Table 2 The changes of respiratory parameters in six eligible patients before and after NPPV application

No.	P/F ratio (mmHg)		RR (/min)		$PaCO_2$ (mmHg)	
	Before	After	Before	After	Before	After
1	201.2	287.4	15	12	32.6	33.0
2	248.3	280.4	13	11	33.3	36.5
3	246.4	298.2	16	14	36.7	28.9
4	351.2	458.4	31	25	34.1	34.7
5	206.6	228.6	18	20	41.3	40.6
6	219.2	398	16	20	25.8	25.7
mean ± SD	245 ± 55	325 ± 85*	18.2 ± 6.5	17.0 ± 5.5	34.0 ± 5.1	33.2 ± 5.3

*$p < 0.05$ compared with before. P/F ratio, partial pressure of arterial oxygen tension to inspiratory oxygen fraction ratio; RR, respiratory ratio; $PaCO_2$, partial pressure of arterial carbon dioxide.

studies examined the effect of NPPV to facilitate a weaning from IMV in patients who required long-term ventilator support and suffered from persistent weaning failure [6-8], our study is quite different from these previous studies in some points. Contrary to previous studies which included medial ICU patients with predominantly hypercapnic COPD patients, our study targeted only patients who have risk factors for developing hypoxemic respiratory failure after cardiovascular surgery. Besides, we applied NPPV after extubation in patients who could maintain sufficient oxygenation at PEEP level of 8 cmH_2O but failed at 5 cmH_2O PEEP following our weaning protocol in this study. We guessed that the major reasons why these six patients required moderate PEEP level were atelectasis, overhydration, and cardiogenic pulmonary edema due to the long procedure of cardiac surgery and large amount of transfusion required for perioperative hemodynamic stability. Thus, it is unclear whether this weaning technique can be generalized to other type of hypoxemic respiratory failure patients. However, one recent small randomized controlled study, including 20 patients, demonstrated that NPPV application after early extubation from moderate level of PEEP was beneficial in non-surgical patients with resolving hypoxemic respiratory failure [16]. Furthermore, early application of nasal CPAP after extubation from 7 cm H_2O PEEP was reported to reduce pulmonary morbidity and length of hospital stay following the surgical repair of thoracoabdominal aortic aneurysms [17]. Thus, weaning strategy through NPPV for patients requiring moderate level of PEEP might be beneficial in wide range of hypoxemic respiratory failure, which should be confirmed by a large randomized controlled trial.

Table 3 The changes of hemodynamic parameters in six eligible patients before and after NPPV application

No.	Systolic BP (mmHg)		HR (beats/min)	
	Before	After	Before	After
1	122	113	89	78
2	145	135	94	87
3	112	121	79	85
4	108	102	82	78
5	138	136	61	65
6	142	128	71	62
mean ± SD	128 ± 16	123 ± 13	79 ± 12	76 ± 10

NPPV, noninvasive positive pressure ventilation; BP, blood pressure; HR, heart rate.

Oxygenation improved significantly after the initiation of NPPV compared with before extubation even though the applied PEEP level was the same (8 cmH_2O). While the exact mechanisms for this improvement is unknown, some possible mechanisms are considered, such as absence of sedation other than dexmedetomidine, increased patient's activity, and improvement of dorsal ventilation leading to reduced V/Q mismatch. Although this improvement of oxygenation could support the use of this weaning strategy, there are some concerns to apply this technique. Delayed intubation after developing respiratory failure is associated with worse outcome [18,19], thereby re-intubation should not be hesitated if respiratory failure once develops. The protocol to prevent delayed re-intubation should be made in all ICU where patients with respiratory failure are treated by NPPV. Tolerance of patients is also one of the key factors in managing NPPV successfully. Although patients were sedated with remifentanil or propofol to increase NPPV tolerance in previous studies [20,21], we used continuous dexmedetomidine infusion, which has little respiratory depressant effects, to relieve discomfort as a routine practice, probably contributing to the high successful rate of NPPV management in our ICU.

There are several limitations to interpret the data herein. *First*, this study is not a randomized controlled trial but an observational study, and the sample size was too small. It remains unknown whether this technique can reduce the length of mechanical ventilation, the rate of complication relating to IMV, the length of ICU stay, and the mortality compared with the conventional weaning strategy. However, all 6 patients enrolled in this study could wean from IMV through application of NPPV without any progression

to respiratory failure and the need of re-intubation, while 3 of 12 patients who were liberated from IMV to oxygen face mask were re-intubated even though they passed SBT at the low PEEP level (5 cmH_2O). Although the rate of re-intubation did not reach significant difference, this might be attributed to the small sample size. Whether this weaning strategy could reduce the rate of re-intubation, it should be evaluated in a randomized controlled trial in the future. *Second*, we performed two sequential SBT for 4 h in this study protocol which could be too long procedure, while some weaning guideline recommends SBT should be performed every 24 h [22]. However, there are no evidences as to the appropriate duration of SBT. *Finally*, there is no rationale for 8 cm H_2O of PEEP level at which trachea were extubated in this study. It may be plausible that patients could be liberated from IMV at higher level of PEEP, which should be examined in a future study.

Conclusions

Application of NPPV after liberation from IMV via tracheal intubation was safe and effective in patients who required moderate level of PEEP for sufficient oxygenation after cardiovascular surgery. The P/F ratio improved significantly 2 h after initiation of NPPV compared with that just before extubation, and all patients could wean successfully without development of respiratory failure and re-intubation. A randomized controlled trial is warranted to confirm the effectiveness of this technique before it is widely used in other ICU.

Abbreviations

COPD: chronic obstructive pulmonary disease; CPAP: continuous positive airway pressure; FIO_2: inspiratory oxygen fraction; ICU: intensive care unit; IMV: invasive mechanical ventilation; NPPV: noninvasive positive pressure ventilation; P/F ratio: PaO_2 to FIO_2 ratio; $PaCO_2$: partial pressure of arterial carbon dioxide; PaO_2: partial pressure of arterial oxygen tension; PEEP: positive end-expiratory pressure; PS: pressure support; SBT: spontaneous breathing trial; SD: standard deviation; SOFA score: sequential organ failure assessment score; SpO_2: O_2 saturation monitored by pulse oximetry.

Competing interests

The authors declare that they have no competing interest.

Authors' contributions

TS planned and conducted the study, collected the data, and drafted the manuscript. TK, ST, YM, and YM participated in planning the study design, conducted the study, and helped in drafting the manuscript. JM gave advice for planning the study, coordinated all the study, and helped in drafting the manuscript. SK and NK participated in planning the study design, analyzed the data, and helped in drafting the manuscript. HM helped to coordinate the study, and supervised all parts of the study. All authors read and approved the final manuscript.

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Perioperative factors affecting the occurrence of acute complex regional pain syndrome following limb bone fracture surgery: data from the Japanese Diagnosis Procedure Combination database

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Abstract

Objective. Complex regional pain syndrome (CRPS) describes a broad spectrum of symptoms that predominantly localize to the extremities. Although limb fracture is one of the most frequently reported triggering events, few large-scale studies have shown the occurrence of and factors associated with CRPS following limb fracture. This study aimed to show the occurrence and identify of those factors.

Methods. Using the Japanese Diagnosis Procedure Combination database, we identified 39 patients diagnosed with CRPS immediately after open reduction and internal fixation (ORIF) for limb fracture from a cohort of 185 378 inpatients treated with ORIF between 1 July and 31 December of each year between 2007 and 2010. Patient and clinical characteristics such as age, gender, fracture site, duration of anaesthesia and use of regional anaesthesia were investigated by logistic regression analyses to examine associations between these factors and the in-hospital occurrence of CRPS after ORIF.

Results. The occurrence of CRPS was relatively high in fractures of the distal forearm, but low in fractures of the lower limb and in patients with multiple fractures. Generally females are considered to be at high risk of CRPS; however, we found a comparable number of male and female patients suffering from CRPS after ORIF for limb fracture. In terms of perioperative factors, a longer duration of anaesthesia, but not regional anaesthesia, was significantly associated with a higher incidence of CRPS.

Conclusion. Although a limited number of CRPS patients were analysed in this study, reduced operative time might help to prevent the development of acute CRPS following limb fracture.

