Outcomes and Prognostic Factors in Patients with Malignant Peripheral Nerve Sheath Tumor

Chindanai Hongsaprabhas, M.D.*, Sorranart Muangsomboon, M.D.*, Chandhanarat Chandhanayingyong, M.D.**, Rapin Phimolsarnti, M.D.**, Saranatra Waikakul, M.D.**, Apichat Asavamongkolkul, M.D.****

**Department of Orthopaedics, Faculty of Medicine, Chulalongkorn University, Bangkok 10330, Thailand, **Department of Orthopaedic Surgery, ***Department of Pathology, Faculty of Medicine Siriraj Hospital, Mahidol University, Bangkok 10700, Thailand.*

ABSTRACT

Objective: To investigate and report the clinical profiles, treatment patterns, and oncologic outcomes in malignant peripheral nerve sheath tumor (MPNST) patients, and to identify the prognostic factors that significantly affect survival.

Materials and Methods: Patients diagnosed with and treated for histologically confirmed MPNST at our institute during the January 1997 to June 2018 study period were included. Patient medical records and surgical specimens were reviewed, and study-related data was extracted and analyzed.

Results: There were 27 males and 32 females with a mean age of 44 years. Most patients presented with mass and most patients were AJCC stage III. Twenty-nine percent of patients had MPNST that was associated with NF-1. At a median follow-up time, 18 patients (30.51%) suffered from local disease recurrence. Two-year and 5-year overall survival was 72% and 46%, respectively. In univariate analysis, chemotherapy treatment and positive tumor margin were adverse prognostic factors for disease-free survival. In multivariate analysis, chemotherapy treatment (hazard ratio (HR): 3.415, 95% CI: 1.367-16.021; p=0.013) and positive tumor margin (HR: 4.680, 95% CI 1.828-10.314; p=0.014) were found to be independent prognostic factors for disease-free.

Conclusion: Chemotherapy treatment and positive tumor margin were identified as independent adverse prognostic factors for disease-free and overall survival, respectively. Accordingly, early detection and appropriate treatment are essential for improved patient outcome.

Keywords: Malignant peripheral nerve sheath tumor; MPNST; prognostic factors; outcomes; survival (Siriraj Med J 2021; 73: 763-771)

INTRODUCTION

Malignant peripheral nerve sheath tumor (MPNST) is a rare and aggressive malignant soft-tissue tumor that is characterized by high risk of local recurrence and distant metastasis.[1] There is a widely held misconception that curative treatment for MPNST is complete tumor removal, with adjuvant chemotherapy and radiotherapy recommended only in large lesions or lesions with high-grade histology.[2] Whether treatment for MPNST involves extensive surgery alone or surgery combined with adjuvant therapies, the prognosis for patients with this condition remains poor.[3] Several studies have reported 5-year overall survival rates that vary from 16% to 52%, and 5-year disease-free survival rates that range from 26% to 49%.[4-13] Neurofibromatosis type 1 (NF-1) or disease recurrence when associated with MPNST were found and reported to be adverse prognostic factors.[10,14]

The aim of this study was to investigate and report

Corresponding author: Apichat Asavamongkolkul
E-mail: apichat.asa@mahidol.ac.th
Received 24 June 2021 Revised 28 September 2021 Accepted 5 October 2021
ORCID ID: https://orcid.org/0000-0002-7868-7426
http://dx.doi.org/10.33192/Smj.2021.99

the clinical profiles, treatment patterns, and oncologic outcomes in MPNST patients. The secondary objective was to identify the prognostic factors that significantly affect survival.

MATERIALS AND METHODS

Seventy-one patients were diagnosed with and treated for histologically confirmed MPNST during the January 1997 to June 2018 study period. Of the 12 patients that were excluded, 3 were denied definitive operative treatment and 9 were lost to follow-up prior to 6 months after commencement of treatment. The remaining 59 patients were enrolled and included in the final analysis. After the protocol for this study was approved by the Institutional Review Board, patient medical records and surgical specimens were reviewed, and study-related data was extracted and analyzed.

A wide excision of tumor was attempted in all MPNST patients (Fig 1A-D). Radiation therapy with high-dose regimen ranging from 45 to 65 Gy was considered in patients with greater risk of recurrence based on operative and pathologic findings. There were, however, no absolute indications for radiation therapy at our center during the study period. Adjuvant chemotherapy, consisting of doxorubicin and ifosfamide, was considered in patients with high-grade disease and distant metastasis. Each patient was discussed at our weekly multidisciplinary musculoskeletal tumor board meeting to determine the most appropriate modality treatment.

