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Neuropathic pain after sarcoma surgery

Prevalence and predisposing factors

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Abstract

Surgery for sarcoma frequently causes nerve damage as the dissection often violates the internervous plane. Nerve damage may cause neuropathic pain (NP), which can result in persistent pain after surgery. This is the first study to investigate the prevalence and associated factors of postoperative NP in patients who underwent surgery for sarcoma of the extremities or pelvis.

Patients (n = 144) who underwent curative surgery at least 6 months prior to the visit for histologically confirmed sarcoma were enrolled. The presence of NP was assessed by administering PainDetect, a widely used questionnaire for detecting NP. Patients with PainDetect scores ≥13 were considered to have NP. The possible factors that might be associated with the development of NP were investigated: patient characteristics, tumor characteristics, extent of surgery, and adjuvant therapy.

Out of 144 patients, 36 patients (25%) had NP. Patients with NP had significantly worse visual analog scale score ($P < .001$), Toronto Extremity Salvage Score ($P < .001$), and Musculoskeletal Tumor Society Rating Scale score ($P < .001$) than patients without NP. Among the possible factors associated with NP, patients with NP were more likely to have undergone pelvic surgery ($P = .002$) and multiple surgeries ($P = .014$) than patients without NP. In logistic regression analysis, pelvic surgery (odds ratio = 5.05, $P = .005$) and multiple surgeries (odds ratio = 2.33, $P = .038$) were independent factors associated with NP after sarcoma surgery.

This study suggests that the prevalence of NP after surgery for sarcoma is considerable. Surgery of the pelvis and multiple surgeries are predictive of postoperative persistent NP.

Abbreviations: MSTS = the Musculoskeletal Tumor Society Rating Scale, NP = neuropathic pain, OR = odds ratio, TESS = the Toronto Extremity Salvage Score, VAS = visual analog scale.

Keywords: extremity, neuropathic, pain, questionnaire, sarcoma

1. Introduction

Neuropathic pain (NP) arises after injury to the nerves or to sensory transmitting systems in the spinal cord and brain. The classical feature of NP, in contrast to nociceptive or inflammatory pain, is a combination of sensory loss with paradoxical hypersensitivity.[1–3] NP has been implicated as the most common cause of chronic postoperative pain in a variety of surgeries, such as mastectomy, thoracotomy, and amputation.[1–7] Chronic postoperative NP persists after the surgical wound has healed and can be severely debilitating for patients. One of the major pathophysiological mechanisms of chronic postoperative NP is damage to the nerves during surgery. Identifying patients with a high risk of developing postoperative NP, using perioperatively available clinicopathologic factors, would be helpful in implementing pre-emptive measures to prevent the development of postoperative NP.[8]

Surgery for sarcoma of the extremities or pelvis often requires extensive tissue dissection to achieve adequate surgical margins for good oncologic outcome. In order to achieve adequate surgical margins, unlike surgeries of other orthopedic specialties, violation of the internervous plane is common during surgery for sarcoma. Because of this feature of sarcoma surgery, patients who undergo surgery for sarcoma of the extremities or pelvis may be prone to developing postoperative NP. To the authors' knowledge, no study has been published regarding postoperative NP in sarcoma surgery.

To fill this gap in the literature, this study aimed to examine the clinical effect of NP, prevalence of NP and to identify preoperative factors associated with the development of NP in patients who underwent surgery for sarcoma of the extremities or pelvis.

2. Materials and methods

2.1. Patients

Patients who visited orthopedic oncology clinic in single tertiary center between September 2015 and December 2015 were asked to participate in the study if they met the following criteria at the time of the visit: curative surgery for histologically confirmed sarcoma of the extremities or pelvis, age over 18 years at the visit, at least 6 months since the last surgery related to sarcoma, limb

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Synopsis: This study suggests that the prevalence of NP after sarcoma surgery is considerable. Surgery in the pelvic location and multiple surgeries are predictive factors of postoperative NP.

The authors have no conflicts of interest to disclose.

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salvaged status at the time of questionnaire, and no major nerve resection or injury related to sarcoma surgery. For the purpose of the study, patients with documented direct nerve damage, which causes NP, such as amputation or postoperative neuroma, was excluded. Two orthopedic oncologists reviewed postoperative MRI to exclude the patients with neuroma. Of the 151 patients who were eligible, 7 refused and 144 accepted participation in the study. Institutional Review Board approval was obtained and informed consent was received from all participants of this study.

