mean follow-up time of 27.9 (range, 2–128) months in all patients. The log-rank test showed Intergroup Rhabdomyosarcoma Study (IRS) group and infiltration of the skull base influenced overall survival ($p=0.001$; $p=0.022$). Advanced IRS stage, lymph node metastasis and tumor size ≥ 5 cm were also associated with an unfavorable outcome on overall survival ($p=0.01$; $p=0.035$; $p=0.02$). The results of multivariate regression analysis showed patients with IRS group I were associated with better prognosis outcome on overall survival.

Conclusion Patients with SNRMS have poor 5-year overall survival, and IRS group is the independent prognostic factor for overall survival.

Keywords Rhabdomyosarcoma · Sinonasal · Prognostic factors · Survival · Skull base

Introduction

Rhabdomyosarcoma (RMS) is the most common malignant soft tissue tumor in children, accounting for more than 50% of all soft tissue sarcomas; however, RMS rarely occurs in adults, accounting for only 3% of all adult soft tissue sarcomas (Ferrari et al. 2003; Gerber et al. 2013). RMS occurs sporadically, and no risk or predisposing factors are found in most cases. The tumor originates from embryonic mesenchymal tissue and has the potential to differentiate into striated muscle tissue.

RMS can occur almost anywhere in the body and exhibit locally aggressive growth. Approximately 35% of RMS cases occur in the head and neck region, and 44.4% of head and neck RMS are parameningeal areas, including the nasal cavity, paranasal sinuses, nasopharynx, mastoid region and middle ear, pterygopalatine fossa and infratemporal fossa (Turner and Richmon 2011). Tumors of parameningeal areas are associated with a poor prognosis not only because of the paucity of distinctive symptoms but also due to the complexity of anatomical structures and theproximity of these tumors to the cranial cavity (Choi et al. 2018). However, nonparameningeal head and neck RMS is considered to have a good prognosis (Orbach et al. 2017). The most common staging systems are the Intergroup Rhabdomyosarcoma Study (IRS) system and TNM-UICC system; the IRS staging system includes both IRS stage and IRS group (Raney et al. 2001). IRS stage separates patients by site of the primary tumor, tumor size and the presence or absence of tumor-involved regional lymph nodes and of distant metastases (Table 1). In

Wanpeng Li and Hanyu Lu contributed equally to this article.

✉ Dehui Wang
wangdehuient@sina.com

[1] Department of Otolaryngology-Head and Neck Surgery, Affiliated Eye Ear Nose and Throat Hospital, Fudan University, 83 Fen Yang Road, Shanghai 200031, China

Table 1 IRS stage system

Stage	Sites of primary tumor	Tumor size (cm)	Regional lymph nodes	Distant metastases
I	Orbit, non-PM head/neck; GU non bladder/prostate; biliary tract	Any size	N0, N1	M0
II	All other sites	≤5	N0	M0
III	All other sites	≤5	N1	M0
		≥5	N0 or N1	
IV	Any site	Any size	N0 or N1	M1

PM parameningeal, *GU* genito-urinary

addition, IRS group classifies RMS patients according to the surgical-pathologic results (Raney et al. 2001).

RMS in the head and neck region has a variety of histological subtypes, including alveolar, embryonic, pleomorphic and mixed types, and embryonic patterns are more prevalent than the other patterns (Fyrmpas et al. 2009). Futhermore, there is increasing recognition that spindle cell/sclerosing RMS is categorized as another morphologically distinct histotype of a RMS; it may occur in the head and neck and may be associated with MyoD1 mutations and poor prognosis (Rekhi and Singhvi 2014; Tsai et al. 2019). Sinonasal RMS (SNRMS) is very rare; only a few retrospective studies and case reports of SNRMS have been conducted in mixed populations of children and adults. In terms of survival, Fyrmpas et al. reported 14 cases of pediatric sinonasal alveolar RMS for which the 5-year overall survival rate was only 53.9% (Fyrmpas et al. 2009). The embryonal subtype of SNRMS had a more favorable prognosis than the alveolar subtype and occurred in younger patients (Sanghvi et al. 2013). In our study, we specifically focused on SNRMS in children and adults, and we reviewed the demographics, management outcomes and prognostic factors associated with this rare malignancy.

Patients and methods

We performed a retrospective chart review of 40 patients who were diagnosed with SNRMS and treated at the Department of Otorhinolaryngology of the Affiliated Eye Ear Nose and Throat Hospital (AEENTH) at Fudan University from March 2007 to March 2018. RMS patients whose lesions originated in the nasal cavity and sinuses were defined as SNRMS. For staging purposes, patients underwent clinical examination, computed tomography, magnetic resonance imaging and positron emission tomography. In our clinical treatment process, the main treatments for SNRMS include surgical treatment, radiotherapy and chemotherapy. Surgical treatment plays a role in resectable tumours or as salvage therapy in non-complete responders to chemoradiation. Radiotherapy and chemotherapy are often used to improve local control and to treat occult metastases. This study was approved by the Institutional Review Board of AEENTH at Fudan University. All patients underwent surgery performed by Dr. Dehui Wang.

Patients' demographics, need for adjunct treatment, surgical approach, pathological type, relapse and overall survival rate were analyzed. In addition, prognostic factors were assessed using the Kaplan–Meier method. Differences in survival distributions according to sex, age, IRS stage (II, III, IV), infiltration of the skull base, lymph node metastasis, tumor size (≥5 cm), pathological subtype and IRS group (I, II, III, IV) were evaluated using the log-rank test. The Cox regression model was used for multivariate survival analysis. The follow-up period was from the initial diagnosis at our institution to date of death or last contact.