Statistical analysis

Descriptive statistics were used to analyze demographic data. Cause-specific mortality, local recurrence, and distant metastasis were the clinical endpoints in this study. Data analysis were performed using statistical package Stata version 14 (StatCorp, College Station, TX, USA) and program R version 4.0.2 for windows. Shapiro-Wilk test and histogram were used to evaluate normal distribution. To summarize the data studied mean (sd) and median (range) were reported for continuous variables when appropriate, frequency and percentage for categorical variables. Kaplan-Meier method and Cox proportional hazard model was used to determine prognostic factors for two events, disease free survival and overall survival. Time to occurrence of event was calculated from the date of surgery to the date when the event occurred, or censored at the date of the last follow-up, death from other cause. Variables of interesting were gender, tumor

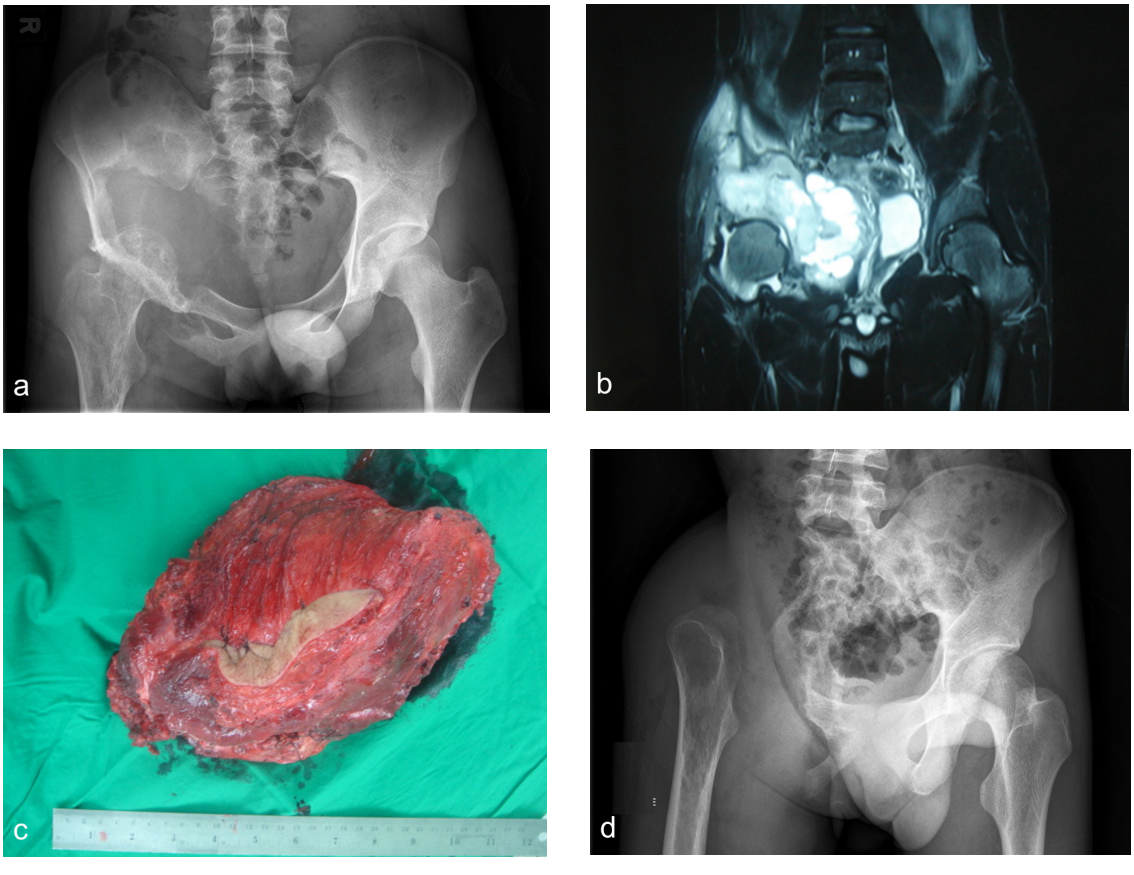

Fig 1. A 19-year-old male with MPNST with right pelvic bone destruction who underwent internal hemipelvectomy without reconstruction: **A)** Initial plain x-ray; **B)** Coronal view of T1-weighted MRI; **C)** Tumor mass after en-bloc resection; **D)** Postoperative plain x-ray

depth, NF-1, primary tumor, chemotherapy, radiotherapy, tumor site, tumor size, surgery technique, margin and severity. In this study, the variables with a univariate significance level of 0.25 or less were selected to perform multivariable Cox regression. We also included other variables from the literature which were reported clinically relevant and eligible for using in the model. Backward elimination technique was employed to select variables into the model. Proportional hazard (PH) assumption was evaluated using PH test based on Schoenfeld residuals and in survival curves plot. Variance inflation factor (VIF) was determined whether there was multi-collinearity among the variables. Candidate variables with VIF > 4 were excluded from data analysis. Goodness of fit was examined for lack of fit using graphical approach; the Cox-Snell residuals against the Nelson-Aalen cumulative hazard function plot. Data analysis was 2-tailed test with significant level 0.05.