2.2. Assessment of neuropathic pain

The presence of NP was assessed by the PainDetect questionnaire. The questionnaire is a well-validated screening tool for assessing NP.[9] It is completed by the patient and consists of 9 items. The first 7 items are neuropathic pain descriptors, each of which are quantified on a 0 to 5 numerical rating scale. The eighth item assesses the temporal characteristic of pain with scores of −1 to 2. The ninth item assesses the presence of radiating pain, with a score of 0 or 2. The aggregate score of the questionnaire can range from −1 to 38, and higher scores indicate more neuropathic symptoms. Scores ≥19 are considered indicative of NP, and scores 13 to 18 indicate a possible neuropathic component.[9] For the purpose of analysis, patients with a score ≥13 were considered to have NP. The mean time from the last surgery to the questionnaire was 52 months (range 6–335 months). All patients were asked to describe the symptoms "in or around" the surgical incision.

2.3. Clinical effect of neuropathic pain assessed by PainDetect questionnaire after sarcoma surgery

Clinical effect of NP assessed by the PainDetect questionnaire was evaluated by measuring the extent to which the PainDetect score related to other widely accepted measures of pain and function. For measure of pain, the visual analog scale (VAS) was assessed. For measure of function, the Toronto Extremity Salvage Score (TESS)[10] and the Musculoskeletal Tumor Society Rating Scale (MSTS)[11] were assessed.

2.4. Factors associated with neuropathic pain

Medical records were reviewed for the following potential factors that might be associated with the presence of NP after surgery for extremity sarcoma: patient characteristics, tumor characteristics, extent of surgery, and adjuvant therapy.

Patient characteristics investigated were age, sex, preoperative pain score (VAS), and oncologic outcome. The mean age at the time of surgery was 36 years (range 18–78), and there were 66 females (46%) and 78 males (54%; Table 1). The mean age at the time of the questionnaire was 43 years (range 0–78). The means of the preoperative VAS was 2.4 (range 0–10). By the time of the questionnaire, 17 patients (12%) had developed metastases, and 17 patients (12%) had developed local recurrence. At the time of the questionnaire, 114 patients (79%) were continuously disease free, 27 patients (19%) showed no evidence of disease, and patients (2%) were alive with disease. In all 17 patients with metastases, sarcoma metastasized to the lung (Table 1).

For tumor characteristics, sarcoma tissue type (soft tissue sarcoma or bone sarcoma), histological type, and anatomical location of the tumor were investigated. There were 70 soft tissue sarcomas (49%) and 74 bone sarcomas (51%). The most common histological types were liposarcoma (n=21, 15%) and

Table 1

Clinicopathologic characteristics of the patients.

Characteristics	
Age (years, SD)*	36.43 (18.23)
Sex (n, %)	
Female	66 (45.8%)
Male	78 (54.2%)
Preoperative pain score (VAS, SD)*	2.4 (2.2)
Time from last surgery (months, SD)*	51.6 (53.1)
Local recurrence (n, %)	
Absent	127 (88.2%)
Present	17 (11.8%)
Metastasis (n, %)	
Absent	127 (88.2%)
Present	17 (11.8%)
Oncologic outcome (n, %)	
CDF	114 (79.2%)
NED	27 (18.8%)
AWD	3 (2.1%)
Tissue type (n, %)	
Soft tissue sarcoma	70 (48.6%)
Bone sarcoma	74 (51.4%)
Histological type	
Osteosarcoma	48 (33.3%)
Chondrosarcoma	21 (14.6%)
Liposarcoma	21 (14.6%)
UPS	13 (9.0%)
Synovial sarcoma	9 (6.3%)
Myxofibrosarcoma	6 (4.2%)
Ewing's sarcoma	5 (3.5%)
UPS of bone	4 (2.8%)
Leiomyosarcoma	3 (2.1%)
Fibrosarcoma	2 (1.4%)
Extraskeletal chondrosarcoma	2 (1.4%)
Others	10 (6.8%)
Location	
Thigh	68 (47.2%)
Lower leg	19 (13.2%)
Pelvis/Hip	15 (10.3%)
Upper arm	11 (7.6%)
Knee	9 (6.3%)
Shoulder	9 (6.3%)
Flank	5 (3.5%)
Ankle/Foot	4(2.8%)
Wrist/Hand	2 (1.4%)
Forearm	1 (0.7%)
Elbow	1 (0.7%)
Tumor size (cm, SD)*	6.6 (4.7)
Operative time (minute, SD)*	203 (142)
Number of surgeries (n, %)	
Once	85 (59.0%)
Multiple	59(41.0%)
Bone resection (n, %)	
Not done	81 (56.3%)
Done	63 (43.8%)
Flap reconstruction (n, %)	
Not done	137 (94.9%)
Done	7 (5.1%)
Radiation therapy (n, %)	
Not done	90 (62.5%)
Done	54 (37.5%)
Chemotherapy (n, %)	
Not done	85 (59.0%)
Done	59 (41.0%)
Preoperative pain score (VAS, SD)*	2.4 (2.2)