Key words: complex regional pain syndrome, bone fracture, open reduction and internal fixation, factors, regional anaesthesia.

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Introduction

Complex regional pain syndrome (CRPS) is a poorly understood syndrome that describes a broad spectrum of sensory, motor and autonomic-like features that predominantly manifest in the extremities. CRPS is usually encountered in patients recovering from limb trauma and they complain of intense pain that is disproportionate to the inciting event. Furthermore, the activities of daily living are significantly impaired in many CRPS patients because of this intense perceived pain [1]. While the underlying pathophysiological mechanisms of CRPS remain controversial, the autonomic-like, trophic and

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motor disturbances are key features of CRPS, with the exception of spontaneous pain and allodynia. To elucidate the mechanisms of CRPS onset, some investigations have categorized CRPS into several subgroups based on the key features or somatosensory abnormalities [2, 3]. Since CRPS patients frequently present with different features (e.g. redness or pallor of the skin) and/or somatosensory abnormalities (e.g. hyperalgesia or hypoaesthesia) at various intervals, CRPS is often categorized on the basis of disease duration and the presence of certain features related to these intervals [4, 5]. Given this close temporal clustering of CRPS symptoms and signs, it may be assumed that focusing on a particular time frame for patients with CRPS provides a relatively homogeneous CRPS subgroup for investigations as to its aetiology.

Since the clinical features of CRPS are so diverse, another approach would be to analyse patient demographic data, particularly in terms of a potential triggering event. Limb fracture is one of the most frequently reported triggering events [6]. In attempting to gather a homogeneous CRPS study population, Schurmann *et al.* [7] recruited patients with a limb fracture and demonstrated that the sympathetic nervous system in the affected limb could possibly predict the development of CRPS. Another investigation that included patients with a fracture reported that no psychological factors could predict the development of CRPS, indicating that anxiety and depression are not predisposing factors for CRPS [8]. Furthermore, a prospective evaluation of CRPS patients after fracture revealed that specific bone fractures (i.e. dislocation and intra-articular fracture) are associated with an elevated incidence of CRPS [9]. Therefore, focusing on the triggering events for CRPS, in addition to the time frame, may help to disentangle the underlying mechanisms of its aetiology. However, the precedent study included a mixed-fracture patient cohort, with varied disease duration (within 1 year) and varied treatments for the fracture. As a result, the study identified a diverse array of features for CRPS; for instance, the prevalence of CRPS at 3 months after fracture increased significantly from that at the time of plaster removal (~6 weeks after the fracture), but decreased again by the 1-year mark [9]. Therefore a focus on the triggering events for CRPS proved inadequate as an independent method to elucidate the mechanisms of CRPS onset.

In the present study we sought to find a close-to-homogeneous population and thus sampled data from CRPS patients with at least one common aetiology (i.e. limb bone fracture), one common treatment [i.e. open reduction and internal fixation (ORIF)] and one common phase of disease (i.e. the acute phase of CRPS immediately after bone fracture). We used a nationwide, inpatient database to collect the data because the incidence of CRPS is very low: 5.5 and 26.2 cases per 100 000 person-years in the USA [10] and the Netherlands [6], respectively. Our objectives were to specify the demographic and medical factors that most likely constitute a risk of developing CRPS and to search for potential interventions to reduce the occurrence of CRPS in these limb fracture patients.

Materials and methods

DPC database

We used the nationwide inpatient database, the Japanese Diagnosis Procedure Combination (DPC) database, to collect the data. The details of the DPC inpatient database are described elsewhere [11, 12]. Briefly, the DPC is a Japanese case-mix classification system linked with a lump-sum payment system. All 82 academic hospitals are obliged to adopt the DPC system, while community hospitals can voluntarily adopt it. A survey of DPC hospitals is conducted between July 1 and December 31 each year by the DPC Research Group, funded by the Ministry of Health, Labour, and Welfare, Japan. The survey includes anonymous data of 3.19 million discharged cases from 952 acute care hospitals in 2010, representing ~45% of all admissions to acute care hospitals in Japan. The database includes the following data: the unique identifier of each hospital; patients' age and sex; main diagnoses, co-morbidities at admission and complications after admission that are coded by the International Classification of Diseases 10th Revision (ICD-10) codes; procedures coded by Japanese original codes; duration of anaesthesia (min); length of stay (days) and in-hospital mortality. Co-morbidities present at admission are clearly differentiated from complications after admission. Attending physicians are obliged to record the diagnoses for each patient at discharge with reference to medical charts to optimize the accuracy of the recorded diagnoses. Data compliance is mandatory to obtain reimbursement of medical fees.

The DPC database is a secondary database of administrative claims data. All the data were de-identified in each hospital and the anonymized data were sent to the study group. Informed consent to each patient was therefore waved because of the anonymous nature of the data. Study approval was obtained from the Institutional Review Board at the University of Tokyo.

Data extraction

We identified the records of all patients in the DPC database who underwent surgical repair (i.e. ORIF) for fracture of upper and lower limbs during 2007–10, including fracture of the shoulder and upper arm (ICD-10 code, S42), fracture of the forearm (S52), fracture at the wrist and hand level (S62), fracture of the femur (S72), fracture of the lower leg (S82), fracture of the foot (S92) and fractures involving multiple regions of the upper and lower limbs (T02.2–T02.6). For each patient we extracted the following data: sex, age, main diagnosis, type of surgery, duration of anaesthesia (ranging from the time of induction of anaesthesia to awakening in recovery), type of anaesthesia, length of stay and discharge status.

Fracture sites were categorized into the following three groups: upper limbs (ICD-10 codes, S42, S52 and S62), lower limbs (S72 and S82 and S92) and multiple regions (T02.2–T02.6). The duration of anaesthesia was categorized into three subgroups: $\leqslant$119 min, 120–179 min or $\geqslant$180 min. Regional anaesthesia included spinal

TABLE 1 Patient characteristics

	All	Upper limb	Lower limb	Both	*P*-value
Total, *n* (%)	185 378 (100.0)	49 650 (100.0)	133 030 (100.0)	2698 (100.0)	—
Age, *n* (%), years					
⩽59	45 444 (24.5)	24 645 (49.6)	19 758 (14.9)	1041 (38.6)	<0.001
60–79	59 846 (32.3)	17 869 (36.0)	40 961 (30.8)	1016 (37.7)	—
⩾80	80 088 (43.2)	7136 (14.4)	72 311 (54.4)	641 (23.8)	—
Sex, *n* (%)					
Male	63 898 (34.5)	24 283 (48.9)	38 376 (28.8)	1239 (45.9)	<0.001
Female	121 480 (65.5)	25 367 (51.1)	94 654 (71.2)	1459 (54.1)	—
Duration of anaesthesia, *n* (%)					
⩽119 min	101 220 (54.6)	23 806 (48.0)	76 769 (57.7)	645 (23.9)	<0.001
120–179 min	53 413 (28.8)	15 958 (32.1)	36 869 (27.7)	586 (21.7)	—
⩾180 min	30 745 (16.6)	9886 (19.9)	19 392 (14.6)	1467 (54.4)	—
Regional anaesthesia	83 945 (45.9)	7861 (16.4)	75 218 (56.9)	866 (32.4)	—
Length of stay, median (IQR), days	26 (14–44)	8 (4–18)	31 (21–50)	36 (21–60)	<0.001
In-hospital death, *n* (%)	2364 (1.3)	120 (0.2)	2215 (1.7)	29 (1.1)	—

IQR: interquartile range.

anaesthesia, epidural anaesthesia and peripheral nerve blocks.