RESULTS

The mean age at presentation was 44 years, with an age range of 13 to 86 years. Twenty-seven males and 32 females were included. Demographic and clinical characteristics of 59 study patients are shown in Table 1. Most patients presented with only one symptom (66.1%) and mass was the most frequent complaint (89.8%), followed by pain (28.8%) and neuropathy (15.3%). Twenty-one patients had been treated at other hospitals before being referred after presenting with local tumor recurrence. Most patients in this study were American Joint Committee on Cancer (AJCC) stage III (47.5%). Twenty-nine percent (17/59) of patients had MPNST that was associated with NF-1. Limb sparing surgeries could be performed in 48 patients (81.3%), with amputation required in the remaining 11 patients. Negative tumor margin could be achieved in 34 patients (57.6%), with 14 patients (23.7%) emerging from surgery with positive margins. Thirty-four patients (57.6%) received adjuvant radiation therapy, 3 patients (5.1%) received only adjuvant chemotherapy, and 11 patients (18.6%) received both adjuvant treatments.

At a median follow-up time of 48 months, 18 patients (30.5%) suffered from local recurrence of the disease. Twenty-nine patients (58%) developed metastasis, and 9 of those had multiple sites metastasis. Pulmonary metastasis was the most common site (44.1%), followed by bone, brain, and other organ at percentages of 11.9%, 3.4%, and 6.8%, respectively. Complications occurred in 15 patients (25.4%), as follows: wound dehiscence (6.8%), superficial wound infection (3.4%), phantom limb pain (5.1%). Two-year and 5-year overall survival was 72% and 46%, respectively. Median overall survival time was 58 months (Fig 2A). Median disease-free survival was 32 months based on analysis of 50 initially non-metastatic patients. Two-year and 5-year disease-free survival was 52% and 40%, respectively (Fig 2B).

Subgroup survival analysis was performed for NF-1 and type of disease presentation. Median overall survival of patients with and without NF-1 was 38 months (95% CI: 13.5-62.5) and 58 months (95% CI: 5.1-11.9), respectively, with no significant difference found between groups (p=0.648). Similarly, no significant difference was observed between patients with recurrent and primary tumor (p=0.978). Median overall survival of patients with recurrent tumor was 46 months (95% CI: 21.7-70.3), while patients with primary tumor had a median survival time of 58 months (95% CI: 0.0-121.2).

In univariate analysis in Table 2, chemotherapy treatment (hazard ratio (HR): 3.176, 95% CI 1.464-6.891; p=0.003) and positive tumor margin (hazard ratio (HR): 4.342, 95% CI 1.828-10.314; p=0.010) were shown to be adverse prognostic factors for disease-free survival (Fig 3A-B). Radiation therapy and type of surgery and AJCC stages III and IV had a non-significantly negative impact on overall survival (Table 3). Of note, AJCC staging could not be calculated as a prognostic factor for disease-free survival, because some of our patients had metastasis initially.

In multivariate analysis, only chemotherapy treatment (hazard ratio (HR): 3.415, 95% CI: 1.367-16.021; p=0.013) and positive tumor margin (hazard ratio (HR): 4.680, 95% CI 1.828-10.314; p=0.014) were found to be independent prognostic factors for disease-free and overall survival, respectively.

DISCUSSION

MPNST is widely known to be a rare and aggressive malignant soft-tissue tumor. They account for approximately 10% of all soft tissue sarcomas.[1,3] The symptoms of MPNST are non-specific. Painless mass is a common chief complaint and most patients suffer from nerve-related symptoms that are caused by tumor compression.[13,15] Our findings revealed mass to be the most common presenting symptom, while weakness and radicular pain were the least common presenting symptoms. The most widely recognized risk factor for MPNST development is NF-1, given that 10-30% of NF-1 patients will develop MPNST during their lifetime.[13] In our series, 28.8% of MPNST developed in NF-1 patients, which is comparable to the incidence reported from other studies.[4,5,11] Asavamongkolkul, *et al.* reported 2 cases of MPNST associated with NF-1, both of whom died shortly after diagnosis with distant metastases.[14] Data from survival meta-analyses reported

TABLE 1. Patient demographic and clinical characteristics.

