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Neurolysis Targeting Both the Aorticorenal Ganglia and Lumbar Sympathetic Plexus for Kidney Tumor–Related Pain

Dear Editor,

Neurolysis of the celiac plexus and/or the retrocrural splanchnic nerves is a valuable approach to treat upper abdominal organ-related pain, particularly pancreatic cancer pain [1]. Few reports, however, have demonstrated celiac plexus block for kidney-related pain. The kidney is governed by a diverse nerve supply, such as sympathetic, parasympathetic, and sensory afferent fibers [2], and its related pain radiates from the flank and back to the hypogastric area, rather than from the upper abdominal region. Although sensory and autonomic nerve supply is relayed *via* the celiac plexus, it is questionable whether patients with kidney-related pain can benefit from celiac plexus neurolysis. We report a case of neurolytic block targeting both the aorticorenal ganglia and the upper lumbar sympathetic plexus for metastatic kidney tumor-related pain.

A 41-year-old man, diagnosed with spindle cell sarcoma in the right lower leg 6 months previously, was admitted to our hospital because of uncontrolled right-side

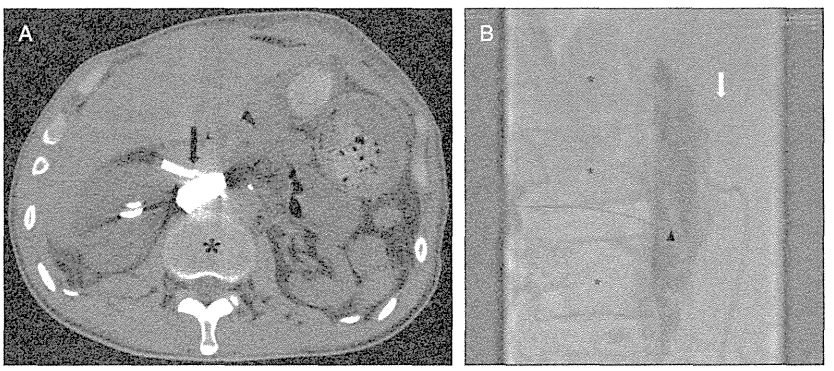

Figure 1 (A) Computed tomographic scan shows the contrast dye spread around the right renal artery (arrow) and right-laterally and posteriorly to the aorta at the level of the L1/L2 intervertebral disk (asterisk). (B) Fluoroscopy shows the contrast dye spread ventrally to the L1–L3 vertebrae (asterisks), including at the level of the right renal artery with an endovascular stent (arrow). The needle tip was located at the level of L2/L3 intervertebral disk (arrowhead). [Color figure can be viewed in the online issue, which is available at wileyonlinelibrary.com.]

umbilical pain. For the 2 weeks prior to admission, the patient experienced abdominal discomfort that gradually worsened. Subsequently, a tumor in the lower part of the right renal medulla associated with lymph node swelling around the right renal and superior mesenteric artery was identified by computed tomography (CT) and magnetic resonance imaging. This was diagnosed as metastatic sarcoma. He complained of sharp intense pain in the right umbilical area and intolerable dull pain spreading down to the right hypogastric region, which required a 75 μg/hour transdermal fentanyl patch, accompanied by continuous intravenous infusion of fentanyl at a rate of 30 μg/hour and a bolus of 50 μg of intravenous fentanyl as a rescue using a patient-controlled analgesia (PCA) device. The average numerical rating scale (NRS) ranged between 4 and 6 out of 10, whereas intense pain over NRS 6 was felt when standing or walking for a long time.

As this pain was visceral rather than somatic in origin, a neurolytic block of the celiac plexus, especially targeting the ipsilateral aorticorenal ganglion, was performed. The procedure was performed using a posterior approach with the patient lying on his left side because the patient had difficulty maintaining in the prone position. Under CT guidance to identify the root of the right main renal artery clearly with an endovascular stent that had been placed previously for renal artery stenosis, a 14-cm 21-gauge needle was inserted at the level of the L2 vertebra and was advanced so that the needle tip was placed just right-laterally of the abdominal aorta and inferior to the root of the right renal artery, where upper lumbar sympathetic plexus, the right aorticorenal ganglion, and renal plexus should be located. After confirming that contrast dye did not flow into the bloodstream or an undesirable area, 15 mL of solution of regional anesthetic and contrast dye (0.2% ropivacaine, iohexol) was injected. The contrast spread around the right renal artery, along with the aorta, at the level of L1–L3 lumbar spine was obtained (Figure 1), whereas the solution did not spread to the root of the celiac artery at the level of Th12L1 intervertebral disk, where the celiac ganglia could be located. After confirming pain relief and no neurological problems, 15 mL of 99.5% ethyl alcohol was injected through the needle.