AWD = alive with disease, CDF = continuous disease free, MSTS = the Musculoskeletal Tumor Society, NED = no evidence of disease, TESS = the Toronto Extremity Salvage Score, UPS = undifferentiated pleomorphic sarcoma, VAS = visual analog scale.

* Numbers represent mean values.

undifferentiated pleomorphic sarcoma (UPS, n = 13, 9%) for soft tissue sarcoma, and osteosarcoma (n = 48, 33%) and chondrosarcoma (n = 21, 15%) for bone sarcoma. Tumors were commonly located at thigh (n = 68, 47%), lower leg (n = 19, 13%), pelvis (n = 15, 10%), and upper arm (n = 11, 8%) regions (Table 1).

The extent of surgery was assessed using the following criteria: tumor size, operative time for the tumor resection surgery, number of surgeries performed for the primary tumor, the performance of bone resection as a part of the surgery, and the performance of flap reconstruction as a part of the surgery. The mean tumor size was 6.6 cm (range 0.2–22.1) and the mean of operative time for tumor resection surgery was 203 minutes (range 30–660). Number of surgeries was assessed by including only surgeries related to the primary tumor: resection of the primary or recurred tumor, flap reconstruction of defect, and complications. The mean number of surgeries related to the sarcoma was 1.6 (range 1–7). Eighty-five patients (59%) underwent 1 surgery, and 59 patients (41%) had 2 or more surgeries. Eighty-one patients (56%) underwent surgery without bone resection and 63 patients (44%) with bone resection. Of the 144 patients, 7 patients (5%) who had undergone flap reconstruction were identified.

For adjuvant therapy, radiation therapy and chemotherapy were investigated. Radiation therapy was administered in 54 patients (38%), all postoperatively with a median dose of 60 Gy (range 50–65 Gy). Chemotherapy was given in 59 patients (41%). For soft tissue sarcoma (STS), an ifosfamide and/or doxorubicin-containing regimen was mostly used. For osteosarcoma, adriamycin, cisplatin, and high dose methotrexate were mostly used for neoadjuvant, adjuvant chemotherapy, or both (Table 1).

2.5. Statistics

Continuous measures were compared using Mann–Whitney *U* test, and categorical variables were compared using Pearson's chi-squared test. All factors associated with the presence of NP in the univariate analysis with $P < .05$ were included in a multivariate logistic regression analysis with backward selection using the likelihood ratio test to evaluate associations linking NP. Clinical effect of NP detected by the PainDetect questionnaire was assessed by calculating Spearman's rank correlation coefficients between the PainDetect score and either the VAS, TESS, or MSTS. Strength of agreement for the correlation coefficient was expressed as follows: strong (≥ 0.70), moderate (>0.5 and <0.7), and weak (≤ 0.5).[12] Statistical analysis was performed using SPSS v.21.0 software (IBM Inc., Armonk, New York).

3. Results

3.1. Clinical effect of neuropathic pain assessed by the PainDetect questionnaire after sarcoma surgery

The mean VAS score at the time of the questionnaire was 1.80 (range 0–10). VAS score at the time of the questionnaire was reported as 0 by 56 (39%) patients. Strong correlation was found between the PainDetect score and VAS score ($r = 0.718$, $P < .001$). The means of the TESS and the MSTS score at the time of the questionnaire were 84 (range 16–100) and 24 (range 2–30), respectively. MSTS and TESS showed moderate correlation with the PainDetect score ($r = -0.587$, $P < .001$ and $r = -0.559$, $P < .001$, respectively). Patients with NP showed significantly worse VAS score ($P < .001$), TESS ($P < .001$), and MSTS score ($P < .001$) than patients without NP (Table 2).

Table 2

Comparison between patients with and without neuropathic pain.