We identified patients who were postoperatively diagnosed with CRPS during hospitalization with an ICD-10 code-based searching algorithm, including the ICD-10 code M89.0 (algodystrophy, shoulder–hand syndrome, Sudeck's atrophy or reflex sympathetic dystrophy) and G56.4 (causalgia). Japanese physicians have quite strictly diagnosed CRPS since 2005 on the basis of the original Japanese criteria [i.e. (i) continuing pain disproportionate to any inciting event and (ii) the presence of at least two symptoms and at least two signs of sensory, sudomotor, oedema, motor and trophic abnormalities] [13]; this criteria follows that set by Bruehl *et al.* [14] and was first published in 2005. Among these patients, a diagnosis of a peripheral nerve injury was further identified by the ICD-10 code that indicates a specified peripheral nerve injury (G56.1, G56.2, G56.3, G57.0, G57.2, G57.3, G57.4, G57.6, S44$, S54$, S64$, S74$, S84$, and S94$). The ICD-10 code includes symptom diagnosis, which sometimes indicates persistent pain itself but does not always indicate the presence of nerve injury [e.g. other nerve root and plexus disorders (G54.8)]. Therefore we gathered data on patients reliably coded with M89.0 and G56.4 to minimize the risk of including non-CRPS patients in a CRPS research sample.

Statistical analyses

We performed univariate comparisons of proportions using the chi-square test. Univariate and multivariate logistic regression analyses were performed to examine the relationships of each factor with the occurrence of postoperative CRPS. Differences were considered to be statistically significant at $P < 0.01$. All analyses were performed using SPSS software, version 19 (IBM SPSS, Armonk, NY, USA).

Results

Of the 11.6 million inpatients included in the DPC database during 2007–10, we identified 185 378 eligible patients. The background characteristics of the patients are shown in Table 1. The mean age (S.D.) of the patients was 68.6 years (23.2). Females suffered from limb fractures more frequently than males. The average duration of anaesthesia was 137 min (S.D. 116). Overall, 45.9% of patients received regional anaesthesia for ORIF. The number of lower limb fractures ($n = 133\,030$) was larger than that of upper limb fractures ($n = 49\,650$) and combined upper and lower limb fractures ($n = 2698$). The median postoperative length of stay was 8 days [interquartile range (IQR) 4–18] and 31 days (IQR 21–50) following upper and lower limb fracture surgery, respectively. Among these, 39 patients matched the ICD-10 code criteria of CRPS and 4 patients were diagnosed with a co-morbid specified nerve injury in addition to CRPS.

Table 2 shows the relationships between various factors and the occurrence of postoperative CRPS. Patients with upper limb fractures had a significantly higher rate of developing CRPS than patients with lower limb fractures (0.058% *vs* 0.006%, $P < 0.001$). Age and sex were not significantly related to the occurrence of CRPS. A longer duration of anaesthesia was significantly associated with more frequent postoperative CRPS. Regional anaesthesia was also significantly related to the development of CRPS.

The results of the logistic regression analyses are shown in Table 3. In the multivariate model, patients with fractures of the forearm, wrist and hand tended to show a relatively higher rate of CRPS [odds ratio (OR) 2.81, $P = 0.012$] as compared with those patients with fractures of the shoulder or upper arm. In contrast, patients with femoral fractures showed a significantly lower rate of CRPS (OR 0.05, $P < 0.001$). Patients ages

TABLE 2 The occurrence of postoperative CRPS

		n	CRPS	(%)	*P*-value
Total		185 378	39	(0.021)	—
Fracture site	Upper limb	49 650	29	(0.058)	<0.001
	Fracture of shoulder and upper arm (S42)	23 971	9	(0.038)	—
	Fracture of forearm (S52)	20 329	17	(0.084)	—
	Fracture of lower end of radius (S525)	*12 485*	*10*	*(0.080)*	—
	Fracture of lower end of both radius and ulna (S526)	*2058*	*4*	*(0.194)*	—
	Fracture of shafts of both radius and ulna (S524)	*1497*	*3*	*(0.200)*	—
	Fracture of forearm, others	*4289*	*0*	*(0)*	—
	Fracture at wrist and hand level (S62)	5350	3	(0.056)	—
	Lower limb	133 030	8	(0.006)	—
	Fracture of femur (S72)	106 880	2	(0.002)	—
	Fracture of lower leg (S82)	21 801	5	(0.023)	—
	Fracture of foot (S92)	4349	1	(0.023)	—
	Multiple regions of upper and lower limbs (T02.2–T02.6)	2698	2	(0.074)	—
Age, years	⩽9	3398	0	(0)	0.140
	10–19	9365	0	(0)	—
	20–29	6451	4	(0.062)	—
	30–39	6841	2	(0.029)	—
	40–49	7553	3	(0.040)	—
	50–59	11 836	2	(0.017)	—
	60–69	21 800	10	(0.046)	—
	70–79	38 046	11	(0.029)	—
	80–89	55 347	6	(0.011)	—
	90–99	23 856	1	(0.004)	—
	⩾100	885	0	(0)	—
Sex	Male	63 898	14	(0.022)	0.851
	Female	121 480	25	(0.021)	—
Duration of anaesthesia, min	⩽119	101 220	8	(0.008)	<0.001
	120–179	53 413	14	(0.026)	—
	⩾180	30 745	17	(0.055)	—
Nerve block	No	98 984	30	(0.030)	0.004
	Yes	83 945	9	(0.011)	—

Values in brackets following the fracture descriptions are International Classification of Diseases 10th Revision codes (ICD-10 codes). CRPS: complex regional pain syndrome.

60–79 years showed a higher rate of CRPS, but this result was not significant (OR 2.15, $P=0.062$). The rates of CRPS were not significantly different between males and females. The group with a long duration of anaesthesia (⩾180 min) showed a higher rate of CRPS as compared with the group with a short duration of anaesthesia (⩽119 min) (OR 5.73, $P<0.001$); however, the use of regional anaesthesia did not significantly contribute to a decrease in the rate of CRPS.

Discussion

In the present study we found that the demographic data of Japanese CRPS patients were different from those of American and Dutch CRPS patients [6, 10]. While the age distribution of our CRPS patients showed one peak around 60 years of age, which is almost compatible with the American and Dutch CRPS populations, a second peak was observed at ~20 years of age, which is quite disparate. We found that patients with upper limb fractures developed CRPS more frequently than those with lower limb fractures. Some previous reports support this observation; e.g. several studies report that Colles' fracture of the radius has a much higher association with CRPS than other fracture sites [6, 10, 15]. However, the precedent prospective study showed a higher incidence of CRPS in patients with lower limb fracture than those with upper limb fracture [9]. A common characteristic among these previous studies and our present study is that fractures to the distal end of either the upper or lower limbs are at a higher risk of co-morbid CRPS.

It has been generally considered that CRPS occurs more frequently in females than in males [6, 10], but our study showed no significant difference between males and females in the rate of CRPS following limb fracture. Because middle-aged and elderly female patients usually also suffer from osteoporosis, the absolute number of patients with bone fracture is much larger for females than for males. As such, this high incidence of female CRPS patients in older cohorts of previous epidemiological studies would be more noticeable [1, 16]. Furthermore, large populations of female CRPS patients might have other

TABLE 3 Logistic regression analyses for the occurrence of postoperative CRPS

	Univariate analysis			Multivariate analysis		
	OR	95% CI	*P*-value	OR	95% CI	*P*-value
Fracture site						
Shoulder or upper arm (S42)	Reference			Reference		
Forearm, wrist or hand (S52 or S56)	2.08	0.94, 4.56	0.069	2.81	1.25, 6.30	0.012
Femur (S72)	0.05	0.01, 0.23	<0.001	0.05	0.01, 0.28	<0.001
Lower leg or foot (S82 or S92)	0.61	0.22, 1.72	0.350	0.66	0.21, 2.05	0.469
Multiple regions (T02.2–T02.6)	1.98	0.43, 9.15	0.384	1.40	0.30, 6.66	0.671
Age, years						
⩽59	Reference			Reference		
60–79	1.45	0.70, 3.01	0.318	2.15	0.96, 4.79	0.062
⩾80	0.36	0.14, 0.93	0.035	1.75	0.61, 5.04	0.300
Sex						
Male	Reference			Reference		
Female	0.94	0.49 ,1.81	0.851	1.21	0.58, 2.52	0.613
Duration of anaesthesia, min						
⩽119	Reference			Reference		
120–179	3.32	1.39, 7.91	0.007	3.15	1.24, 7.97	0.016
⩾180	7.00	3.02, 16.22	<0.001	5.73	2.31, 14.24	<0.001
Regional anaesthesia						
No	Reference			Reference		
Yes	0.35	0.17, 0.75	0.006	1.11	0.46, 2.68	0.817

Values in brackets following the fracture descriptions are International Classification of Diseases 10th Revision codes (ICD-10 codes). CRPS: complex regional pain syndrome.

causative aetiologies aside from bone fracture as compared with male patients. Our present findings show that females with bone fractures do not appear to have a higher risk of developing CRPS as compared with their male counterparts.