Following the procedure, pain at rest was alleviated to an average NRS of 1–2 out of 10, which was not exacerbated even when walking for a long time. Intravenous fentanyl as PCA was discontinued by tapering for a week, whereas the fentanyl patch was continued for the residual mild abdominal pain. Two weeks after the procedure, he was transferred to a regional hospital with improved pain control.

Noxious stimuli derived from the kidneys pass through the renal plexus, which travels through the celiac ganglia and aorticorenal ganglia [2]. In addition, some sensory fibers directly travel through the upper lumbar sympathetic and aortic plexus [3]. However, it remains unclear which ganglia or plexus is the most responsible for kidney-related pain.

In this patient, the contrast spread along the lateral wall of the aorta at the level of the upper lumbar spine, and extended around the right renal artery, whereas it did not spread to the celiac artery where celiac ganglia should be located. Furthermore, 15 mL of neurolytic agent, which was less than in previously reported studies in which more than 30 mL was used [1,4], was sufficient to alleviate the intractable pain, indicating that satisfactory pain relief was obtained by the blockade of the ipsilateral aorticorenal ganglion and the upper lumbar sympathetic plexus alone. On the other hand, when performing celiac plexus block for upper organ malignancy, celiac artery is considered as the most reliable landmark at the level of Th12 or L1 [4]. For kidney-related visceral pain, however, it may be optimal for the needle tip to be advanced in the caudal direction so that the aorticorenal ganglia and the lumbar sympathetic plexus can be blocked at the same time. This approach can be performed in the same way as the classic lumbar sympathetic plexus block targeting superior ganglion. As no clinical trial regarding the effectiveness of neurolysis for kidney-related visceral pain has been performed, further clinical reports are required to confirm our findings.

In conclusion, neurolysis, targeted to the aorticorenal ganglia and the upper lumbar sympathetic plexus, may provide a key to successful treatment for renal-related visceral pain.

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Validity and Reliability of the Japanese Version of the Newest Vital Sign: A Preliminary Study

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Abstract

Health literacy (HL) refers to the ability to obtain, process, and understand basic health information and services, and is thus needed to make appropriate health decisions. The Newest Vital Sign (NVS) is comprised of 6 questions about an ice cream nutrition label and assesses HL numeracy skills. We developed a Japanese version of the NVS (NVS-J) and evaluated the validity and reliability of the NVS-J in patients with chronic pain. The translation of the original NVS into Japanese was achieved as per the published guidelines. An observational study was subsequently performed to evaluate the validity and reliability of the NVS-J in 43 Japanese patients suffering from chronic pain. Factor analysis with promax rotation, using the Kaiser criterion (eigenvalues $\geq$1.0), and a scree plot revealed that the main component of the NVS-J consists of three determinative factors, and each factor consists of two NVS-J items. The criterion-related validity of the total NVS-J score was significantly correlated with the total score of Ishikawa et al.'s self-rated HL Questionnaire, the clinical global assessment of comprehensive HL level, cognitive function, and the Brinkman index. In addition, Cronbach's coefficient for the total score of the NVS-J was adequate (alpha = 0.72). This study demonstrated that the NVS-J has good validity and reliability. Further, the NVS-J consists of three determinative factors: "basic numeracy ability," "complex numeracy ability," and "serious-minded ability." These three HL abilities comprise a 3-step hierarchical structure. Adequate HL should be promoted in chronic pain patients to enable coping, improve functioning, and increase activities of daily living (ADLs) and quality of life (QOL).