Characteristics	With neuropathic pain (n = 36)	Without neuropathic pain (n = 108)	*P* value
Age, years	45.9 (±18.1)	42.1 (±17.1)	.306
Sex			.562
Female	15 (42%)	51 (47%)	
Male	21 (58%)	57 (53%)	
Preoperative pain score (VAS)	2.5 (±2.1)	2.3 (±2.3)	.607
Time from last surgery	55.3 (±55.5)	50.3 (±52.5)	.890
Local recurrence			1.000
Absent	32 (89%)	95 (88%)	
Present	4 (11%)	13 (12%)	
Oncologic outcome			.890
CDF	29 (81%)	85 (79%)	
NED	6 (17%)	21 (19%)	
AWD	1 (3%)	2 (2%)	
Tissue type			.564
Soft tissue sarcoma	17 (47%)	57 (53%)	
Bone sarcoma	19 (53%)	51 (47%)	
Location			.002*
Extremity	27 (75%)	102 (94%)	
Pelvis	9 (25%)	6 (6%)	
Tumor size, cm	6.6 (±4.8)	6.6 (±4.7)	.957
Operative time, minutes	196 (±141)	205 (±143)	.865
Number of surgeries			.014*
Once	15 (41.7%)	70 (64.8%)	
Multiple	21 (58.3%)	38 (35.2%)	
Bone resection			.628
Not done	19 (53%)	62 (57%)	
Done	17 (47%)	46 (43%)	
Radiation therapy			.842
Not done	22 (61%)	68 (63%)	
Done	14 (39%)	40 (37%)	
Chemotherapy			.282
Not done	24 (67%)	61 (56%)	
Done	12 (33%)	47 (44%)	
Current pain score (VAS)	3.8 (±2.6)	1.1 (±1.5)	<.001
TESS score	72.9 (±19.8)	88.0 (±15.6)	<.001
MSTS score	19.3 (±6.9)	25.5 (±4.8)	<.001

AWD = alive with disease, CDF = continuous disease free, MSTS = the Musculoskeletal Tumor Society, NED = no evidence of disease, TESS = the Toronto Extremity Salvage Score, VAS = visual analog scale.

* means statistically significant.

3.2. Prevalence of neuropathic pain after sarcoma surgery

Overall, the mean PainDetect score was 8.2 (median 7.0; range 0–28; Fig. 1). As for the 7 NP descriptors, the mean of the total score of the 7 items was 7.47 (range 0–27; Fig. 2). Sensation of numbness was the item with the highest score (1.87, range 0–5) and was rated as "very strongly," "strongly," or "moderately" numb in 53 patients (37%). Pain triggered by light touching showed the lowest score (0.53, range 0–5) and was rated as "never," "hardly noticed," or "slightly" in 134 patients (93%) (Fig. 2). As for the temporal characteristic of pain, 93 patients (65%) reported to have experienced a temporal pattern of pain. The most commonly reported pattern was pain attacks without pain between them (57%), followed by persistent pain with slight fluctuations (30%), persistent pain with pain attacks (12%), and pain attacks with pain between them (1%). Twenty-seven patients (19%) reported radiating pain. Definite NP was present in 7% (n = 10) of the patients, with an additional 18% (n = 26) having probable NP. In all, of the 144 patients, 36 patients (25%) were identified to have NP with PainDetect scores ≥ 13.