Characteristic	Overall (n=59)	Disease free (n=50)
Gender (Female)	32 (54.2)	28 (56.0)
Mean age (year)	44	45
Follow up (months)	48 (24 – 178)*	51.5 (24 – 178)*
Number of chief complaint		
One	39 (66.1)	35 (70.0)
Two	18 (30.5)	14 (28.0)
Three	2 (3.4)	1 (2.0)
Chief complaint		
Mass	53 (89.8)	46 (92.0)
Pain	17 (28.8)	13 (26.0)
Neuropathy	9 (15.3)	5 (10.0)
Others	2 (3.4)	2 (4.0)
Presentation (Primary case)	37 (62.7)	30 (61.2)
Visit (Referred case)	45 (76.3)	38 (76.0)
Tumor site		
Neck and trunk	16 (27.1)	13 (26.0)
Extremity	42 (71.2)	36 (72.0)
Neck and Extremity	1 (1.7)	1 (2.0)
Size (More than 5 cm.)	40 (67.8)	33 (66.0)
Depth (Deep)	53 (89.8)	44 (88.0)
Grading		
Low	7 (11.9)	7 (14.0)
Intermediate	12 (20.3)	10 (20.0)
High	40 (67.8)	33 (66.0)
AJCC staging		
I	5 (8.5)	5 (11.9)
II	11 (18.6)	11 (26.2)
III	28 (47.5)	26 (61.9)
IV	7 (11.9)	0 (0.0)
Margin status		
Negative	34 (57.6)	29 (58.0)
Closed	7 (11.9)	6 (12.0)
Positive	14 (23.7)	12 (24.0)
NF-1 (Yes)	17 (28.8)	13 (26.0)
Distant metastases**	29 (58.0)	29 (58.0)
Radiation therapy (Yes)	34 (57.6)	29 (58.0)
Chemotherapy (Yes)	14 (23.7)	12 (24.0)
Dealth	24 (40.7)	

NF-1, neurofibromatosis type 1; AJCC, American Joint Committee on Cancer.
*Median (range). ** nine cases have event before begin study.

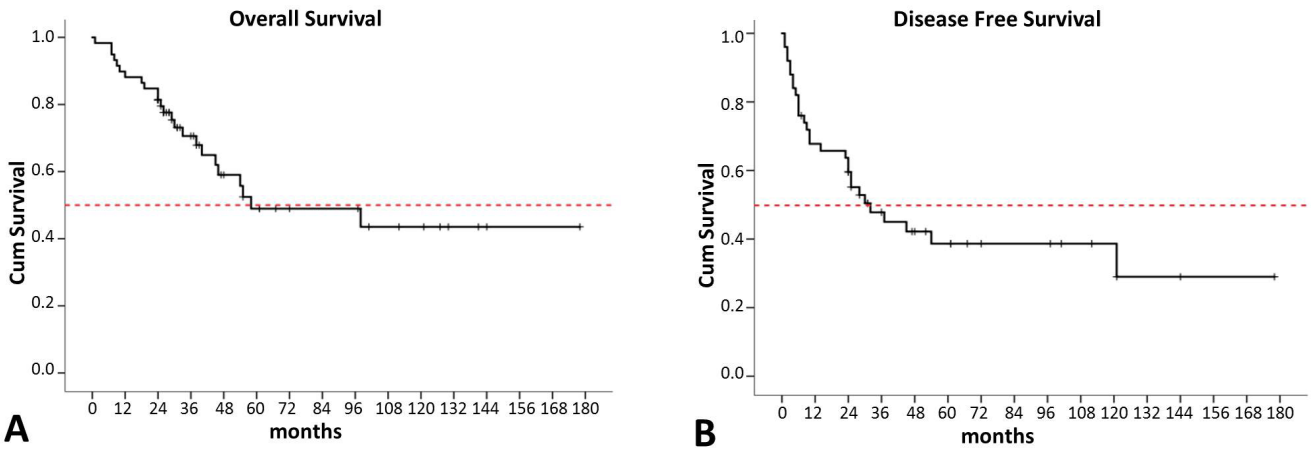

Fig 2. Survival rate of overall survival **(A)** and disease-free survival **(B)**

TABLE 2. Univariate and multivariate Cox proportional hazard regression for disease free survival (n=50).