The estimated overall incidence of CRPS was 0.026% and 0.0055% per year in the Dutch and American general populations, respectively [6, 10]. Although bone fracture is one of the major causes of CRPS and patients with bone fracture are generally at increased risk for the development of CRPS, the rate of CRPS in patients with ORIF for limb fracture in our study was 0.021%. This is lower than the estimated 22% following the International Association for the Study of Pain (IASP) criteria [17] and ~5% following the criteria of Bruehl *et al.* [14] for the only other study to prospectively evaluate the development of CRPS in ~600 patients with limb bone fracture within 6 weeks after injury [9]. The IASP criteria include a combination of (i) the presence of an initiating noxious event or a cause of immobilization; (ii) continuous pain, allodynia or hyperalgesia with which pain is disproportionate to any inciting event; (iii) evidence at some time of oedema, changes in skin blood flow or abnormal sudomotor activity in the region of the pain and (iv) the absence of a condition that would otherwise account for the degree of pain and dysfunction [17]. Comparatively the criteria by Bruehl *et al.* [14] include (i) continuing pain disproportionate to any inciting event and (ii) the presence of at least one symptom and two signs each of a sensory, vasomotor, sudomotor/oedema and motor/trophic nature. The IASP criteria are highly sensitive but with a low specificity, whereas the criteria by Bruehl *et al.* have a moderate-to-high sensitivity as well as a relatively high specificity. The fact that Japanese physicians have quite strictly diagnosed CRPS since 2005 on the basis of the original Japanese criteria [13] might contribute to the different prevalence rates between our study and the earlier prospective study [9]. In addition, a genetic contribution to pain perception in CRPS patients has been reported [18], and the genetic differences between Japanese and Dutch patients might contribute to the differences in the incidence of CRPS between these two investigations.

We consider that such distinct characteristics of our patients are possibly attributable to our efforts to gather a close-to-homogeneous population and thus recruiting only patients who were diagnosed with CRPS during hospitalization immediately after ORIF for limb bone fracture. Early in the postoperative period, physicians are generally reluctant to assign a diagnosis of CRPS. This may explain why the prevalence of the diagnosis of CRPS increased between 6 weeks to 3 months in the precedent prospective study [9]. We sampled data from CRPS patients within the very acute phase of the postoperative period. Such a limited observation period might result in a possible underestimation of the true prevalence of CRPS. Because of the difference in health care systems between Japan and Western countries, our length of hospital stay was generally longer than those in other reports [19].

There will be a certain number of patients with false-negative diagnoses of CRPS. Approaching this topic

from a different angle, in many patients, complaints begin and continue after the inciting event. However, it is clinically uncommon for patient complaints to begin during the period of time elapsed from the inciting event [16]. In addition, there was close temporal clustering of CRPS in ours and other cohorts [4, 5]. Thus it is unlikely that our data would include a considerable number of the false-negative cases. We should consider the likelihood of false-positive cases in the present study. Since the DPC system did not include any records of signs and symptoms of CRPS, we cannot confirm the diagnostic validity of our study retrospectively. However, to enhance specificity in the diagnosis of CRPS, we sampled patients who were reliably coded with CRPS (ICD-10 codes M89.0 and G56.4) and did not include those who were coded with a symptomatic diagnosis of neural disorders. This was because CRPS should be diagnosed in the absence of an alternative condition that would otherwise account for the pain. In addition to these considerations, and because of the reluctance of physicians to assign a diagnosis of CRPS early in the postoperative period, we assume that our data describe a well-selected, albeit small, cohort with few false-positive cases.

To cluster a close-to-homogeneous CRPS subgroup, we gathered only patients who were diagnosed with CRPS during hospitalization immediately after ORIF for limb fracture. Our approach may thus permit better identification of risk factors for the development of CRPS after ORIF for limb fracture early during the postoperative period with distinct characteristics. It should be noted therefore that the results cannot be generalized across all CRPS patients, but is applicable to those patients within a specific CRPS subgroup.

The underlying pathophysiological mechanisms of CRPS remain controversial. One possible explanation is that CRPS stems from neuropathic pain. Limb fractures, including dislocations, can induce peripheral nerve injuries. We found 4 of 39 patients diagnosed as a specified nerve injury; this figure is much larger than the reported 1–2% incidence of nerve injuries induced by limb trauma [20]. In the majority of reported cases, a diagnosis of peripheral nerve injury was made within 4 days of admission [21]. Because our observation period was sufficient, with a median length of stay of at least 8 days, our data would have been satisfactory to detect most of the peripheral nerve injuries occurring subsequent to fracture. Here we found that a longer duration of anaesthesia was associated with a higher incidence of CRPS. This longer requirement for anaesthesia might suggest the occurrence of more severe fractures in our patients and thereby a higher rate of nerve injury. Supporting evidence for this consideration comes from the fact that more severe traumas, such as crushing injuries, can lead to a higher rate of nerve injury [20]. Indeed, in the present study, patients with multiple fractures to the upper and lower limbs were plausibly considered to be the result of high-energy trauma. However, these multiple-fracture patients showed a relatively low association with CRPS. In contrast, we found that patients with fractures to the distal end of either the upper or lower limbs were at a higher risk of co-morbid CRPS. The frequency of nerve injuries to the humerus or femur in response to fracture is reported to be similar to that of the ulna or tibia [20]. These results argue against the hypothesis that more severe traumatic injury is followed by an increased prevalence of nerve injury and suggest that neuropathic pain alone cannot explain the underlying causes of CRPS.

This study aimed to search for any interventions that could contribute to a reduction in the development of CRPS patients in our subgroup of patients. We focused on the relationship between regional anaesthesia and the occurrence of CRPS because regional anaesthesia combined with general anaesthesia may be better than general anaesthesia alone for treating bone fracture patients with ORIF by blocking afferent nociceptive signals from the wound and the bone fracture into the central nervous system and helping to prevent the development of CRPS that can persist long after healing [22]. However, we did not find this to be the case. Instead, in perioperative factors we found that a longer duration of anaesthesia was associated with a higher occurrence of CRPS. In Japan, tourniquet inflation is used to decrease blood loss and improve the operative field visually during standard ORIF for distal end fractures of the upper and lower limbs. We can assume that the longer duration of anaesthesia implies not only a longer operation time, but also a longer inflation period using the tourniquet. Nerve compression and ischaemia by tourniquet inflation induces an increase in spontaneous activity and expansion of the receptive fields of the spinal nociceptive neurons, especially those with receptive fields located proximal to the tourniquet. This results in widely expanded areas of hyperalgesia and allodynia, such as CRPS, in the exposed limb [23]. If we consider that regional anaesthesia could prevent CRPS, one possible underlying cause of the pathological pain associated with CRPS is the central sensitization of the spinal nociceptive neurons induced by continuous nociceptive inputs from wound, bone fracture and ischaemic tissue and neuropathic inputs from nerve compression by tourniquet inflation. However, this mechanism is unlikely, given the present result that regional anaesthesia showed no relationship to the prevalence of CRPS. We propose the ischaemia–reperfusion injury theory as an alternative explanation for the relationship between a higher rate of CRPS and the longer duration of anaesthesia. Reperfusion subsequent to prolonged occlusion of the blood flow to one limb results in hyperalgesia and allodynia, and moreover the exposed limb exhibits an initial phase of CRPS features, such as hyperaemia and oedema [24]. A large body of clinical evidence suggests that, in at least a subset of CRPS patients, the fundamental cause of abnormal pain sensations and CRPS-based symptomatology is ischaemia–reperfusion injury followed by sustained inflammation due to microvascular pathology in deep tissues [25]. Our proposal is supported by the present results that, although there was a longer duration of anaesthesia with ORIF procedures for both upper and lower limb fractures

than with a single ORIF procedure for either an upper or lower limb fracture, multiple fractures showed a relatively low association with CRPS. Therefore a longer inflation period with a tourniquet on an exposed limb may be the cause of CRPS.