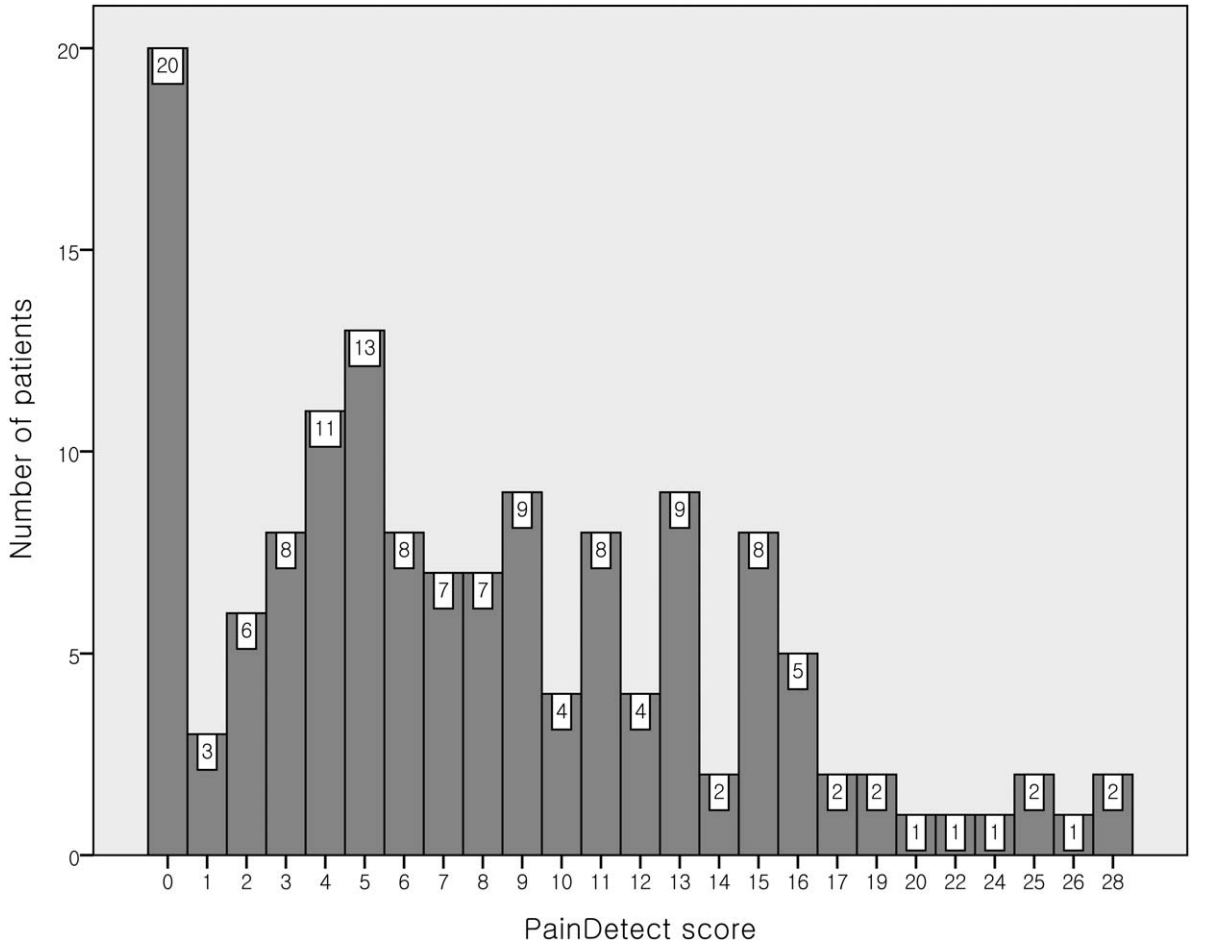

Figure 1. Histogram of total PainDetect scores. *Y*-axis depicts number of patients of each score.

3.3. Comparison of characteristics between patients with and without neuropathic pain

Patients with NP were more likely to have undergone pelvic surgery ($P=.002$) and more than 2 surgeries ($P=.014$). Among the possible factors associated with NP, no significant differences were found with respect to age, sex, preoperative pain score, time from the last surgery, local recurrence, oncologic outcome, sarcoma tissue type, tumor size, operative time, bone resection, radiation therapy, or chemotherapy (Table 2).

3.4. Predictive factors of neuropathic pain in sarcoma surgery

In univariate logistic regression analysis of associated factors of NP after sarcoma surgery, pelvic tumor location ($P=.002$) and multiple surgeries ($P=.016$) were significant (Table 3). In multivariate analysis, pelvic tumor location (odds ratio [OR]= 5.05, $P=.005$) and multiple surgeries (OR=2.33, $P=.038$) remained as independent factors associated with postoperative NP in sarcoma surgery (Table 3).