Results

A summary of the patients included in this series is depicted in Table 2. Forty patients were identified, of whom 25 (62.5%) were males, and 15 (37.5%) females. The median age was 33 years (range, 2–67 years). There were 13 cases of left-side lesions, 23 cases of right-side lesions and 4 cases of bilateral lesions. The majority of SNRMS cases were found in the nasal cavity ($N=30$; 75%), followed by the ethmoid sinus ($n=26$; 65%), maxillary sinus ($n=20$; 50%) and skull base ($n=18$; 45%). Other sites of invasion are shown in Table 3. Seven patients (17.5) underwent surgical intervention before referral to our institution. Eighteen patients (45%) had IRS stage II SNRMS, 21 patients (52.5%) were diagnosed with stage III disease and 1 patient (2.5%) was diagnosed with stage IV disease. Seven patients (17.5%) had lymph node metastases. Eighteen patients (45%) had IRS stage II SNRMS, 21 patients (52.5%) were diagnosed with stage III disease and 1 patient (2.5%) was diagnosed with stage IV disease.

All patients underwent surgical treatment, 34 patients (85%) only underwent endoscopic resection, endoscopy combined with Caldwell-Luc surgery was performed in three patients and other surgical procedures included

Table 2 Characteristics of sinonasal rhabdomyosarcoma patients

Characteristics	Total = 40
Gender	
Male	25
Female	15
Median age (range)	33 (2–67)
Age (years)	
≤3	1
4–10	4
11–18	7
>18.3	28
Laterality	
Left	13
Right	23
Bilateral	4
IRS stage	
II	18
III	21
IV	1
IRS group	
I	12
II	18
III	9
IV	1
Surgical approach	
Endoscopic resection	34
Weber-Fergusson incision	1
Endoscopic resection + Caldwell-Luc approac	3
Endoscopic resection + extracranial approach	2
Maxillectomy	5
Adjuvant therapy	
Chemotherapy	5
Radiotherapy	2
Radiochemotherapy	26
No radiochemotherapy	2
Unknown	5
Histological subtype	
Alveolar	6
Embryonal	18
Pleomorphic	2
Mixed	1
Rhabdomyosarcoma, not otherwise specified	13
All patients with follow-up (mean months of survival, range)	27.9 (2–128)
Recurrent	20
Outcome	
Remission	12
Deceased	18
Alive with disease	6
Unknown	4

Table 3 The invading location of sinonasal rhabdomyosarcoma

Location	No of cases
Nasal cavity	30
Maxillary sinus	20
Ethmoid sinus	26
Sphenoid sinus	10
Frontal sinus	8
Skull base	18
Orbit	16
Nasopharynx	2
Intracalvarium	4
Infratemporal fossa	2
Pterygopalatine fossa	1
Subcutaneous maxillofacial region	1

Weber–Fergusson incisions ($n=1$) and endoscopic resection combined with an extracranial approach ($n=2$). In addition, five patients underwent maxillectomy. Surgery prior to or after adjuvant radiochemotherapy was performed in 26 patients (65%). Radiation therapy alone was carried out in two patients (5%), chemotherapy alone was performed in five patients (12.5%) and five patients failed to report whether adjuvant therapy was administered. The histological subtype of SNRMS in most patients was the embryonal subtype ($n=18$; 45%), followed by the alveolar subtype ($n=6$; 15%). Thirteen patients (32.5%) were diagnosed with RMS not otherwise specified (NOS), two patients presented with the pleomorphic subtype and mixed-type RMS was observed in one patient. The number of patients with IRS group I, II, III and IV was 12, 18, 9 and 1, respectively.

The overall 1-, 3- and 5-year survival rates were 77.0%, 46.5% and 46.5%, respectively, during a median follow-up time of 27.9 months (range 2–128) in all patients (Fig. 1). Twenty patients (50%) experienced a local recurrence, and 18 patients (45%) died due to tumor progression. Remission was confirmed on a physical exam and/or disappearance of the tumor was confirmed by imaging studies in 12 patients (30%), and 6 patients (15%) remained alive with disease.

Prognostic factors for the treatment outcomes of SNRMS are shown in Table 4. Infiltration of the skull base influenced survival; the 5-year survival rate of these patients was 0% in contrast with patients without skull base involvement, in whom the 5-year survival rate was 65.7% ($p=0.022$, Fig. 2). Lymph node metastasis adversely affected outcomes; these patients had a 14.3% 5-year cumulative survival rate, whereas patients without lymph node metastasis had an improved survival rate of 54.3% ($p=0.035$, Fig. 3). There was significantly poorer survival in patients with tumors ≥ 5 cm in size than in those with tumors < 5 cm in size (23.9% vs 59.6%; $p=0.02$, Fig. 4). Patients with IRS stage II disease had a better prognosis than those with IRS