Several limitations in this study should be acknowledged. First, the recorded diagnoses in the administrative claims database are generally less well validated than those in planned prospective surveys. Second, because the database does not include information on the patients' signs and symptoms or laboratory data, underreporting or biased reporting (withholding sensitive cases) may have potentially led to over- and underestimation of the true occurrence rate of CRPS. Third, although the database represents 45% of acute care in patients in Japan, community hospitals voluntarily participated in the DPC system and patients were not randomly sampled. Fourth, our database lacks the actual duration of the tourniquet time during ORIF. We speculate that ischaemia–reperfusion injury may be a critical event for the initiation of CRPS in a specific subset of patients with limb fracture treated with ORIF. Prospective studies are required to confirm this hypothesis to develop treatment and preventative strategies for CRPS. Our approach of sampling CRPS patients with specified disease duration and aetiology may help to disentangle the underlying pathophysiological mechanisms of our specific subgroups of CRPS patients in a stepwise manner.

Rheumatology key messages

- Forearm fracture is associated with a higher risk of complex regional pain syndrome (CRPS).
- The risk of developing CRPS is equal in male and female limb fracture patients.

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ORIGINAL ARTICLE

Long-Term Outcomes of Percutaneous Radiofrequency Thermocoagulation of Gasserian Ganglion for 2nd- and Multiple-Division Trigeminal Neuralgia

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■ **Abstract**

Objectives: The objective of this study was to examine the long-term outcome of percutaneous radiofrequency thermocoagulation (PRT) of the Gasserian ganglion for the 2nd division and multiple division trigeminal neuralgia (TN), compared to the isolated 3rd division TN.

Methods: One hundred and forty-eight procedures performed in 89 patients with typical TN between April 2004 and September 2011 in a single pain center were retrospectively analyzed. Baseline characteristics of these patients, immediate outcome, duration pain-free, and complications were obtained from their medical records and questionnaires sent in June 2012. Duration pain-free was assessed by Kaplan–Meier analysis.

Results: Of the 148 PRT of the Gasserian ganglion, 37 procedures were performed for isolated 2nd-division TN (V2 TN), 67 procedures were for both 2nd- and 3rd-division TN (V2 + V3 TN), and 38 procedures were for isolated 3rd-division TN (V3 TN). The remaining 6 procedures were performed for V1 + V2 TN and V1 + V2 + V3 TN. Immediate success rates of PRT for V2 TN, V2 + V3 TN, and V3 TN were 100%, 86.6%, and 100%, respectively, whereas the durations pain-free for V2 TN and V2 + V3 TN were significantly shorter than that for V3 TN (9, 12, and 36 months, respectively: $P = 0.012$).

Conclusion: For 2nd-division TN and multiple-division TN, less long-term pain relief after PRT of the Gasserian ganglion can be expected compared with that for isolated trigeminal 3rd-division neuralgia, even if immediate pain relief is achieved. ■

Key Words: trigeminal neuralgia, trigeminal neuralgia, idiopathic, radiofrequency ablation, Gasserian ganglion, outcomes

INTRODUCTION

Trigeminal neuralgia (TN) is a neuropathic disorder, characterized by paroxysmal electric shock-like pain confined to the distribution of one or more divisions of the trigeminal nerve. To patients refractory to medication therapy, surgical treatments such as microvascular decompression (MVD), Gamma knife radiosurgery, and percutaneous destructive procedures can be selected as therapeutic options. Among these

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procedures, percutaneous radiofrequency thermocoagulation (PRT), characterized by the lack of a need for endotracheal anesthesia and short hospitalization, remains the most common procedure.[1] Although the recurrence rate appears to be higher than for MVD,[1–3] this procedure can be selected for elderly patients who reject other invasive procedures or for patients who recur after MVD, Gamma knife radiosurgery or other percutaneous destructive procedures such as alcohol injection, glycerol rhizotomy, and balloon compression.

Although several studies have shown the efficacy of PRT of the Gasserian ganglion,[4–7] the long-term outcome has not been well evaluated according to each trigeminal branch other than the isolated 3rd division, which is easily accessible.[8] Since thermocoagulation for 2nd-division or multiple-division TN is technically more difficult than for isolated 3rd-division TN because of its anatomical distribution, the duration of pain relief appears to be shorter despite its excellent immediate outcome. Therefore, we investigated the long-term outcome of PRT of the Gasserian ganglion, targeted for 2nd-division or multiple-division TN compared with isolated 3rd-division TN.

METHODS

The institutional committee of Shiotani Pain Clinic approved this study protocol. Between April 2004 and September 2011, 89 patients with medically refractory idiopathic TN underwent PRT of the Gasserian ganglion. All procedures were performed under fluoroscopy. Patients were sedated by injection of 0.05 mg/kg midazolam during the procedures. A 22-gauge, straight radiofrequency lesioning electrode with a stylet (Sluyter-Mehta cannula) was inserted through the foramen ovale, and the tip of the electrode was positioned appropriately in the Gasserian ganglion. Final location of the electrode tip was adjusted by the patient's response to electrical stimulation of 0.1 to 0.3 V at 50 Hz. When the proper location of the electrode had been confirmed, 0.2 mL of 2% lidocaine was injected through the needle to produce anesthesia in the diseased division and radiofrequency themocoagulation was then performed at 90°C for 180 seconds. In principle, a single lesion was made per procedure.

The immediate success of the treatment was examined at 2 weeks after the procedures. Immediate success was defined as satisfactory pain relief in the involved divisions. Additional PRT of the Gasserian ganglion or a peripheral nerve branch was performed if satisfactory pain relief was not achieved in the diseased area at the first clinical visit after the procedure. These additional procedures were considered as the part of initial intervention. Once satisfactory pain relief was obtained, the patients were then followed up every 3 months. Patients were questioned about the degree of pain relief, sensory loss, and treatment complications such as dysesthesia, muscle weakness, and eye problems at each clinical visit. Complete recurrence is defined as constant lancinating paroxysmal pain recurring partially and fully in the same divisions and repeat treatment being required. The level of initial sensory loss was graded as anesthesia: complete loss of touch sensation, severe hypesthesia: loss of $\geq 50\%$ of touch sensation, and mild hypesthesia: loss of $< 50\%$ of touch sensation. Repeated PRT of the Gasserian ganglion or PRT or alcohol block of the peripheral nerve was performed when complete recurrence was found.

In June 2012, questionnaires were mailed to all patients to ask them about the present degree of pain relief. Data regarding the recurrence of pain was retrieved from the questionnaires and the medical records. Patients who neither visited periodically after the procedure nor returned questionnaires were considered to be lost to follow-up, and patients who did not return questionnaires were counted in the analysis alone up to their last contact.

The probability of remaining pain free was calculated by Kaplan–Meier analysis, and comparisons between the subgroups were performed using log-rank test. Statistical significance was assigned at P value of < 0.05.

RESULTS

Between April 2004 and September 2011, 148 PRT of the Gasserian ganglion were performed for 89 patients with typical TN. Patients with atypical facial pain and those with TN secondary to brain tumor or multiple sclerosis were excluded. The patient characteristics are described in Table 1. Most patients received oral medication such as carbamazepine or alternative anticonvulsant before visiting our clinic. Two patients did not take any medication owing to their side effects. Prior to visiting our clinic, 56 patients (62.9%) underwent one or more surgical treatments such as MVD, Gamma knife radiosurgery, PRT, or alcohol block. In most patients, the 2nd (V2), 3rd (V3), or both divisions were affected, whereas 6 patients had pain in the 1st (V1) division accompanied by V2 and/or V3.