Variables	Univariate analysis		Multivariate analysis	
	HR (95 % CI)	p value	HR (95 % CI)	p value
Gender: (Female)	1.159 (0.551-2.435)	0.697	-	-
Tumor depth: (Deep)	1.263 (0.381-4.190)	0.702	0.552 (0.132-2.310)	0.416
NF-1: (No)	1.134 (0.459-2.799)	0.785	-	-
Presentation: (Recurrence)	1.510 (0.708-3.222)	0.286	-	-
Chemotherapy: (Yes)	3.176 (1.464-6.891)	**0.003**	3.415 (1.293-9.022)	**0.013**
Radiotherapy: (Yes)	1.548 (0.725-3.305)	0.259	0.509 (0.167-1.551)	0.235
Site: (extremity)	1.065 (0.449-2.525)	0.887	2.465 (0.862-7.049)	0.092
Size: (> 5 cm.)	1.229 (0.559-2.702)	0.608	1.136 (0.450-2.873)	0.787
Surgery: (limb salvage)	2.649 (0.791-8.866)	0.114	3.481 (0.817-14.836)	0.092
Margin*:				
Close	4.342 (1.828-10.314)	**0.010**	4.680 (1.367-16.021)	**0.014**
Negative	0.571 (0.130-2.505)	0.458	0.570 (0.120-2.718)	0.481
Grade: (High)	1.902 (0.838-4.318)	0.124	1.094 (0.408-2.930)	0.858
AJCC Staging: (III + IV)	1.468 (0.651-3.308)	0.355	-	-

* Positive qualified reference group.

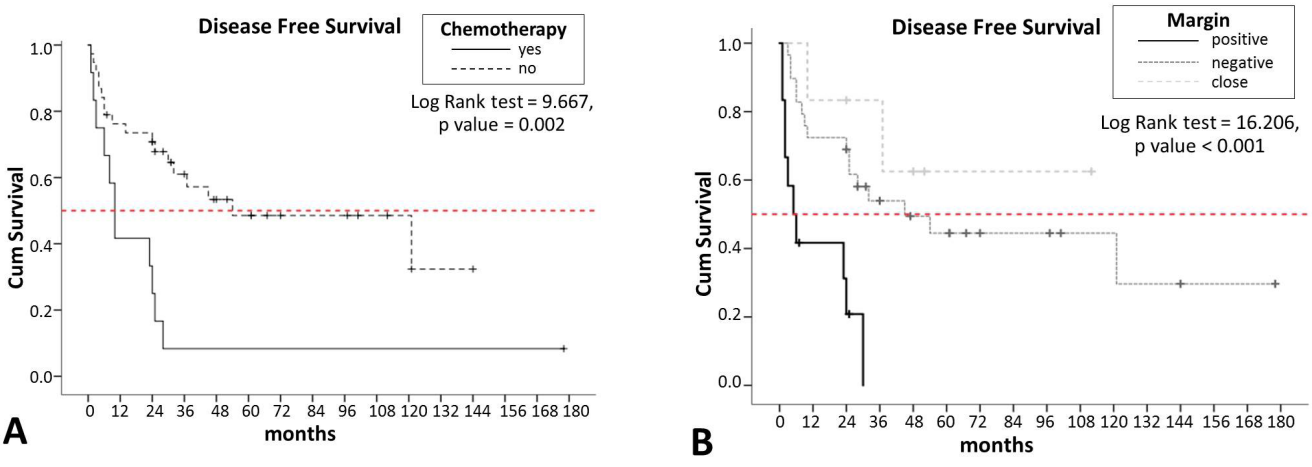

Fig 3. Disease free survival rate related to chemotherapy treatment **(A)** and tumor margin **(B)**

TABLE 3. Univariate and multivariate Cox proportional hazard regression for overall survival (n=59).

Variables	Univariate analysis		Multivariate analysis	
	HR (95 % CI)	p value	HR (95 % CI)	p value
Gender: (Female)	1.406 (0.614-3.217)	0.420	-	-
Tumor depth: (Deep)	1.139 (0.265-4.890)	0.861	-	-
NF-1: (Yes)	1.228 (0.508-2.968)	0.648	-	-
Presentation: (Primary)	1.021 (0.442-2.317)	0.978	-	-
Chemotherapy: (Yes)	1.644 (0.699-3.867)	0.255	-	-
Radiotherapy: (Yes)	1.918 (0.793-4.638)	0.148	2.095 (0.826-5.312)	0.119
Site: (extremity)	1.152 (0.427-3.112)	0.780 (0.540-4.324)	1.528	0.425
Size: (> 5 cm.)	1.386 (0.573-3.355)	0.469 (0.631-4.370)	1.660	0.305
Surgery: (limb salvage)	1.678 (0.495-5.687)	0.406	-	-
Margin*:				
Close	1.952 (0.762-5.001)	0.164	1.669 (0.616-4.519)	0.314
Negative	0.573 (0.130-2.526)	0.462	0.474 (0.103-2.182)	0.338
Grade: (High)	2.430 (0.903-6.544)	0.079	1.799 (0.638-5.069)	0.267
AJCC Staging: (III + IV)	2.251 (0.838-6.048)	0.107	-	-