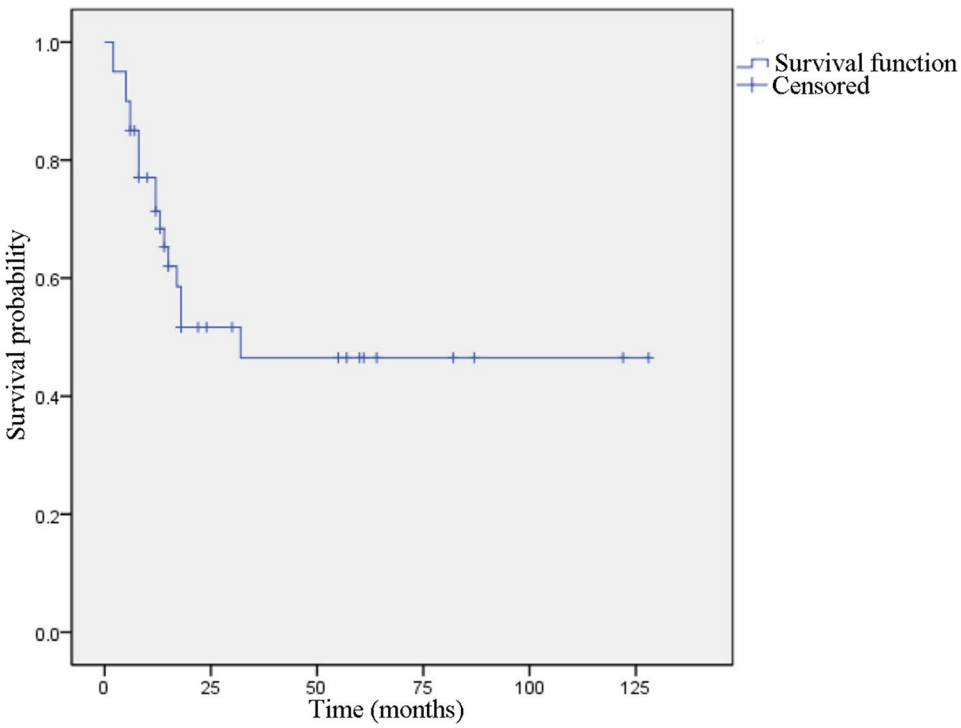

Fig. 1 Kaplan–Meier curve of the overall survival probability of patients with sinonasal rhabdomyosarcoma

Table 4 Log-rank test of prognostic factors for sinonasal rhabdomyosarcoma

	N	%	*p* value
Sex			
Male	25	62.5	0.252
Female	15	37.5	
Age (year)			
4–10	4	10.0	0.797
11–18	7	17.5	
> 18	28	70.0	
Infiltration of the skull base			
Yes	18	45.0	0.022
No	22	55.0	
Lymph node metastasis			
Yes	7	17.5	0.035
No	33	82.5	
Tumor size by IRS staging, cm			
< 5	22	55.0	0.020
≥ 5	18	45.0	
IRS stage			
II	18	45.0	0.010
III	21	53.0	
IRS group			
I	12	24.0	0.001
II	18	45.0	
III	9	22,5	
Histological subtype			
Embryonal	18	45	0.345
Alveolar	6	15	

stage III disease ($p = 0.01$, Fig. 5); 5-year survival rates were 69.6% and 15.1% for the stage II and stage III groups, respectively. Patients with IRS group I were associated with better prognosis outcome on overall survival ($p = 0.001$, Fig. 6). The 5-year survival rate of males (35.8%) was lower than that of females (62.2%), but there was no significant difference between the two groups ($p = 0.252$). Age categories did not influence overall survival ($p = 0.797$, Fig. 7). Regarding the specific histologic subtype, embryonal SNRMS was associated with lower survival rates than alveolar SNRMS. However, survival comparisons did not reveal significant differences between the two groups ($p = 0.345$). The results of multivariate regression analysis showed IRS group was the independent prognostic factor for overall survival (Table 5).

The surgical approach for SNRMS varies according to the lesion size and location. A 23-year-old female presented with a tumor invading the right ethmoid sinus, orbit, maxillary sinus and nasolacrimal duct. The lesions of the right maxillary sinus and ethmoid sinus were resected by endoscopic surgery, after which a right pyriform foramen incision was made to remove the anterior and medial walls of the maxillary sinus, and the lesions from the nasolacrimal duct to the highest point of the lacrimal sac were also removed. This patient is disease-free for more than 61 months after surgery. A 40-year-old female underwent modified Denker surgery for RMS involving the entire right maxillary sinus, and she is in remission for more than 122 months after total resection. There were two cases of lesions invading the anterior skull base and intracranial area, and endoscopic resection of

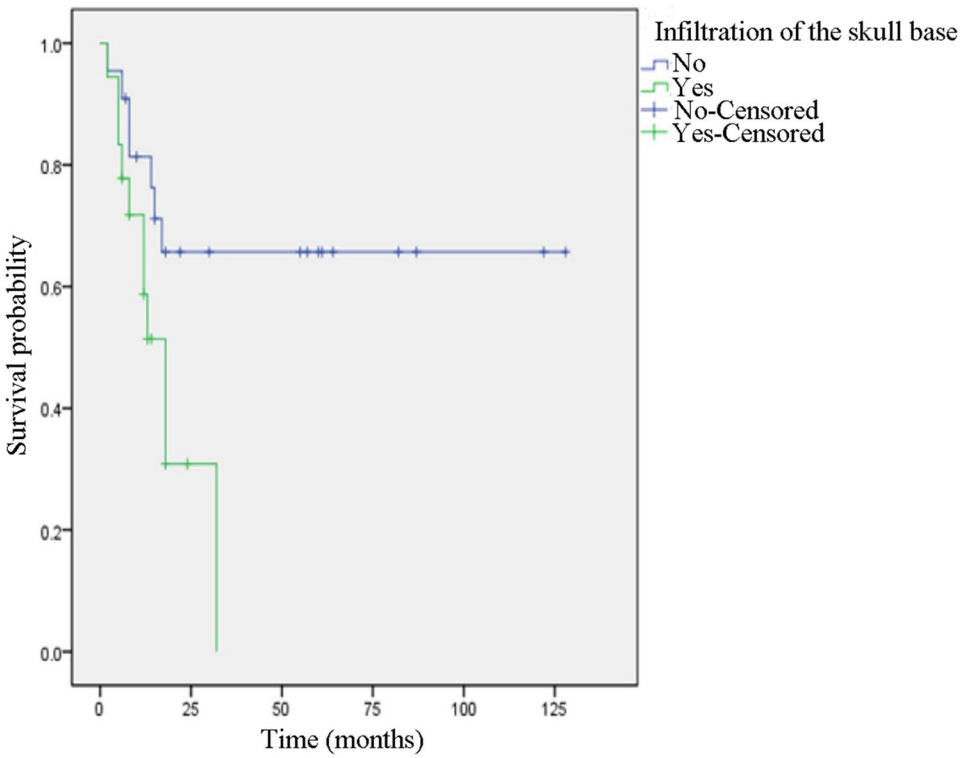

Fig. 2 Kaplan–Meier curves for the survival of patients with or without skull base involvement ($p = 0.022$)