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Introduction

Pain is defined as "an unpleasant sensory and emotional experience associated with actual or potential tissue damage, or described in terms of such damage" [1]. Pain is the most common patient-reported complaint in clinical practice, and is strongly associated with quality of life (QOL). Therefore, pain has been suggested as an important QOL indicator for patients with chronic illness (e.g., cancer) [2]. In clinical practice, patients' pain recognition and persistency are profoundly influenced by the strength of noxious stimuli and affective status, as well as various other factors [e.g., medical knowledge, social skills, activities of daily living (ADLs), economic status, interpersonal relationships]. The biopsychosocial model proposes that clinical pain management must incorporate psychological and social factors, along with biological variables [3]. In this model, pain is considered an interactive and psychophysiological pattern of behaviors that cannot be separated into distinct, independent psychosocial and physical components. Numerous studies support the usefulness of cognitive behavioral therapy and other psychological approaches to chronic pain management, in addition to those that support a pharmacotherapeutic approach [4,5]. These psychological approaches yield similar outcomes, and commonly focus on educating patients with chronic pain to build coping skills and improve functioning. Successful treatment with pharmacotherapies requires the education of chronic pain patients regarding proper drug administration, side effects, and communicating with their physicians about unrelieved pain and prescription changes [6]. Thus, it is important to educate patients on the management of chronic pain. For example, opioids are prescribed to alleviate patients' chronic pain and improve their overall functioning. However, concerns regarding opioid abuse, addiction, adverse outcomes (e.g., respiratory depression and/or deep sedation from overdosing, and withdrawal symptoms from unintended discontinuation), and tolerance have been increasing. To address such concerns, chronic pain patients need to have adequate numeracy

skills to ensure that they consume the right amounts of opioids. In other words, it is highly important that their physicians teach them how to count and take the correct number of pills dutifully.

Health literacy (HL) refers to the capacity to obtain, process, and understand basic health information and services, and is necessary to make appropriate health decisions. In other words, HL is a social skill that embodies the ability to access necessary information in order to maintain and promote better health [7]. More specifically, it refers to the ability to read, understand, and use health care information to make decisions and follow treatment instructions. From the viewpoint of health care professionals, patients need to possess a particularly sophisticated level of understanding to receive the care they need, and lower HL is commonly found among older adults and patients with chronic illnesses [8]. Lower HL has been associated with lengthier hospitalizations, greater use of emergency care, a lower rate of screening examinations, poorer medication compliance, and a lower ability to interpret labels and health messages, as well as lower overall health status and higher mortality among older adults [9]. Several HL assessment tools have already been developed. One such assessment is the Newest Vital Sign (NVS), which is comprised of 6 questions about an ice cream nutrition label and assesses HL numeracy skills [10]. HL numeracy skills facilitate adherence to medication regimens [11]. This is particularly important for opioid medications, where adequate adherence to dosing schedules is necessary to avoid unfavorable consequences (e.g., respiratory depression, addiction, and withdrawal symptoms upon abrupt discontinuation). Assessment of HL numeracy skills is consequently of great importance in clinical practices for treating chronic pain [12]. English, Turkish, Dutch, and Spanish versions of the NVS have already been validated in primary care patients; however, a highly necessary Japanese version has yet to be validated. In the present study, we developed and validated a Japanese version of the NVS (NVS-J) in patients with chronic pain. While the original NVS assessments were conducted via face-to-face interviews, the NVS-J was designed as a questionnaire available for routine use in a variety of situations.

Materials and Methods

Participants

This study was approved by the Institutional Ethics Committee, Faculty of Medicine, The University of Tokyo (#3678), and consistent with the Declaration of Helsinki. A unique aspect of the NVS is that it can potentially be used to screen for limited numeracy skills. The original NVS was validated in primary care patients. However, as we mentioned earlier, numeracy skills are vital to patients with chronic pain who are using opioid analgesics. Therefore, we focused on chronic pain patients in our research.

A subset of patients who had been seen more than three times in our outpatient clinic, the Department of Anesthesiology and Pain Relief Center, The University of Tokyo Hospital, were enrolled in the study. During the study period of January–February 2012, the participants eligible for recruitment were randomly selected from the appointment logs of the attending physicians. All of the participants reported pain of an intensity of 3 or higher out of 10 on an 11-point numerical rating scale (NRS: 0 = no pain, 10 = worst pain imaginable), and the attending physicians evaluated their pain as necessitating continuous treatment. Participants with cultural or language barriers, or poor mental health statuses, that prevented them from understanding or responding to the questionnaires were excluded from this study. Among 44 identified eligible patients, 43 provided oral informed consent to participate in the study, and completed the questionnaires. Demographic data were obtained on each participant through the self-report questionnaire [i.e., age, sex, height, body weight, occupation, intensity of pain (NRS), smoking history (Brinkman index = daily number of cigarettes * year), and education level].