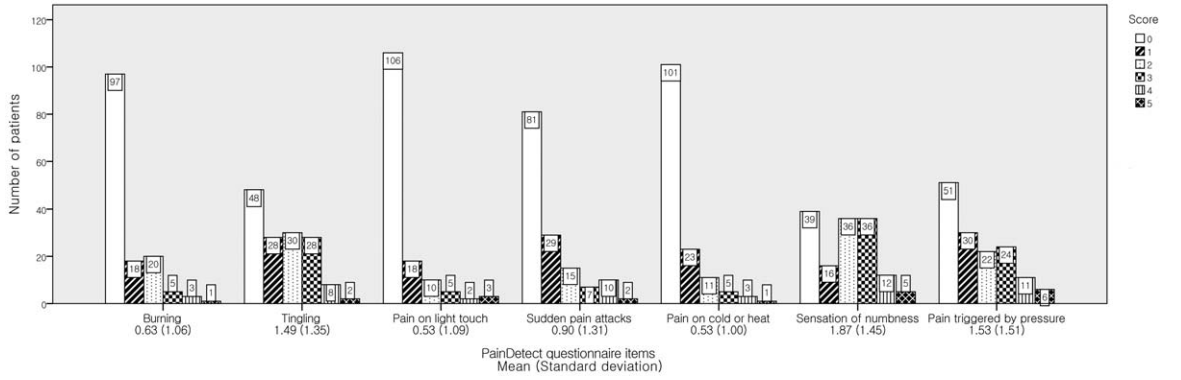

Figure 2. Histogram of PainDetect scores for each descriptor. *Y*-axis depicts number of patients of each score.

Table 3

Factors associated neuropathic pain.

Factors	Univariate			Multivariate		
	OR	95%CI	*P*	OR	95%CI	*P*
Age, years	1.01	0.99 to 1.03	.389			
Sex			.563			
Female	1.00					
Male	1.25	0.58 to 2.69				
Preoperative pain score (VAS)	1.01	1.00 to 1.03	.159			
Time from last surgery	1.00	1.00 to 1.00	.631			
Local recurrence			.913			
Absent	1.00					
Present	0.91	0.28 to 3.00				
Oncologic outcome			.890			
CDF	1.00					
NED	0.83	0.31 to 2.28				
AWD	1.47	0.13 to 16.77				
Tissue type			.564			
Soft tissue sarcoma	1.00					
Bone sarcoma	1.25	0.59 to 2.66				
Location			.002*			.005*
Extremities	1.00			1.00		
Pelvis	5.67	1.86 to 17.31		5.05	1.61 to 15.80	
Tumor size	1.00	0.92 to 1.09	.978			
Operative time	1.00	0.99 to 1.00	.770			
Number of surgeries			.016*			.038*
Once	1.00			1.00		
Multiple	2.58	1.19 to 5.58		2.33	1.05 to 5.18	
Bone resection			.628			
Not done	1.00					
Done	1.21	0.57 to 2.57				
Radiation therapy			.842			
Not done	1.00					
Done	1.08	0.50 to 2.35				
Chemotherapy			.284			
Not done	1.00					
Done	0.65	0.29 to 1.43				

AWD = alive with disease, CDF = continuous disease free, NED = no evidence of disease, VAS = visual analog scale.
* Means statistically significant.

4. Discussion

Persistent NP is a major component of chronic postoperative pain in various surgeries and can be a source of considerable disability and psychological distress for patients.[13] A large component of NP is thought to be caused by nerve injury during surgery.[8] As complete removal of the tumor takes priority over preservation of normal tissue in sarcoma surgery, nerve injuries are frequent in sarcoma surgery. Although the nerve injuries can be identified in cases of major nerve resection or amputation, the majority of the nerve injuries are not identifiable in sarcoma surgery. Thus, patients undergoing surgery for sarcoma may have a high probability of developing postoperative NP. Identification of predictive factors of postoperative NP is needed for planning effective strategies to treat NP. This study investigated the clinical effect of NP in sarcoma patients, the prevalence of NP after sarcoma surgery and examined various potentially associated factors. Pelvic surgery and multiple surgeries were identified as independent predictors of postoperative NP.

Because pain is essentially a subjective experience with patient-specific symptoms, NP is commonly diagnosed with a patient-reported questionnaire.[1,9] In this study, the PainDetect questionnaire was used to identify NP in patients who underwent surgery for extremity sarcoma. The questionnaire was originally conceptualized and validated by Freynhagen et al[9] for use with patients with back pain. This easy-to-use questionnaire incorporates patient-reported items including seven weighted sensory descriptor items and two items relating to spatial and temporal characteristics of individual pain patterns. The questionnaire was originally developed for patients with back pain but has been utilized in a variety of diseases, such as osteoarthritis, diabetic neuropathy, post-herpetic neuralgia, carpal tunnel syndrome, shoulder impingement syndrome, fibromyalgia, and sickle cell disease.[14–18] It has been used to assess NP in several postoperative settings such as mastectomy,[19] thoracotomy,[20] and arthroscopic surgery of the knee.[21]

In this study, patients who underwent pelvic surgery had a significantly greater risk of developing NP than those who had extremity surgery. Pelvic sarcomas frequently present with larger tumors and necessitate dissection that is more extensive and longer operative time than extremity sarcomas. Moreover, the extensive nerve plexus of the pelvis may be at risk of injury from stretch during retraction as well as from frank transection.[13] These findings align with those of previous studies, in which patients undergoing more extensive surgery had higher chance of developing postoperative NP in various types of surgeries.[20,22] From the data in this study, tumor size and operative time were not associated with the development of NP. Therefore, extensive dissection and complexity of anatomical structure in pelvic area

may be more significant causes of NP than tumor size or operative time.