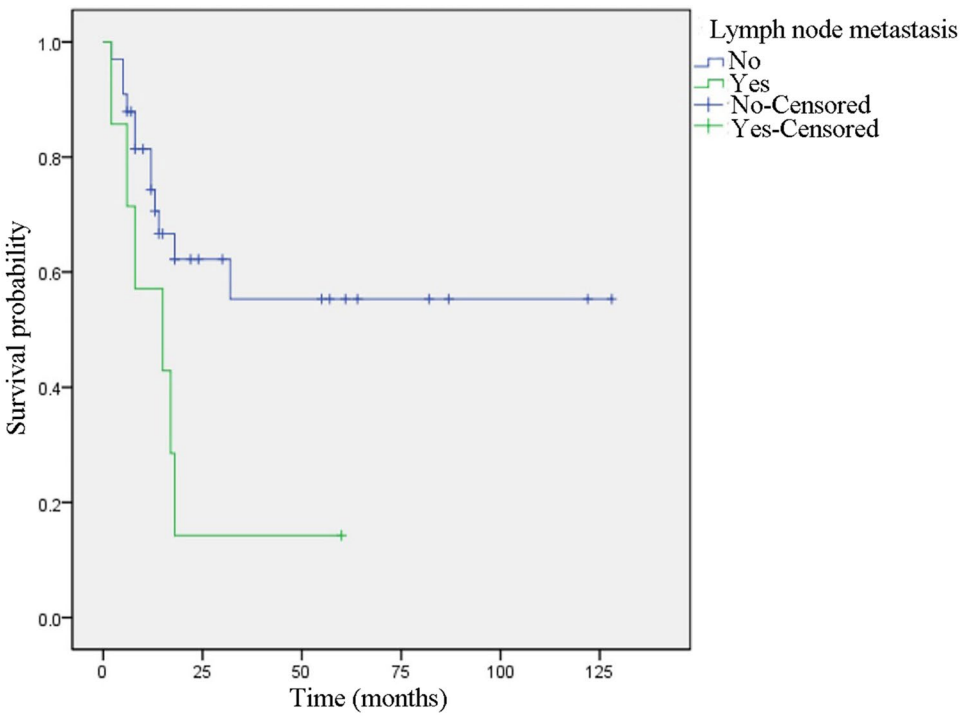

Fig. 3 Kaplan–Meier curves for the survival of patients with lymph node metastasis and N-neck ($p = 0.035$)

the tumor combined with an extracranial approach was performed. The tumors eroded the local dura mater and exhibited substantial adhesions to brain tissue. The adhesions between the lesions and brain tissue were separated, and the tumors and eroded dura mater were removed completely.

Nine patients belonged to RMS group III and had gross residual tumors due to invasion of significant structures. In six patients, the tumor invaded intraorbital tissues, and only periorbital lesions could be removed to the largest extent possible. In two patients, the tumor invaded

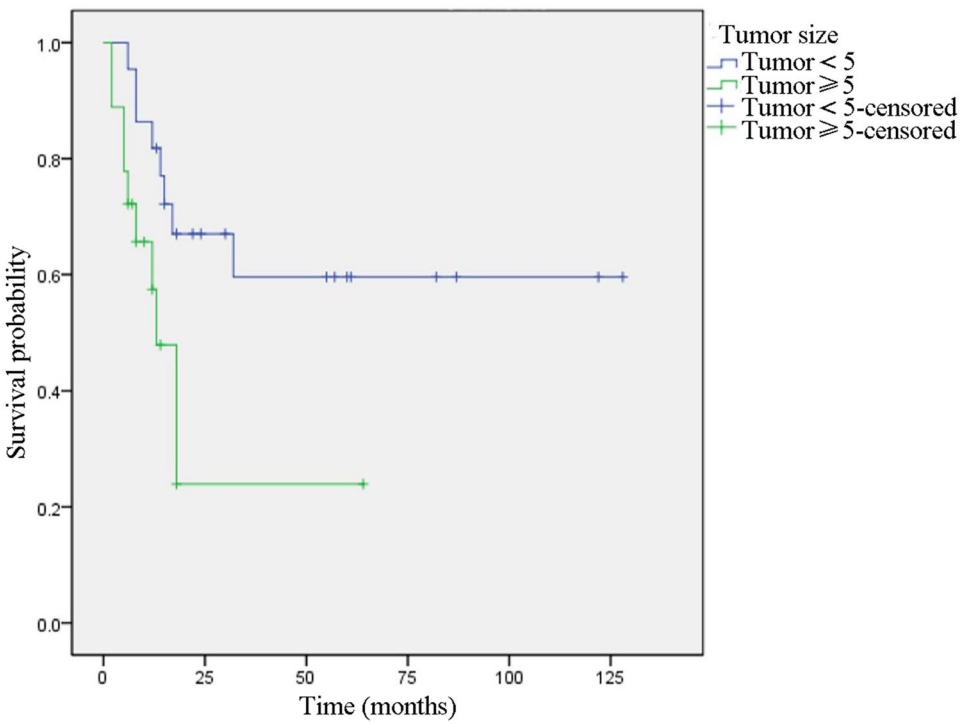

Fig. 4 Kaplan–Meier curves for the survival of patients with tumors ≥ 5 cm and tumors < 5 cm ($p = 0.02$)