Table 1. Baseline Characteristics of Patients

Age at the first procedure at our clinic, mean (range)	69.4 (38–88)
Sex, no. (%)	
Female	59 (66.3)
Male	30 (33.7)
Prior drug treatment, no. (%)	
Carbamazepine or other anticonvulsant	87 (97.8)
None	2 (2.2)
Prior procedure, no. (%)	
Microvascular decompression	5 (5.6)
Gamma-knife	18 (20.2)
Radiofrequency thermocoagulation or alcohol injection	39 (43.8)
None	27 (30.3)
Distribution of pain localization, no. (%)	
V2 only	19 (21.3)
V3 only	29 (32.6)
V1 and V2	3 (3.4)
V2 and V3	35 (39.3)
V1, V2, and V3	3 (3.4)

Of 148 PRT of the Gasserian ganglion, 37 procedures were performed for isolated 2nd-division TN (V2 TN), 67 procedures were for both 2nd- and 3rd-division TN (V2 + V3 TN), and 38 procedures were for isolated 3rd-division TN (V3 TN). The remaining 6 procedures were performed for V1 + V2 TN and V1 + V2 + V3 TN. Ten patients were lost to follow-up.

The immediate success rates of the procedures at 2 weeks after the procedure were 100% for isolated V3 TN, 100% for isolated V2 TN, and 86.6% for V2 + V3 TN. Nine procedures (13.4%) for V2 + V3 TN required an additional procedure at the first clinical visit after discharge, and all of those patients had complete pain relief after the additional procedure. Six patients who had pain in the V1 division required additional PRT or alcohol block of the supraorbital nerve, which is a peripheral branch of the ophthalmic nerve. The PRT for V3 TN showed better long-term outcome than those for V2 TN or V2 + V3 TN ($P = 0.0012$). The probabilities of pain relief of V3 TN being maintained were 80.2% at 12 months and 54.9% at 24 months, whereas those of V2 TN and V2 + V3 TN were 40.5% and 49.3% at 12 months, and 19.6% and 17.1% at 24 months, respectively. The median pain-free durations for patients with V2 TN, V2 + V3 TN, and V3 TN were 9, 12, and 36 months, respectively (Figure 1).

Of 104 procedures for V2 TN and V2 + V3 TN, 39 (37.5%) were associated with anesthesia, 30 (28.8%) with severe hypesthesia, and 10 (9.6%) with mild hypesthesia in the selective 2nd division at 2 weeks of the initial procedure. For the remaining 26 (24.8%) procedures, information on sensory loss was not available from the medical records. The median pain-free durations were 18 months in patients with anesthesia,

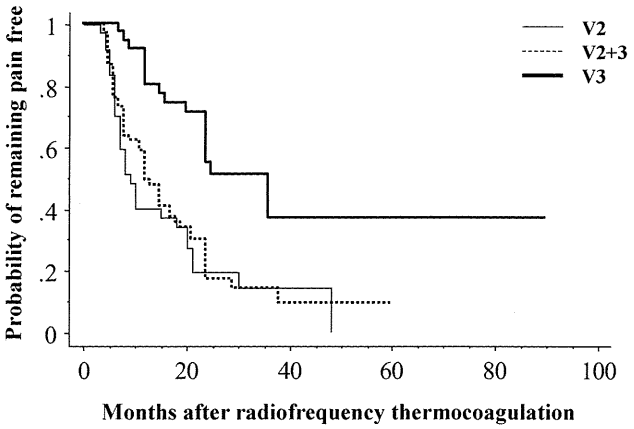

Figure 1. Kaplan–Meier analysis showing the probability of remaining pain-free after radiofrequency thermocoagulation according to the affected division. 37 procedures were for isolated V2 TN, 38 procedures for isolated V3 TN, and 67 procedures for V2 + V3 TN.

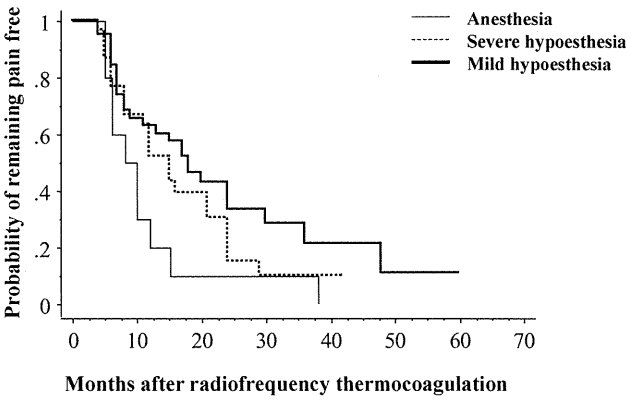

Figure 2. Kaplan-Meier analysis showing the probability of remaining pain-free after radiofrequency thermocoagulation for V2 and V2 + 3TN according to the severity of sensory loss of the V2 division.

15 months in patients with severe hypesthesia, and 9 months in patients with mild hypesthesia. The probability of remaining pain-free differed significantly between patients with anesthesia and those with mild hypesthesia ($P = 0.017$) (Figure 2).

Of 37 procedures for V2 TN, 28 (75.7%) patients required repeated PRT of the Gasserian ganglion or PRT of infraorbital nerve from 3 to 48 months after the initial procedure. Likewise, of 73 procedures for multiple-division TN, 57 (78.1%) patients required repeated PRT of the Gasserian ganglion or PRT of peripheral nerves from 4 to 38 months. Of these 57 patients, 2 (3.5%) patients were treated for recurrence in V1, 47 (82.5%) were for recurrence in V2, and 8 (14.0%) were for recurrence in V3 (Table 2). There was no mortality

Table 2. Treatments for Pain Recurrence

		Multiple-division TN (N = 57)		
		Recurred division		
	Isolated V2 TN (N = 28)	V1 (N = 2)	V2 (N = 47)	V3 (N = 8)
Repeat PRT of GG	16	0	33	7
PRT of infraorbital nerve	12	0	14	0
PRT of mandibular nerve	0	0	0	1
PRT or alcohol block of supraorbital nerve	0	2	0	0

GG, Gasserian ganglion; PRT, percutaneous radiofrequency thermocoagulation.

related to the procedures. Major complications included 10 cases of weakness of masticatory muscles (12.2%), 4 intolerable dysesthesia (4.9%), and 4 eye problems without keratitis (4.9%).

DISCUSSION

The present study examined the long-term outcomes of PRT of the Gasserian ganglion, targeted for 2nd-division or multiple-division TN. We showed that (1) the immediate success rate was high regardless of the affected division, except for V1 division; (2) the long-term outcomes of pain relief were better in the isolated V3 TN than in V2 TN or V2 + V3 TN; and (3) the duration pain-free for V2 TN and V2 + V3 TN depended on the degree of sensory loss in the V2 division.

Although the present study was unable to clarify the precise mechanism of differences in durability of response in patients between with V3 division and with multiple divisions TN, it could be the result of anatomical and/or technical difficulties of selective thermocoagulation to approach maxillary fibers. When treating V2 pain, adjusting the position of the electrode is technically tough because the electrode needs to be placed more medial and deeper to touch the maxillary fibers rather than the mandibular fibers. If advanced too deep, it could involve the ophthalmic fibers, which affect the corneal sensation, indicating the difficulty of selective thermocoagulation of the V2 division.[9] Nevertheless, for V2 TN and V2 + V3 TN, even if the electrode contacts only the inferior part of maxillary fibers, thermal effects of radiofrequency could spread to destroy the upper part of the maxillary fibers away from the electrode. In such cases however, the durability of nerve destruction by diffused heat may not last as long as that by direct effects. That could, in turn, account for our findings that, despite the high immediate success rate, the probability of being pain-free was considerably lower in V2 TN and V2 + V3 TN than in isolated V3 TN, for which direct lesion was easy to achieve. A curved tip electrode could be beneficial to achieve a more precise approach to affected nerve fibers, and concurrently to obviate undesirable side effect. However, there is no report to date regarding the rate of recurrence when used the curved tip electrode compared to smaller straight tip electrode.[10]

Once the appropriate location of the needle was determined, a single thermocoagulation was made after injecting a small dose of lidocaine into the Gasserian ganglion. This method is much simpler and less stressful for both physicians and patients to complete each procedure with immediate success and with no need for additional intravenous anesthesia for lesioning. Moreover, it is less likely to cause harm as long as the operator confirms that contrast dye stays within the trigeminal cistern without flowing into a blood vessel or the subarachnoid space. However, the efficacy of thermocoagulation could not be assessed intra-operatively, resulting in the variability of sensory loss and long-term efficacy. Such variability of treatment efficacy was more likely to be observed when treating for V2 and V2 + 3 TN than for V3 TN, in which the durability of pain relief was comparable with previous studies.[11–14] In particular, in the treatment of V2 + V3 TN, discrepancy in the severity of the lesion may occur between the V2 and V3 regions. In fact, we have often experienced situations in which the V3 division is well thermocoagulated while not achieving a sufficient lesion in the V2 division. Some may recommend several lesions be made to reduce the unevenness of lesioning by altering the location of the electrode based on patients' self-assessment.[11] However, it may be challenging to obtain reliable assessment for the degree and extent of lesioning obtained from patients under sedation. Additionally, since it often takes a few days to reach an ultimate outcome, we believe that several lesions per procedure could result in overtreatment.