Measures

All patients were asked to complete the following 4 questionnaires: 1) the NVS-J; 2) a simple dementia screening test that assessed cognitive functioning (a total score of 12 or less out of 15 indicated possible dementia) [13]; 3) the Brief Pain Inventory (BPI) (Japanese version) for assessing ADLs [14]; and 4) a self-rated HL Questionnaire (HLQ) by Ishikawa et al., in which functional, communicative, and critical HL were assessed separately, with the total score of all three HL perspectives indicating an individual's comprehensive HL level [15]. Further, the attending physicians of each participant completed a clinical global impression scale of participants' comprehensive HL levels (CGI-HL) that consisted of a 5-point Likert-type scale (1 = "very poor," 2 = "poor," 3 = "fair," 4 = "moderate," 5 = "good"), on the basis of the following appraisals: 1) the participant always keeps his/her consultation appointments, 2) the participant understands the

Table 1. Participant demographics.

	Mean	SD
Age (yrs)	64.5	14.4
Male/Female	25/18	
Height		
Male (cm)	167.2	6.5
Female (cm)	151.1	6.9
Weight		
Male (kg)	64.4	10.6
Female (kg)	47.8	8.4
BMI		
Male	23.0	3.4
Femle	20.9	3.3
Brink Mann Index	247.3	480.1

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Table 2. Distribution of total NVS-J scores.

NVS-J score	0	1	2	3	4	5	6
Number (n = 43)[%]	13 [30.2]	7 [16.3]	4 [9.3]	8 [18.6]	4 [9.3]	6 [14.0]	1 [2.3]

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psycho-education concept about chronic pain management presented by the attending physician, 3) the participant can adequately adhere to medication regimens, 4) the participant can answer open questions, and 5) the participant can communicate coherently with the attending physician.

Development of a Japanese version of the NVS

Translation and cross-cultural adaptation of the NVS-J was performed in accordance with the established guidelines [16,17]. First, a forward translation of the original NVS into Japanese involving independent translations by a professional native Japanese translator and bilingual Japanese physician was obtained. Then, an expert committee including specialists in pain management, public health, and methodology, synthesized the two translations. Finally, two native English translators, who were uninformed about the nature of the study, completed back-translations of the translated NVS; thereafter, the back-translations were sent to an expert committee to detect cultural bias. When the NVS-J was deemed free of cultural bias, it was considered complete and suitable for administration to participants.

Data analysis

A score of two or less on the CGI-HL was considered in this study as indicative of low HL. Sensitivity and specificity ratios, as well as the stratum-specific likelihood ratio (SSLR) were then calculated for the NVS-J score of each participant. The cut-off point for the NVS-J was set for screening purposes on the basis of these parameters and the area under the receiver operating characteristic (ROC) curve.

Feasibility. The feasibility of the NVS-J was determined by analyzing the number of unanswered questions.

Validity. Construct validity was established through an exploratory factor analysis with principal components extraction. The Kaiser criterion (eigenvalues >1.0) and scree plot were used to determine the number of factors. Criterion-related validity was assessed through the calculation of a Pearson correlation coefficient between the dementia screening score, BPI, NRS, NVS-J, HLQ, and physicians' impressions. The following are generally accepted rankings for coefficients: 1.0–0.81 (excellent), 0.80–0.61 (very good), 0.60–0.41 (good), 0.40–0.21 (fair), and 0.20–0 (poor) [18].

Reliability. Internal consistency was measured with Cronbach's alpha. Alpha coefficients of a magnitude ≥ 0.70 were considered evident of adequate scale reliability at the level of group comparisons [19]. Repeatability was assessed by a test-retest method. Intra-class correlation coefficients (ICCs) between test and retest scores were calculated based on data from participants who reported no symptom changes between the times of the two surveys. Coefficients >0.80 were considered indicative of excellent reliability [20].

All statistical analyses were performed using the Statistical Package for the Social Sciences (SPSS version 11.0) software.

Table 3. Percentage of correct answers for each NVS-J question.