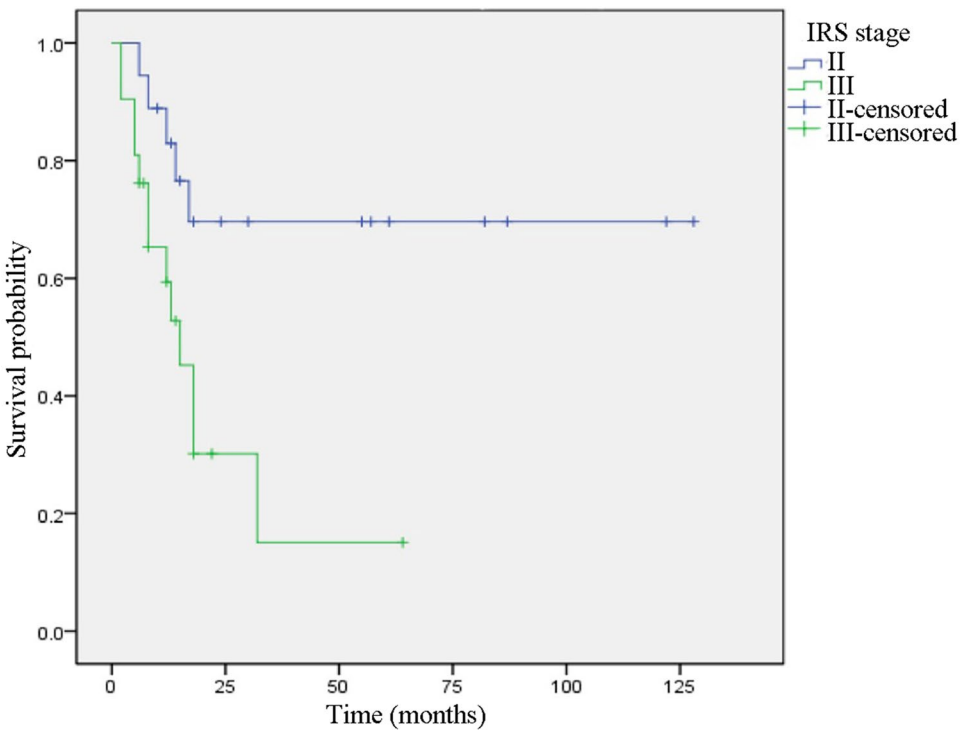

Fig. 5 Kaplan–Meier curves for the survival of patients with IRS stages II and III disease ($p = 0.01$)

the cranium and had obvious adhesions to brain tissue. These intracerebral tumors were difficult to remove via an exclusively endoscopic approach. In one patient, a widely extended mass was observed in the left nasal cavity and nasopharynx. This mass surrounded the internal carotid artery and could not be completely removed.

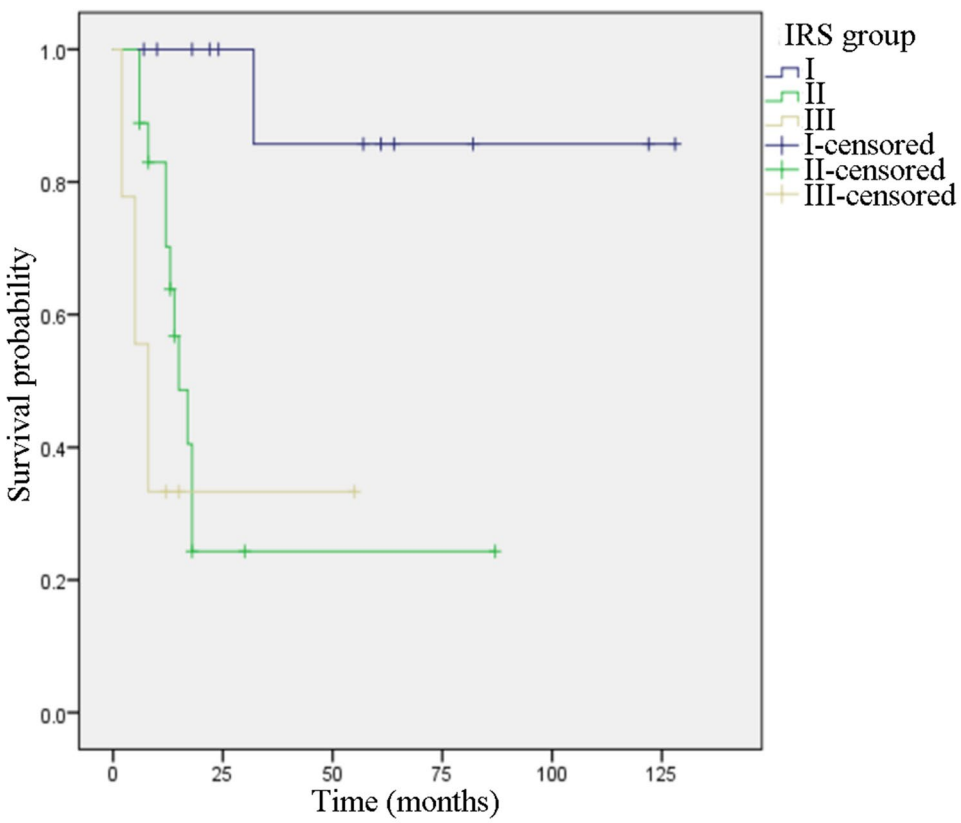

Fig. 6 Kaplan–Meier curves for the survival of patients with IRS group I, II and III disease ($p = 0.001$)