In this study, patients with multiple surgeries had a significantly greater risk of developing NP. The difficulty in surgical dissection due to the effects of previous surgery, such as scarring and violation of the normal anatomy, may result in damage to peripheral nerves. Moreover, repeat injuries to the peripheral nerves could contribute to the development of NP. Similar observations were made in inguinal hernia repair and shoulder surgeries, in which repeated surgeries resulted in unsatisfactory pain relief.[23,24] Identified significant predictive factors of pelvic and multiple surgery were related more of anatomic or technical issue than specific disease, extremity sarcoma.

Orthopedic literature on postoperative NP is scarce. In shoulder replacement surgery, the prevalence of NP was reported as 13%.[25] In osteoarthritis of knee, the prevalence of NP assessed by PainDetect was reported as 37%,[26] but this data did not reflect postoperative pain. However, orthopedic literature on chronic postoperative pain, which mostly results from NP, is not scarce. The prevalence of chronic postoperative pain varies from 7% to 23% after hip replacement and 10% to 34% after knee replacement.[27] Taken together, the prevalence of persistent NP in extremity sarcoma surgery could conceivably be higher than that in other types of orthopedic surgery.

The results of this study highlight the potential for prevention strategies for postoperative NP in sarcoma surgery. Preoperatively, identifying patients with risk factors of developing postoperative NP is needed. Intraoperatively, the use of less invasive and more precise dissection is needed to avoid nerve damage.[2] Perioperative multimodal pharmacological analgesia that targets NP as well as inflammatory pain may be effective.[7] Postoperatively, patients may need to be assessed for signs of NP. Antidepressants or anticonvulsants can be administered in the postoperative period.[28]

There are a few limitations in this study. First, NP was assessed by the PainDetect questionnaire as a screening tool. However, these screening tools do not identify about 10% to 20% of patients with clinician-diagnosed NP[29] and is not validated tool in patients with postsurgical NP. However, the questionnaire showed significant correlations with pain VAS and functional scores that were commonly used in extremity sarcoma in this study. The additional use of objective measures such as quantitative sensory testing or laser evoked potential would have aided in confirming the findings of this study.[29] Second, as the neuropathic component of postoperative pain becomes more significant when recovery progresses, serial examinations of the changes in the PainDetect score over the postoperative period could further show the validity of the study. Third, a relatively small number of patients from a single institution limit the interpretation of the results in this study. A larger number of patients from multiple institutions would be necessary to verify the results of this study.

In conclusion, this study suggests that the prevalence of NP after sarcoma surgery is considerable. Surgery in the pelvic location and multiple surgeries are predictive factors of postoperative NP.

References

[1] Baron R, Binder A, Wasner G. Neuropathic pain: diagnosis, pathophysiological mechanisms, and treatment. Lancet Neurol 2010;9:807–19.

[2] Kehlet H, Jensen TS, Woolf CJ. Persistent postsurgical pain: risk factors and prevention. Lancet 2006;367:1618–25.

[3] Macrae WA. Chronic post-surgical pain: 10 years on. Br J Anaesth 2008;101:77–86.

[4] Duffy JR, Warburg FE, Koelle SF, et al. Pain-related psychological distress, self-rated health and significance of neuropathic pain in Danish soldiers injured in Afghanistan. Acta Anaesthesiol Scand 2015;59:1367–76.

[5] Johansen A, Romundstad L, Nielsen CS, et al. Persistent postsurgical pain in a general population: prevalence and predictors in the Tromso study. Pain 2012;153:1390–6.

[6] Macrae WA. Chronic pain after surgery. Br J Anaesth 2001;87:88–98.

[7] Shipton E. Post-surgical neuropathic pain. ANZ J Surg 2008;78:548–55.

[8] Kalkman CJ, Visser K, Moen J, et al. Preoperative prediction of severe postoperative pain. Pain 2003;105:415–23.