* Positive qualified reference group.

a lower odds ratio for survival in MPNST patients associated with NF-1; however, the prognosis for these patients has improved in studies published in recent years.[12]

Magnetic resonance imaging (MRI) is a valuable investigation prior to histo-pathologic study. The main objective is to differentiate MPNST from benign peripheral nerve sheath tumor using criteria that includes peripheral enhancement, mass dimension, perilesional edema, and intratumoral cystic lesion. The presence of two or more of these features is suggestive of malignancy with a specificity of 90%.[16] In contrast, target sign is also helpful in differentiating benign neurofibroma from MPNST.[17] Fluorodeoxyglucose positron emission tomography (FDG-PET) has been reported as being able to differentiate MPNST and forecast patient prognosis.[2,4]

Most patients in our series were in the advance stage – predominantly AJCC stage III (47.5%) The aggressive nature of the tumors in our study was reflected, as follows: 67.8% of tumors were high grade, 89.8% were deeply located, and 67.8% were larger than 5 cm in diameter, which was comparable to data reported from other studies.[8,10,11,13,18] The number of patients who received isolated adjuvant radiation therapy, isolated adjuvant chemotherapy, and combined adjuvant treatments was 43%, 4%, and 20%, respectively, which was comparable to data from other studies.[8-11,13] Adjuvant radiation therapy is recommended for tumors with high grade, large size, tumor recurrence, and closed margin. Alternatively, adjuvant chemotherapy is considered in tumors with high grade, large size, and metastasis. Although MPNST has relatively low sensitivity to radiation, adjuvant irradiation to doses more than 60 Gy is still associated with improved local control, but not with overall disease survival.[2,6] Carbon ion irradiation is becoming more popular due to its higher biological effectiveness compared to photons or protons, but a study in MPNST treatments revealed that it provided short-term benefits, especially in patients with gross residual or unresectable tumor.[19]

Local recurrence is common in MPNST. Incidence of recurrence ranges from 32% to 65%.[2,8-11,13] There were 18 patients (30.5%) who developed local recurrence in this study. However, we were not able to correlate recurrence with initial presentation from survival analysis.

Twenty-nine patients (50.8%) developed metastasis, and 9 of those had multiple sites metastasis. Pulmonary metastasis was the most common site (44.1%), followed by bone, brain, and other locations at percentages of 11.9%, 3.4%, and 6.8%, respectively, and these rates are comparable to rates published in other reports.[6,8-11,13] Five-year overall survival and disease-free survival in this study was 46% and 40%, respectively. Our survival rates are comparable to rates from other studies that described 5-year overall survival rates that varied from 16% to 52%, and 5-year disease-free survival rates that ranged from 26% to 49%.[4-13]

A variety of significant favorable prognostic factors have been reported from several studies. (Table 4) In the present study, chemotherapy treatment and positive tumor margin was shown to be an adverse prognostic factor for disease-free survival. Cashen, *et al*. identified Musculoskeletal Tumor Society (MSTS) Rating Scale as an adverse prognostic outcome.[7] MPNST with rhabdomyoblastic differentiation or malignant triton tumor (MTT) was reported to be associated with poor prognosis and more aggressive tumor behavior.[20] Brekke, *et al*. reported that p53-positive MPNST patients are a high-risk group and they are candidates for adjuvant treatment.[21]

Chemotherapy for soft-tissue sarcoma is limited in benefit and in variety. Chemotherapy options that include vincristine, doxorubicin, ifosfamide, and etoposide have a positive effect among metastatic MPNST patients, but not in non-metastatic patients.[22] A positive trend for adjuvant radiation, but not for chemotherapy, was observed for disease-free survival and overall survival.[13,23,24] Interestingly, we found chemotherapy treatment to be an adverse prognostic factor for disease-free survival. Targeted therapy is becoming a compelling treatment option for patients with MPNST (e.g., erlotinib, sorafenib); however, some targeted therapy studies are still ongoing and some have shown no clinical response.[2] Moreover, there are studies that have demonstrated the feasibility of anti-survivin and oncolytic measles virus as a novel treatment for MPNST patients that should be studied in future clinical trials, especially in the NF-1-related group.[25-27]

This study has some mentionable limitations. First and consistent with the retrospective nature of this study, some patient data may have been incomplete. Second, the size of the study population was relatively small. As a result, our study may have lacked sufficient power to identify all significant associations. Third, the patients enrolled in this study were from a single center, the largest tertiary referral hospital. Most patients were referred to our institute with complicated and intransigent conditions.