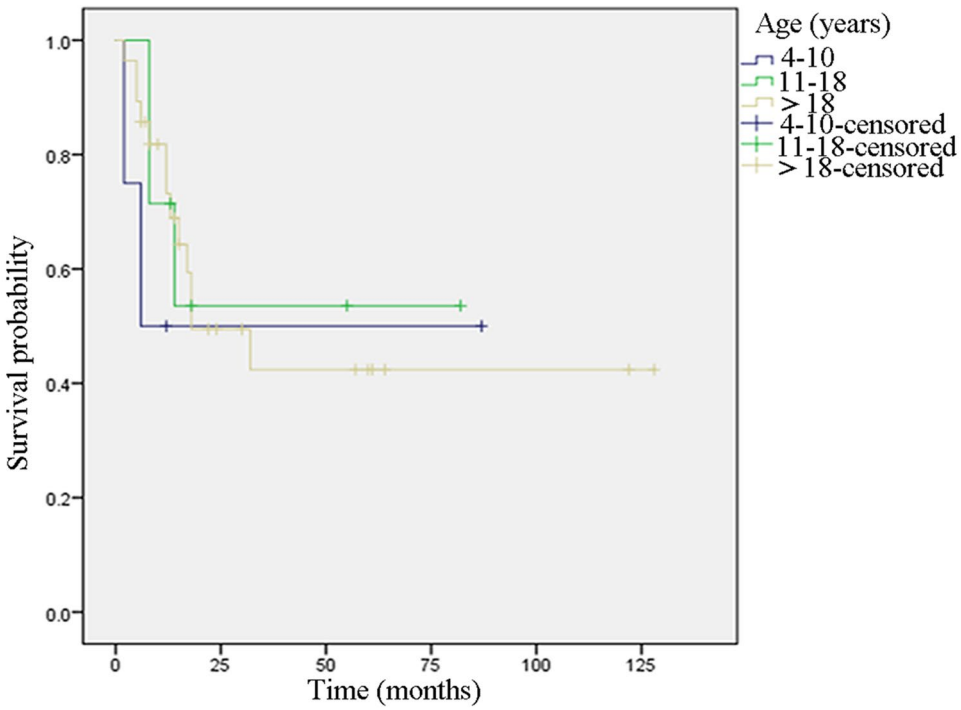

Fig. 7 Kaplan–Meier curves for the survival of patients with age categories ($p = 0.797$)

Table 5 Univariate and multivariate Cox regression analyses of prognostic factors associated with overall survival in patients with sinonasal rhabdomyosarcoma

Variable	Univariate			Multivariate		
	HR	95% CI	*p*	HR	95% CI	*p*
IRS group						
I	1		0.016	1		0.017
II	12.920	1.623–102.843	0.016	9.813	1.072–89.786	0.043
III	22.901	2.688–195.135	0.004	24.049	2.476–233.639	0.006
Infiltration of skull base						
No	1		0.03	1		0.841
Yes	2.933	1.107–7.767		0.839	0.151–4.677	
IRS stage						
II	1		0.017	1		0.188
III	3.560	1.253–10.115		3.133	0.572–17.151	
Tumor size						
< 5 cm	1		0.029	1		0.828
≥ 5 cm	2.913	1.118–7.586		1.194	0.241–5.912	
Lymph node metastasis						
No	1		0.047	1		0.369
Yes	2.713	1.015–7.257		1.660	0.549–5.016	
Sex						
Female	1		0.266			
Male	1.799	0.639–5.060				
Age (year)						
4–10	1		0.806			
11–18	0.599	0.093–3.359	0.525			
> 18	0.647	0.145–2.880	0.567			
Histological subtype						
Embryonal	1		0.366			
Alveolar	0.499	0.110–2.253				

HR hazard ratio, *CI* confidence interval at 95% level

Discussion

Head and neck RMS is a rare malignant soft tissue tumor that accounts for a small portion of head and neck neoplasms, presenting for 0.041 per 100,000 patients per year (Turner and Richmon 2011). However, Head and neck RMS is the most prevalent soft tissue malignancy in children. The incidence of RMS confined to the nasal cavity and paranasal sinuses is even lower, with a reported 0.034 cases per 100,000 patients over the past 20 years (Sanghvi et al. 2013). The ratio of males to females with RMS in some studies has been reported to be up to 1.7:1 (Hicks and Flaitz 2002; Ognjanovic et al. 2009), while Turner cited an equal distribution of RMS between males and females in a population-based study (Turner and Richmon 2011). However, our series contradicted Turner's study, as an overall male predominance was found for SNRMS, with a 1.7:1 ratio of males to females.

Turner et al. demonstrated that the relative 5-year survival rate of parameningeal sites in the head and neck RMS was 49.1%, while the 5-year survival rate of nonorbital nonparameningeal and orbital sites was 70.3% and 84.3%, respectively (Turner and Richmon 2011). Sanghvi et al. showed a 5-year survival rate of 49.45% for SNRMS RMS (Sanghvi et al. 2013). However, one study reported that the overall 5-year disease-specific survival rate of SNRMS was only 35.1% (Unsal et al. 2017). In our series, the 5-year survival rate in 40 patients with SNRMS was 46.5%, which was well within the range reported in the literature (Callender et al. 1995; Sanghvi et al. 2013; Wharam 1997; Wurm et al. 2005). Our current analysis showed that the survival rate of SNRMS was lower than that of nonparameningeal RMS in previous studies, and this decreased survival may be attributed to the proximity of the lesion location to the important organs and complex anatomical structures. In addition, the symptoms of nasal cavity lesions are not specific, sometimes leading to late diagnosis of SNRMS.