	Kcal	Cup	Gram	%	Allergy	Reason
Correct (%)	37.2	18.6	51.2	25.6	41.9	37.2

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Results

Participant characteristics

The sociodemographic and clinical characteristics of the participants are displayed in Table 1. The total score distribution of the NVS-J is presented in Table 2. The percentage of participants who answered correctly is shown for each NVS-J question in Table 3.

Validity

Factor analysis with promax rotation, using the Kaiser criterion (eigenvalues ≥ 1.0), and a scree plot revealed that the main component of the NVS-J consists of three determinative factors that constitute 100% of the variance (Table 4). The first of these determinative factors consisted of the first and second questions, and was termed "basic numeracy ability," which referred to the capacity of participants to perform a simple calculation. The second factor consisted of the third and fourth questions, and was termed "complex numeracy ability," which referred to the ability of participants to extract necessary information from a nutrition label and perform complex calculations. Finally, the third factor consisted of the fifth and sixth questions, and was termed "serious-minded ability," which referred to the ability of participants to make reasonable health-related decisions. This factor was assessed by instructing participants to imagine they had been diagnosed with an allergic condition and asking whether they would consider avoiding allergenic foods.

In the analysis of criterion-related validity, the total NVS-J score was significantly correlated with the total HLQ score ($p = 0.004$, $R = 0.43$), functional HL score in the HLQ ($p = 0.009$, $R = 0.39$), and profoundly with the CGI ($p < 0.0001$, $R = 0.72$). Furthermore, we observed that the NVS-J was significantly correlated with cognitive function ($p = 0.016$, $R = 0.37$) and the Brinkman index of smoking history ($p < 0.05$, $R = -0.30$). These results also indicated the criterion-related validity of the NVS-J. Conversely, the total score of the NVS-J did not demonstrate any correlation with communicative and critical HL scores in the HLQ ($p = 0.064$, $R = 0.39$; $p = 0.11$, $R = 0.25$; respectively), body mass index ($p = 0.79$, $R = -0.042$), or pain intensity ($p = 0.98$, $R = -0.004$).

Reliability

Cronbach's coefficient for the total NVS-J score was adequate (alpha = 0.72). We were able to recruit 18 participants for a test-retest study, all of whom reported no changes in their symptoms. The data for each participant were evaluated. The average period between the two surveys was 12.2 weeks [standard deviation (SD): 1.7]. A significant correlation between the two surveys was

Table 4. Factor analysis of the NVS-J.

Factor analysis	Factor1	Factor2	Factor3
Kcal	0.831	−0.179	−0.031
Gram	0.709	0.210	0.046
%	−0.182	0.828	−0.029
Cup	0.238	0.640	0.017
Allergy	0.000	−0.040	0.855
Reason	−0.012	0.043	0.834

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demonstrated by a Pearson's correlation analysis ($p<0.001$, $R = 0.82$), which suggests good reproducibility. The applicable rate is shown in Table 5. There were no unanswered questions on any surveys administered during either time point in the data that were analyzed.

Cut-off point for low HL

The area under the ROC curve for the CGI-HL was 0.87. The theoretical maximum of this value is 1.00, which indicates perfect discrimination. A score of 2 on the NVS-J showed very high sensitivity (94.7%) but moderate specificity (75.0%); a score of 1 showed high sensitivity (84.2%) and relatively high specificity (83.3%). Further, the SSLR score of 1 was the maximum (5.05) among all the scores (Table 6). Therefore, a score of 1 on the NVS-J would be the suitable clinical cut-off point for screening purposes of low HL. This is compatible with the original cut-off point.

Discussion

This study demonstrated that the NVS-J has good validity and reliability. The results obtained in this study were comparable to those in previous studies [10,21]. With regard to criterion-related validity, significant correlations between the NVS-J, HLQ, and the CGI-HL by the physicians were observed. Furthermore, the NVS-J score was significantly correlated with cognitive function and smoking history, suggesting that the NVS-J would reflect overall numeracy ability and health practices. With regard to construct validity, we conducted a factor analysis and found that the six items of the NVS-J consist of three determinative factors, which can be defined as "basic numeracy ability," "complex numeracy ability," and "serious-minded ability." A factor analysis of this nature has not yet been attempted with regard to the NVS. One was not performed in the original NVS study conducted by Barry et al. (2005) in the US, or in the validation study of the screen by Rowlands et al. (2013) in the UK [10,21]. The factor analysis was fundamental in revealing covert psychometric properties of the NVS-J and the relationships between them. Here, we compared the present factor structure of the NVS-J to the HLQ. The HLQ assesses three components of HL: functional, communicative, and critical HL [15]. Functional HL refers to the ability to read and comprehend basic medical information. Communicative HL denotes the ability to extract important information and independently apply that information to personal health maintenance. Communicative HL is thus more advanced than functional HL, but still relatively basic. Critical HL refers to the extent to which individuals can thoroughly examine the necessity and suitability of medical information, and use that information to make decisions about personal health maintenance. These three HL abilities comprise a 3-step hierarchical structure. The present three extracted factors of the NVS-J are likely consistent with these core HL abilities in the HLQ [15].