CONCLUSION

Patients with MPNST in this series had survival rates that are comparable to those reported in other studies. Chemotherapy treatment and positive tumor margin were identified as independent adverse prognostic

TABLE 4. Significant favorable prognostic factors.

Publications	Year	Number of cases	Significant favorable prognostic factors
Anghileri[8]	2005	205	- smaller tumor size - lack of local recurrence - extremity located
Stucky[11]	2012	175	- tumor size < 5 cm - lack of local recurrence - low histologic grade - extremity located
Zou[9]	2009	140	- tumor size < 10 cm - low intensity p53 staining
Wong[6]	1998	134	- smaller tumor size - low histologic grade - perineural histologic subtype
Lafemina[10]	2012	105	- tumor size <5 cm - low histologic grade - lack of local recurrence - extremity located
Cashen[7]	2004	80	- anatomical location - MSTS staging - lower part of lower extremity
Brekke[21]	2009	64	- tumor size < 8 cm - complete surgical resection - lower intensity p53 staining
Okada[22]	2007	56	- tumor size < 7 cm - lack of metastasis
Baehring[15]	2003	54	- tumor size < 5 cm, complete surgical resection, young age, radiation therapy, lack of chemotherapy
This study	2021	51	- lack of chemotherapy, negative tumor margin

MSTS, Musculoskeletal Tumor Society; AJCC, American Joint Committee on Cancer

factors for disease-free and overall survival, respectively. Accordingly, early detection and appropriate treatment are essential for improved patient outcome.

ACKNOWLEDGEMENTS

The authors gratefully acknowledge Miss Krabkaew Soparat, M.Sc and Miss Nichakorn Khomawut for assistance with data analysis and research coordination.

Conflict of interest declaration: The authors hereby declare no personal or professional conflicts of interest regarding any aspect of this study.

Funding disclosure: This was an unfunded study.

REFERENCES

1. Weiss SW GJ. Malignant tumors of the peripheral nerves. Enzinger FM and Weiss SW ed Soft tissue tumors. 5th edition ed. St. Louis: C.V. Mosby; 2008. p. 903-44.
2. Bradford D, Kim A. Current treatment options for malignant peripheral nerve sheath tumors. Curr Treat Options Oncol 2015; 16:328.
3. Cai Z, Tang X, Liang H, Yang R, Yan T, Guo W. Prognosis and risk factors for malignant peripheral nerve sheath tumor: a systemic review and meta-analysis. World J Surg Oncol 2020; 18:257.
4. Sordillo PP, Helson L, Hajdu SI, Magill GB, Kosloff C, Golbey