Our experience showed that pain in the V2 division was more likely to recur than pain in the V3 division, and the degree of sensory loss in the V2 division may be a decisive factor for the durability of pain relief for V2 TN and V2 + V3 TN. With recurrence in the V2 division, satisfactory pain relief was obtained by either repeat PRT of the Gasserian ganglion or PRT of the infraorbital nerve. PRT of the infraorbital nerve is an even simpler thermoneurotomy than that of the Gasserian ganglion, and we selected this peripheral procedure

if the recurrent pain was limited to the infraorbital area, not including the superior alveolar area. In 6 patients who had V1 pain, pain relief was not accomplished only by PRT of the Gasserian ganglion because we intentionally tried to avoid lesioning ophthalmic fibers. However, it was complemented by additional percutaneous destructive procedures of the supraorbital nerve that did not affect corneal sensation. These peripheral procedures were also effective as a treatment when recurrence was limited to the V1 division. Some may argue that the recurrence rate was high especially as to V2 and multiple division TN. Since the recurred pain could be treated effectively by repeat procedure, we do not believe that they were serious events.

There are some reports recommending balloon compression or glycerol rhizotomy for TN confined to the V1 or V2 division, or TN affecting more than one division.[2,9] However, there is no prospective study to compare the outcome of PRT to those of balloon compression or glycerol rhizotomy. The median pain-free duration of these procedures has been reported to be from 6 to 42 months,[15–19] which may depend on previous procedures and medical history.[2] History of previous surgery, and frequent repeat balloon compression and glycerol rhizotomy have been reported to be associated with a higher risk of technical failure,[9,15–17] which may not be seen in frequent repeat PRT.[13] In our series, nearly half of the patients had one or more relevant factors in their surgical history prior to visiting our clinic, and we believe these recurrent cases could benefit from PRT rather than from other percutaneous procedures.

There are, however, some disadvantages reported in PRT, such as a higher rate of corneal sensation deficit compared with that in other percutaneous destructive procedures.[9,20] In our series, the incidences of eye problems, dysesthesia, and weakness of masticatory muscles after the procedure were similar to those in other studies on balloon compression[21–23] or glycerol rhizotomy.[12,24,25] Masticatory muscle weakness was likely to be seen early after the procedures. However, this symptom recovered gradually and did not seem to have a major detrimental effect on the patients' daily life.

There are several limitations affecting the interpretation of the data herein. *First*, owing to the constraints associated with retrospective analyses, the follow-up intervals among the subjects varied and 11.2% were lost to follow-up. An insufficiency of systematic recording of sensory loss might also preclude more accurate evaluation of the durability in the present study. *Second*, there are few reports addressing the therapeutic effects dependent on each trigeminal division and it may not be appropriate to simply compare our results with previous reports in which wide variations in technique and equipment existed. Some may argue that our treatment approach cannot be extrapolated to other institutions. A prospective study should be warranted to validate the results of present study.

CONCLUSIONS

Although the immediate success rate is high, the durability of pain relief of PRT for 2nd-division TN and multiple-division TN could not be expected to be as great as for isolated trigeminal 3rd-division neuralgia. However, the recurrence of pain can be treated safely and effectively by repeated PRT of the Gasserian ganglion or percutaneous destructive procedures of peripheral nerves.

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LETTERS TO THE EDITOR

A Rare Cause of Lumbar Radiculopathy: Perineural Cyst

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Dear Editor,

Lumbosacral perineural cysts are formed by the arachnoid membrane of the nerve root at the lumbosacral level. Sacral perineural cysts called Tarlov cysts were identified by Tarlov for the first time in 1938 [1]. Langdown et al. reported that Tarlov cysts, which are a relatively common finding on lumbosacral magnetic resonance imaging (MRI) scans, have a prevalence of 1–2%, and only 13% of these cysts are symptomatic [2]. Symptomatic perineural cysts, which are relatively less common when compared with Tarlov cysts, are found in the lumbar region where they cause nerve root compression, which then leads to radiculopathy mimicking disc herniation [3]. Herein, we report a case with lumbosacral radiculopathy due to a perineural cyst that responded well to a transforaminal epidural steroid injection.

A 19-year-old male patient was admitted to the Physical Medicine and Rehabilitation Clinic presenting with complaints of lower back and left leg pain ongoing for 6 weeks. He had no history of trauma, heavy lifting, morning stiffness, night pain, fever, nor weight loss, and his pain was relieved by rest. His physical examination showed bilateral paravertebral muscle spasm, limited and painful lower back flexion. Straight leg raise test was positive at 40 degrees on the left and negative on the right. Achilles and patellar deep tendon reflexes were normal bilaterally. Sensory and motor examination revealed normal results except his left extensor hallucis longus strength of 4/5. His lumbar MRI scan revealed a 7 × 4-mm cystic lesion with well-defined contours (perineural cyst) in close proximity with the left L5 root (Figure 1A and B). We thought that the symptoms were due to this compression and did a left L5 fluoroscopy-guided transforaminal epidural steroid injection. His pain level before the procedure was 5/10 in visual analogue scale (VAS) that regressed to 0/10 after the injection.

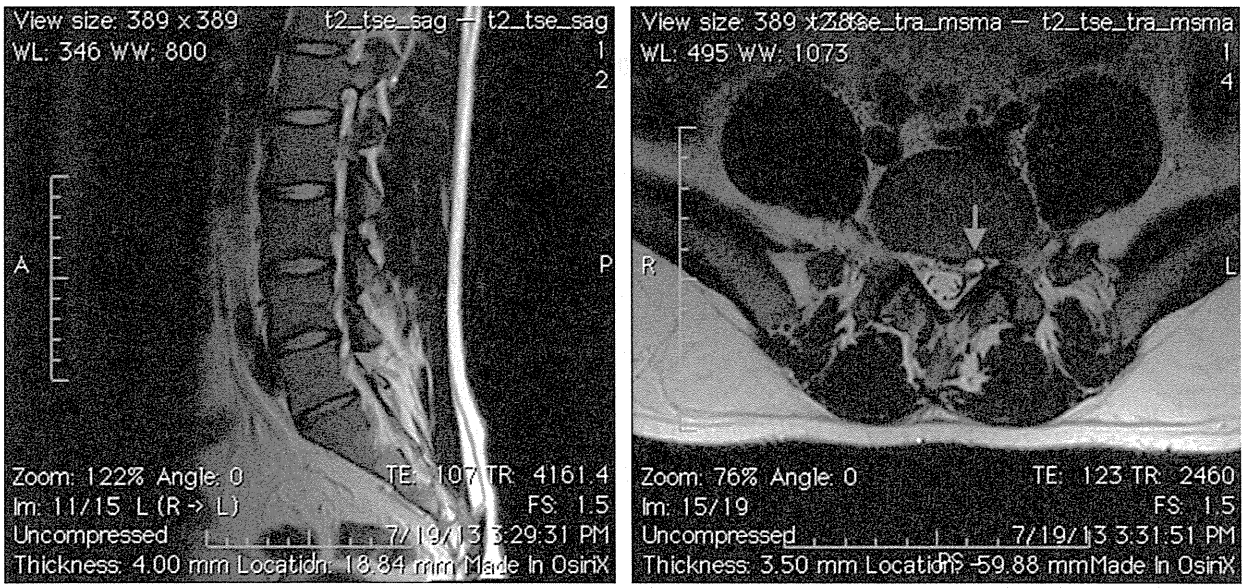

Figure 1 Lumbar spine T2-weighted sagittal (A) and axial (B) magnetic resonance imaging (MRI) scans showing a 7 × 4-mm cystic lesion (red arrows) with well-defined contours (perineural cyst) in close proximity with the left L5 root. [Color figure can be viewed in the online issue, which is available at wileyonlinelibrary.com.]