IRS group was used to classify patients based on clinically and pathologically determined extent of disease and degree of initial surgical resection. Siddiqui et al. reported 157 cases of pediatric SNRMS from the National Cancer Database and showed IRS group was not a predictor for decreased survival

on multivariate analyses (Siddiqui et al. 2019). However, in our study, log rank analysis demonstrated that Patients with IRS group I were associated with better prognosis outcome, and multivariate regression analysis suggested that IRS group was an independent prognostic factor for overall survival. Our findings are contrary to those reported by Sidiqui et al., which may be related to the fact that most of our patients are adults.

The prognostic role of lymph node metastasis is controversial in the previous literatures, and some published studies hold that the clinical finding of lymph node metastasis is a significant prognostic factor for head and neck RMS (Sultan et al. 2009; Wu et al. 2014). However, Unsal et al. did not find this to be the case with the presence of nodal involvement (Unsal et al. 2017). In our patients, multivariate regression analysis showed no significant correlation between lymph node metastasis and prognosis. Classification according to the IRSG stage showed that a tumor size ≥ 5 cm in RMS was a poor prognostic factor regardless of lesion location (Raney et al. 2001). Other research reports that limited their analyses to the head and neck region confirmed this observation (Fyrmpas et al. 2009; Wu et al. 2014), while a study of 286 patients with SNRMS who were evaluated from 1973 to 2013 indicated that a tumor size ≥ 5 cm did not decrease the survival rate (Unsal et al. 2017). In this study, our results also demonstrated that tumors ≥ 5 cm in size was not a risk factor. IRS staging reflects the tumor location, size, lymph node involvement and distant metastasis. Log rank analysis showed patients with stage II disease had a better prognosis than those with stage III disease. However, the IRS stage is not a significant prognostic factor in the multivariate regression method, which was also consistent with another study by Siddiqui et al. (2019).

Multiple studies have shown that alveolar-type RMS is associated with a poorer prognosis than other subtypes of RMS (Haussler et al. 2018; Ognjanovic et al. 2009; Turner and Richmon 2011). However, Sanghviet al. compared alveolar and embryonal histological subtypes using the log-rank survival method and found no significant differences (Sanghvi et al. 2013). In our series, the survival rates between cases of embryonal ($n = 18$) and alveolar RMS ($n = 6$) showed no significant difference. Approximately 83.3% (5/6) of patients with stage III disease had alveolar RMS, and 33.3% (6/18) of these patients had embryonal RMS. Curiously, the survival rate for alveolar-type RMS (62.5%) was higher than that for embryonal RMS (30.1%). Recently, there is evidence that the prognosis of alveolar-type RMS with PAX-FOXO1 fusion positive status is worse than that of patients with fusion negative status (Skapek et al. 2013). Thus, we suspect that PAX-FOXO1 fusion negative status may exist in most our patients with alveolar RMS, which leads to a better survival rate of alveolar RMS than embryonic RMS, but further studies are required to confirm this. Notably, our study sample included a group of patients with RMS NOS (32.5%; 13/40); of these patients, 84.6% (11/13) were older than 18 years. RMS NOS was not a specific subtype. Instead, this nomenclature was reserved for cases in which RMS could be diagnosed but any further definitive classification was impossible because of limited biopsy quality (e.g., small or crushed tissue samples) or lack of pathologist experience. RMS NOS seemed to be more common in adults, and the rate we observed was similar to that described in similar studies (Stepan et al. 2017).

The management of RMS often requires multimodal therapy, including surgery, chemotherapy and radiotherapy (Casey and Wolden 2018; Stepan et al. 2017). Multidrug chemotherapy combined with radiotherapy is the mainstay of treatment for RMS, and many studies have reported that surgery prior to or after cytoreductive chemotherapy is recommended if complete resection is feasible and if there is no intracranial invasion (Daya et al. 2000; Healy et al. 1991). Microscopic residual disease after resection can be treated with less intensive radiotherapy and chemotherapy. Surgical intervention plays a role for treating resectable tumors or as a remedy for tumors that have an incomplete response to radiotherapy and chemotherapy. The IRSG showed that overall survival for patients with any type of RMS improved from 55% to 71% over the study period from 1972 to 1997 with multimodality treatment (Raney et al. 2001). In addition, Wurm et al. studied 15 patients with nasal or paranasal sinus RMS, and the 5-year survival rate was 66% in the group subjected to tumor resection with subsequent radiotherapy compared with 33% in the group of patients who exclusively received primary radiotherapy (Wurm et al. 2005). In our patients, surgery prior to or after adjuvant therapy was performed in 91.4% (33/35) of patients; 74.3% (26/35) of patients were administered chemoradiotherapy, and 37.1% (13/35) were administered adjuvant therapy before surgical resection. Our clinical experience has shown that preoperative adjuvant therapy can reduce the size of extensive, invasive and difficult-to-resect tumors and facilitate early clinical staging, thereby improving resection and survival rates.

Conclusion

Patients with SNRMS have poor 5-year overall survival, and IRS group is the independent prognostic factor for overall survival. Management of SNRMS requires a combination of surgery, chemotherapy and radiotherapy. Surgical intervention plays a role for treating resectable tumors or as a remedy for tumors with an incomplete response to radiotherapy and chemotherapy.

Funding This work was financially supported by the National Natural Science Foundation of China (No. 81870703).

Compliance with ethical standards

Conflict of interest The author(s) declared no potential conflicts of interest with respect to the research, authorship and/or publication of this article.