RB, et al. Malignant schwannoma--clinical characteristics, survival, and response to therapy. Cancer 1981;47:2503-9.
5. Ducatman BS, Scheithauer BW, Piepgras DG, Reiman HM, Ilstrup DM. Malignant peripheral nerve sheath tumors. A clinicopathologic study of 120 cases. Cancer 1986;57:2006-21.
6. Wong WW, Hirose T, Scheithauer BW, Schild SE, Gunderson LL. Malignant peripheral nerve sheath tumor: analysis of treatment outcome. Int J Radiat Oncol Biol Phys 1998;42:351-60.
7. Cashen DV, Parisien RC, Raskin K, Hornicek FJ, Gebhardt MC, Mankin HJ. Survival data for patients with malignant schwannoma. Clin Orthop Relat Res 2004; 426: 69-73.
8. Anghileri M, Miceli R, Fiore M, Mariani L, Ferrari A, Mussi C, et al. Malignant peripheral nerve sheath tumors: prognostic factors and survival in a series of patients treated at a single institution. Cancer 2006;107:1065-74.
9. Zou C, Smith KD, Liu J, Lahat G, Myers S, Wang WL, et al. Clinical, pathological, and molecular variables predictive of malignant peripheral nerve sheath tumor outcome. Ann Surg 2009;249:1014-22.
10. Lafemina J, Qin LX, Moraco NH, Antonescu CR, Fields RC, Crago AM, et al. Oncologic Outcomes of Sporadic, Neurofibromatosis-Associated, and Radiation-Induced Malignant Peripheral Nerve Sheath Tumors. Ann Surg Oncol 2013;20:66-72.
11. Stucky CC, Johnson KN, Gray RJ, Pockaj BA, Ocal IT, Rose PS, et al. Malignant peripheral nerve sheath tumors (MPNST): the Mayo Clinic experience. Ann Surg Oncol 2012;19:878-85.
12. Kolberg M, Holand M, Agesen TH, Brekke HR, Liestol K, Hall KS, et al. Survival meta-analyses for >1800 malignant peripheral nerve sheath tumor patients with and without neurofibromatosis type 1. Neuro Oncol 2013;15:135-47.
13. Goertz O, Langer S, Uthoff D, Ring A, Stricker I, Tannapfel A, et al. Diagnosis, treatment and survival of 65 patients with malignant peripheral nerve sheath tumors. Anticancer Res 2014; 34:777-83.
14. Asavamongkolkul A, Jiranantakan T, Waikakul S, Phompitaksa K, Muangsomboon S. Malignant peripheral nerve sheath tumor with neurofibromatosis type 1: a 2-case report and review of the literature. J Med Assoc Thai 2001;84:285-93.
15. Baehring JM, Betensky RA, Batchelor TT. Malignant peripheral nerve sheath tumor: the clinical spectrum and outcome of treatment. Neurology 2003;61:696-8.
16. Wasa J, Nishida Y, Tsukushi S, Shido Y, Sugiura H, Nakashima H, et al. MRI features in the differentiation of malignant peripheral nerve sheath tumors and neurofibromas. AJR Am J Roentgenol 2010;194:1568-74.
17. Bhargava R, Parham DM, Lasater OE, Chari RS, Chen G, Fletcher BD. MR imaging differentiation of benign and malignant peripheral nerve sheath tumors: use of the target sign. Pediatr Radiol 1997;27:124-9.
18. Wakely PE, Jr., Ali SZ, Bishop JA. The cytopathology of malignant peripheral nerve sheath tumor : A report of 55 fine-needle aspiration cases. Cancer Cytopathol 2012;120:334-41.
19. Jensen AD, Uhl M, Chaudhri N, Herfarth KK, Debus J, Roeder F. Carbon Ion irradiation in the treatment of grossly incomplete or unresectable malignant peripheral nerve sheaths tumors: acute toxicity and preliminary outcome. Radiat Oncol 2015;10:109.
20. Kamran SC, Howard SA, Shinagare AB, Krajewski KM, Jagannathan JP, Hornick JL, et al. Malignant peripheral nerve sheath tumors: prognostic impact of rhabdomyoblastic differentiation (malignant triton tumors), neurofibromatosis 1 status and location. Eur J Surg Oncol 2013;39:46-52.
21. Brekke HR, Kolberg M, Skotheim RI, Hall KS, Bjerkehagen B, Risberg B, et al. Identification of p53 as a strong predictor of survival for patients with malignant peripheral nerve sheath tumors. Neuro Oncol 2009;11:514-28.
22. Okada K, Hasegawa T, Tajino T, Hotta T, Yanagisawa M, Osanai T, et al. Clinical relevance of pathological grades of malignant peripheral nerve sheath tumor: a multi-institution TMTS study of 56 cases in Northern Japan. Ann Surg Oncol 2007; 14:597-604.
23. Longhi A, Errani C, Magagnoli G, Alberghini M, Gambarotti M, Mercuri M, et al. High grade malignant peripheral nerve sheath tumors: outcome of 62 patients with localized disease and review of the literature. J Chemother 2010;22:413-8.
24. Zehou O, Fabre E, Zelek L, Sbidian E, Ortonne N, Banu E, et al. Chemotherapy for the treatment of malignant peripheral nerve sheath tumors in neurofibromatosis 1: a 10-year institutional review. Orphanet J Rare Dis 2013;8:127.
25. Ghadimi MP, Young ED, Belousov R, Zhang Y, Lopez G, Lusby K, et al. Survivin is a viable target for the treatment of malignant peripheral nerve sheath tumors. Clin Cancer Res 2012;18:2545-57.
26. Deyle DR, Escobar DZ, Peng KW, Babovic-Vuksanovic D. Oncolytic measles virus as a novel therapy for malignant peripheral nerve sheath tumors. Gene 2015;565:140-5.
27. Widemann BC, Italiano A. Biology and management of undifferentiated pleomorphic sarcoma, myxofibrosarcoma, and malignant peripheral nerve sheath tumors: State of the art and perspectives. J Clin Oncol 2018;36:160-7.