We found three cases with lumbar perineural cysts mimicking lumbar disc herniation by causing nerve root compression in the literature search. Our case resembles the one published by Takatori et al., where the patient presented with pain at his lower back and left leg, and a perineural cyst compressing the nerve root at L5 on the left side was found during the MRI scan [3].

In our case, patient's complaints of left radicular pain and the fact that a perineural cyst was found at L5 level on the patient's left side during MRI scanning in accordance with his complaint suggest that presence of the cyst might be the source of his pain. However, in our case, the MRI scans revealed a bulging at L4–L5 level, but it was decided that this was not significant enough to cause the patient's symptoms.

Today, both surgical and conservative methods can be used for the treatment of lumbosacral perineural cysts; however, which method is more effective remains a matter of debate. There are studies which suggest that oral or epidural steroid treatments should be considered as the first choice of treatment in cases of perineural cysts presenting with complaints of lower back and radicular pain [4]. Supporting the findings of these studies, in our study, an hour after a left L5 transforaminal epidural steroid injection was administered to the patient, his pain level was decreased from 5 to 0 in VAS that remained for 6-month follow-up.

In conclusion, even though they are usually asymptomatic, it should be kept in mind that symptomatic lumbosacral perineural cysts that can mimic disk herniation should be taken into consideration when obtaining a differential diagnosis between the causes of lower back and radicular extremity pain and that transforaminal epidural steroid injection might be a good treatment option for these cysts.

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Chronic Neck Pain and Episodic Vertigo and Tinnitus

The patient was managed by B Peng, X Pang, and H Yang. The report was prepared by B Peng.

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Dear Editor,

The term "cervical vertigo" was coined by Ryan and Cope [1] in 1955, which involves vertigo, tinnitus, hearing loss, and neck pain. To date, however, the syndrome remains only a theoretical possibility awaiting a reliable clinical test to demonstrate its independent existence. We present a case with cervical vertigo syndrome that is diagnosed and managed successfully to support its existence and provide direct clinical evidence.

In July 2012, a 54-year-old female presented with 24 years of history of chronic neck pain and episodic vertigo and tinnitus irresponsive to extensive conservative therapies. The patient was free of any other neurological symptoms. Her general and otolaryngologic and neurological exams were completely normal. Cervical spine MRI scan indicated the cervical lordosis disappeared and cervical 5/6 disc protruded slightly (Figure 1). The computerized tomography angiography (CTA) scan of the cerebral vessels showed that the left vertebrobasilar artery was normal, whereas the right vertebrobasilar artery was absent (Figure 2).

Cervical discography was recommended to identify the pain-generating site [2,3]. The patient underwent provocative discography at C5/6 and C6/7 discs. The result of discography identified the C5/6 disc as the source of pain. Accordingly, C5/6 disc decompression was recommended using radiofrequency nucleoplasty [3,4]. Cervical disc nucleoplasty percutaneous disc decompression utilized patented Coblation technology for partial disc removal. The Coblation Mode was used at the tip of the Perc-DC Spine Wand (DC SpineWand, Arthro-Care Spine, Stockholm, Sweden). The patient felt the

symptoms of neck pain and vertigo almost completely disappeared after treatment. In last follow-up in August 2013, her symptoms never relapsed. The patient was reexamined with CTA and color Doppler duplex scan of left vertebrobasilar artery the second day after treatment. The diameters of left vertebrobasilar artery were measured from CTA before and after treatment. The peak systolic maximal blood flow velocity (Vmax, cm/s) and the intervascular flow volume (mL/min) of left vertebrobasilar artery were calculated and compared according to the results of color Doppler ultrasound evaluation before and after treatment. The results showed that the diameter of left vertebral artery increased dramatically after treatment (starting segment: 4.3 vs 3.5 mm; atlas transverse process segment: 3.8 vs 3.3 mm). The Vmax also increased after treatment (57.2 vs 51.8 cm/s) and so did the flow volume (175.8 vs 117.4 mL/min).

Insufficient blood supply to posterior circulation is called vertebrobasilar insufficiency. The most common complaint in patients with vertebrobasilar insufficiency is vertigo. It has been showed that the patients with cervical spondylosis complaining of vertigo have significant lower blood flow parameters than nonvertigo patients with cervical spondylosis [5]. Clinical studies have indicated that anterior cervical discectomy and fusion can eliminate the accompanied vertigo syndrome in the patients with cervical radiculopathy or myelopathy [6]. A potential association between cervical spondylosis and vertebral artery occlusion resulting in vertigo due to vertebrobasilar insufficiency was suggested [7].

Because the patient did not respond to conservative therapies, the percutaneous radiofrequency nucleoplasty

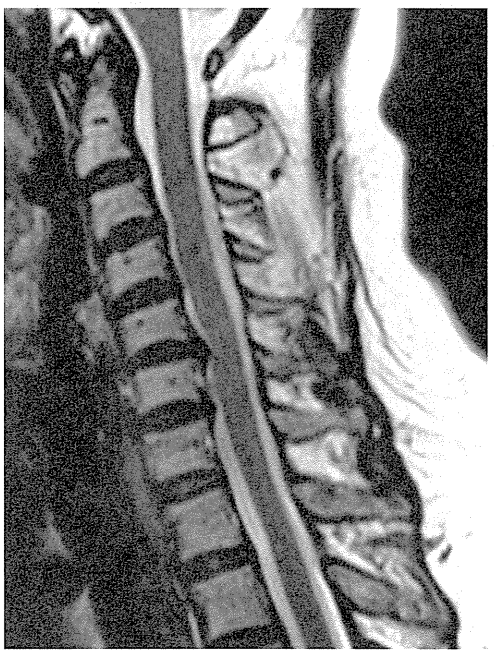

Figure 1 MRI showed C5/6 disc protrusion.

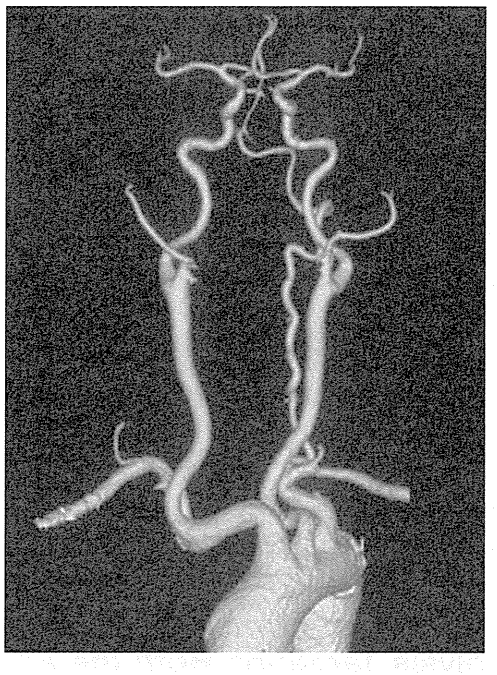

Figure 2 Computerized tomography angiography (CTA) showed the absence of right vertebrobasilar artery.

should be considered [3,4]. Open fusion surgery cannot guarantee relief especially when treatment is for the patient with chronic neck pain without radiculopathy or myelopathy. As the patient is congenitally defected with the absence of the right vertebrobasilar artery, the posterior circulation cannot be compensated by collateral circulation from the right vertebrobasilar artery. When left vertebrobasilar artery is occluded under stimulation, there will be insufficiency of blood supply. According to our current study, we think that there is a direct link between cervical disc pathology and vertebrobasilar insufficiency as mediated by sympathetic nerves. Degenerative painful disc may have a significant increase in inflammatory cytokines that could theoretically irritate the sympathetic nerves that innervate cervical disc and cause vertebral artery insufficiency [8,9], which subsequently induces ischemia of vestibulocochlear organ.

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