[9] Freynhagen R, Baron R, Gockel U, et al. painDETECT: a new screening questionnaire to identify neuropathic components in patients with back pain. Curr Med Res Opin 2006;22:1911–20.

[10] Kim HS, Yun J, Kang S, et al. Cross-cultural adaptation and validation of the Korean Toronto Extremity Salvage Score for extremity sarcoma. J Surg Oncol 2015;112:93–7.

[11] Enneking WF, Dunham W, Gebhardt MC, et al. A system for the functional evaluation of reconstructive procedures after surgical treatment of tumors of the musculoskeletal system. Clin Orthop Relat Res 1993;241–6.

[12] Terwee CB, Bot SD, de Boer MR, et al. Quality criteria were proposed for measurement properties of health status questionnaires. J Clin Epidemiol 2007;60:34–42.

[13] Jung BF, Ahrendt GM, Oaklander AL, et al. Neuropathic pain following breast cancer surgery: proposed classification and research update. Pain 2003;104:1–3.

[14] Baron R, Tolle TR, Gockel U, et al. A cross-sectional cohort survey in 2100 patients with painful diabetic neuropathy and postherpetic neuralgia: differences in demographic data and sensory symptoms. Pain 2009;146:34–40.

[15] Gwilym SE, Keltner JR, Warnaby CE, et al. Psychophysical and functional imaging evidence supporting the presence of central sensitization in a cohort of osteoarthritis patients. Arthritis Rheum 2009;61:1226–34.

[16] Gwilym SE, Oag HC, Tracey I, et al. Evidence that central sensitisation is present in patients with shoulder impingement syndrome and influences the outcome after surgery. J Bone Joint Surg Br 2011;93:498–502.

[17] Sonohata M, Tsuruta T, Mine H, et al. The relationship between neuropathic pain, and the function of the upper limbs based on clinical severity according to electrophysiological studies in patients with carpal tunnel syndrome. Open Orthop J 2013;7:99–102.

[18] Koroschetz J, Rehm SE, Gockel U, et al. Fibromyalgia and neuropathic pain—differences and similarities. A comparison of 3057 patients with diabetic painful neuropathy and fibromyalgia. BMC Neurol 2011;11:55.

[19] Henderson JR, Tao A, Kirwan CC, et al. Immediate breast reconstruction does not increase postmastectomy pain. Ann Surg Oncol 2014;21:113–7.

[20] Steegers MA, Snik DM, Verhagen AF, et al. Only half of the chronic pain after thoracic surgery shows a neuropathic component. J Pain 2008;9:955–61.

[21] Valdes AM, Suokas AK, Doherty SA, et al. History of knee surgery is associated with higher prevalence of neuropathic pain-like symptoms in patients with severe osteoarthritis of the knee. Semin Arthritis Rheum 2014;43:588–92.

[22] Shipton EA, Tait B. Flagging the pain: preventing the burden of chronic pain by identifying and treating risk factors in acute pain. Eur J Anaesthesiol 2005;22:405–12.

[23] Sondenaa K, Nesvik I, Breivik K, et al. Long-term follow-up of 1059 consecutive primary and recurrent inguinal hernias in a teaching hospital. Eur J Surg 2001;167:125–9.

[24] Mikkelsen T, Werner MU, Lassen B, et al. Pain and sensory dysfunction 6 to 12 months after inguinal herniotomy. Anesth Analg 2004;99:146–51.

[25] Bjornholdt KT, Brandsborg B, Soballe K, et al. Persistent pain is common 1–2 years after shoulder replacement. Acta Orthop 2015;86:71–7.

[26] Hochman JR, Davis AM, Elkayam J, et al. Neuropathic pain symptoms on the modified painDETECT correlate with signs of central sensitization in knee osteoarthritis. Osteoarthritis Cartilage 2013;21:1236–42.

[27] Beswick AD, Wylde V, Gooberman-Hill R, et al. What proportion of patients report long-term pain after total hip or knee replacement for osteoarthritis? A systematic review of prospective studies in unselected patients. BMJ Open 2012;2:e000435.

[28] Fassoulaki A, Sarantopoulos C, Melemeni A, et al. EMLA reduces acute and chronic pain after breast surgery for cancer. Reg Anesth Pain Med 2000;25:350–5.

[29] Cruccu G, Sommer C, Anand P, et al. EFNS guidelines on neuropathic pain assessment: revised. Eur J Neurol 2010;17:1010–8.