References

Callender TA, Weber RS, Janjan N, Benjamin R, Zaher M, Wolf P, El-Naggar A (1995) Rhabdomyosarcoma of the nose and paranasal sinuses in adults and children. Otolaryngol Head Neck Surg 112:252–257. https://doi.org/10.1016/S0194-59989570246-6

Casey DL, Wolden SL (2018) Rhabdomyosarcoma of the Head and Neck: a Multimodal Approach. J Neurol Surg B Skull Base 79:58–64. https://doi.org/10.1055/s-0037-1617450

Choi PJ, Iwanaga J, Tubbs RS, Yilmaz E (2018) Surgical interventions for advanced parameningeal rhabdomyosarcoma of children and adolescents. Cureus 10:e2045. https://doi.org/10.7759/cureus.2045

Daya H, Chan HS, Sirkin W, Forte V (2000) Pediatric rhabdomyosarcoma of the head and neck: is there a place for surgical management? Arch Otolaryngol Head Neck Surg 126:468–472

Ferrari A et al (2003) Rhabdomyosarcoma in adults. A retrospective analysis of 171 patients treated at a single institution. Cancer 98:571–580. https://doi.org/10.1002/cncr.11550

Fyrmpas G, Wurm J, Athanassiadou F, Papageorgiou T, Beck JD, Iro H, Constantinidis J (2009) Management of paediatric sinonasal rhabdomyosarcoma. J Laryngol Otol 123:990–996. https://doi.org/10.1017/S0022215109005337

Gerber NK et al (2013) Adult rhabdomyosarcoma survival improved with treatment on multimodality protocols. Int J Radiat Oncol Biol Phys 86:58–63. https://doi.org/10.1016/j.ijrobp.2012.12.016

Haussler SM, Stromberger C, Olze H, Seifert G, Knopke S, Bottcher A (2018) Head and neck rhabdomyosarcoma in children: a 20-year retrospective study at a tertiary referral center. J Cancer Res Clin Oncol 144:371–379. https://doi.org/10.1007/s00432-017-2544-x

Healy GB, Upton J, Black PM, Ferraro N (1991) The role of surgery in rhabdomyosarcoma of the head and neck in children. Arch Otolaryngol Head Neck Surg 117:1185–1188

Hicks J, Flaitz C (2002) Rhabdomyosarcoma of the head and neck in children. Oral Oncol 38:450–459

Ognjanovic S, Linabery AM, Charbonneau B, Ross JA (2009) Trends in childhood rhabdomyosarcoma incidence and survival in the United States, 1975–2005. Cancer 115:4218–4226. https://doi.org/10.1002/cncr.24465

Orbach D et al (2017) Nonparameningeal head and neck rhabdomyosarcoma in children and adolescents: lessons from the consecutive International Society of Pediatric Oncology Malignant Mesenchymal Tumor studies. Head Neck 39:24–31. https://doi.org/10.1002/hed.24547

Raney RB et al (2001) The Intergroup Rhabdomyosarcoma Study Group (IRSG): major lessons from the IRS-I through IRS-IV studies as background for the current IRS-V treatment protocols. Sarcoma 5:9–15. https://doi.org/10.1080/13577140120048890

Rekhi B, Singhvi T (2014) Histopathological, immunohistochemical and molecular cytogenetic analysis of 21 spindle cell/sclerosing rhabdomyosarcomas. APMIS 122:1144–1152. https://doi.org/10.1111/apm.12272

Sanghvi S, Misra P, Patel NR, Kalyoussef E, Baredes S, Eloy JA (2013) Incidence trends and long-term survival analysis of sinonasal rhabdomyosarcoma. Am J Otolaryngol 34:682–689. https://doi.org/10.1016/j.amjoto.2013.04.012

Siddiqui SH et al (2019) Clinicopathologic traits and prognostic factors associated with pediatric sinonasal rhabdomyosarcoma. Int Forum Allergy Rhinol 9:363–369. https://doi.org/10.1002/alr.22267

Skapek SX et al (2013) PAX-FOXO1 fusion status drives unfavorable outcome for children with rhabdomyosarcoma: a children's oncology group report. Pediatr Blood Cancer 60:1411–1417. https://doi.org/10.1002/pbc.24532

Stepan K et al (2017) Outcomes in adult sinonasal rhabdomyosarcoma. Otolaryngol Head Neck Surg 157:135–141. https://doi.org/10.1177/0194599817696287

Sultan I, Qaddoumi I, Yaser S, Rodriguez-Galindo C, Ferrari A (2009) Comparing adult and pediatric rhabdomyosarcoma in the surveillance, epidemiology and end results program, 1973 to 2005: an analysis of 2600 patients. J Clin Oncol 27:3391–3397. https://doi.org/10.1200/jco.2008.19.7483

Tsai JW et al (2019) The expanding morphological and genetic spectrum of MYOD1-mutant spindle cell/sclerosing rhabdomyosarcomas: a clinicopathological and molecular comparison of mutated and non-mutated cases. Histopathology 74:933–943. https://doi.org/10.1111/his.13819

Turner JH, Richmon JD (2011) Head and neck rhabdomyosarcoma: a critical analysis of population-based incidence and survival data. Otolaryngol Head Neck Surg 145:967–973. https://doi.org/10.1177/0194599811417063

Unsal AA, Chung SY, Unsal AB, Baredes S, Eloy JA (2017) A population-based analysis of survival for sinonasal rhabdomyosarcoma. Otolaryngol Head Neck Surg 157:142–149. https://doi.org/10.1177/0194599817696292

Wharam MD Jr (1997) Rhabdomyosarcoma of Parameningeal Sites. Semin Radiat Oncol 7:212–216. https://doi.org/10.1053/SRAO00700212

Wu Y, Li C, Zhong Y, Guo W, Ren G (2014) Head and neck rhabdomyosarcoma in adults. J Craniofac Surg 25:922–925. https://doi.org/10.1097/SCS.0000000000000704

Wurm J, Constantinidis J, Grabenbauer GG, Iro H (2005) Rhabdomyosarcomas of the nose and paranasal sinuses: treatment results in 15 cases. Otolaryngol Head Neck Surg 133:42–50. https://doi.org/10.1016/j.otohns.2005.03.023