In fact, our research revealed correlations between patients' NVS-J scores and total scores on the HLQ. NVS-J scores were also associated with functional HL, which is the fundamental subscale of the HLQ. These results indicate that the NVS-J has good criterion-related validity in evaluating overall HL and fundamental HL. On the other hand, NVS-J scores were not correlated with scores on the communicative and critical subscales of the HLQ. Its potential use for detecting limited numeracy skills makes the NVS one of a kind, as the HLQ cannot currently be used to ascertain such skills in individuals. Therefore, the NVS-J can be used independently or on its own to evaluate HL, especially numeracy skills.

Further, the distribution of scores attained by participants on the NVS-J, detailed in Table 2, varied from the one observed on the original NVS. However, our analysis utilizing ROC Curves clearly demonstrated that a score <2 on the NVS-J had moderately high sensitivity (84.2%) and specificity (83.3%) for predicting limited literacy, consistent with assessments by patients' attending physicians. This cut-off point was similar to that used in the original NVS study, in which the researchers also observed that scoring <4 could predict adequate literacy based on the stratum-specific likelihood ratios they obtained. However, our ratios (see Table 6) did not enable us to clearly categorize individuals in terms of whether they had adequate or robust health literacy. Therefore, differing from the original NVS, the present NVS-J could predict limited literacy when scores were <2 with a moderately high degree of specificity, but could not separate patients with adequate health literacy from those who had high health literacy.

Individuals with limited health literacy are less knowledgeable about their health problems [22–27], endure lengthier hospital-

Table 5. Applicable rate of the respective questions.

	Kcal	Cup	Gram	%	Allergy	Reason
Applicable rate (%)	90.1	86.0	79.1	74.4	81.4	79.1

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Table 6. Stratum-specific likelihood ratios for NVS-J cut-off scores by the CGI-HL.

Score of the NVS-J	Sensitivity	Specificity	Stratum-specific likelihood ratio (SSLR)
0	47.4	87.5	3.79
1	84.2	83.3	5.05
2	94.7	75.0	3.79
3	94.7	41.7	1.62
4	100	29.2	1.41
5	100	4.17	1.04
6	100	0.00	1.00

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izations [28,29], pay higher health care costs [30,31], and are less healthy [32–36] than those with adequate or high health literacy. Health information can be tailored for delivery to patients in an understandable format, provided patients have adequate health literacy. Additionally, patients with low health literacy have poor knowledge of pain medications, including their proper use and intake. Opioid analgesics are potent and thus commonly prescribed for chronic pain treatment; however, these drugs carry significant dependence and abuse risk for a portion of patients. Health care professionals should consequently be trained to recognize patterns of opioid abuse and misuse, and educate chronic pain patients on proper opioid administration. Training and ongoing education should be provided for chronic pain patients on effective dosing schedules and risks of pain medications, particularly opioids, that have a high potential for misuse, abuse, dependence, and life-threatening withdrawal symptoms. Patients should be required to demonstrate adequate numeracy ability prior to receiving an opioid prescription intended for self-administration. Furthermore, chronic pain patients should be capable of understanding the specifics of non-pharmacological coping strategies that may improve functioning, ADLs, and QOL. Given that HL encompasses these basic cognitive abilities, HL assessment is essential for chronic pain patients, as well as patients suffering from other chronic illnesses (e.g., congestive heart failure, diabetes mellitus, and asthma).

Limitations

The sample size of this study was small. In the original Newest Vital Sign (NVS) study by Barry et al. (2005) that enrolled 250 participants [10], the validity of the NVS was not directly associated with patients' health literacy (HL) levels as evaluated by health care professionals. Instead, by including the Test of Functional Health Literacy in Adults (TOFHLA), which can be used to assess medical linguistic problems [37], the original NVS demonstrated sensitivity and specificity for detecting low levels of HL. However, we felt that a conventional test/assessment utilizing medical words might be insufficient for detecting low HL levels in our study population (chronic pain patients). We thus decided to evaluate HL by also asking patients' attending physicians to complete a clinical global impression scale of patients' comprehensive HL levels, as they had expertise in educating patients on health and helping them understand health related information in their clinical practice. Because of this, the number of participants was fairly limited, but we were able to more precisely screen for limited HL with a higher degree of sensitivity and specificity. While the results of our preliminary study demonstrated the validity of the NVS-J in screening for limited HL, further research is required. From our pilot data, we could calculate the ideal sample size for more confirmatory investigations of its validity.

Author Contributions

Conceived and designed the experiments: TK M. Sumitani KK. Performed the experiments: M. Sumitani TO. Analyzed the data: M. Suka HI MK MO HS KK. Contributed reagents/materials/analysis tools: AI. Wrote the paper: TK M. Suka HI HS.

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Research Article Open Access

Classification of the Pain Nature of CRPS Type 1, Based on Patient complaints, into Neuropathic Pain and Nociceptive/Inflammatory Pain, Using the McGill Pain Questionnaire

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Abstract

Objectives: The precise causes of Complex Regional Pain Syndrome (CRPS) are as yet not well known. Some consider CRPS type 1 without apparent nerve injury to arise due to a prolonged inflammatory state after initial trauma and its underlying pathophysiology indicates Nociceptive/Inflammatory Pain (NocP) components. Yet others have shown clear direct evidence of nerve injury in CRPS type 1-affected limbs, and they consider CRPS type 1to be Neuropathic Pain (NeP). The McGill Pain Questionnaire (MPQ) has the potential to diagnose pain disorders as well as suggest the underlying pathophysiology.

Methods: We investigated pain characteristics of 165 NeP and 66 NocP patients, by using the 78 words of the MPQ, and thereby developed a discriminant function which efficiently discriminates NocP from NeP. We then applied this function to 36 CRPS type 1 patients' complaints and classified their pain into either NocP or NeP.

Results: The discriminant probability of the function was 81.0% (chi-square, p=0.24) and this function revealed 47.2% of CRPS type 1 patients' complaints were classified as NocP and 52.8% as NeP. These subgroups showed almost comparable demographic data.

Considerations: Our results indicate that CRPS type 1 cannot be classified as NeP or NocP dichotomously according to pain descriptions. This raises the possibility that CRPS type 1 represents a "mixed" pain mechanism comprised of both NeP and NocP.

Introduction

Pain is inherently subjective. To understand another people's pai, we must accurately interpret what others say or show by their behaviors. In many investigations of pain, various measurements and questionnaires are used to evaluate pain as objectively as possible. Among these, the McGill Pain Questionnaire (MPQ) is one of the most widely-used and well-validated questionnaires [1]. The MPQ consists of 78 pain descriptors, which are classified into 20 sub-groups. Furthermore, the 20 sub-groups can be scored and assessed in view of four major dimensions of pain: sensory, affective, evaluative and miscellaneous pain. Some investigations have suggested that the MPQ is clinically useful for diagnosing the pain complaints of patients on the basis of the nature of their pain descriptions [2-4]. Patients with certain pain syndromes frequently select characteristic words in the MPQ to describe their pain. For example, cancer pain patients consistently characterize their pain as shooting, sharp, gnawing, burning and heavy, while those with neuropathic pain tend to describe theirs as burning, shooting, tingling, piercing, and so on [1,5,6].We previously succeeded in demonstrating two categories of neuropathic pain [one involves superficial-pain descriptions (e.g., burning, tingling, piercing and so on), and the other deep-somatic descriptions (e.g., squeezing, cramp-like, twisting and so on)] which are differently alleviated according to mirror visual feedback treatment [7]. Thus, the nature of pain is useful for suggesting underlying the pathophysiological mechanism(s), and the MPQ has the potential to diagnose pain disorders and reveal the causative pathophysiology.

Following a noxious event, Complex Regional Pain Syndrome (CRPS) may occur accompanied by severe pain disproportionate to the initiating event, edema, skin color asymmetry, skin temperature asymmetry, atrophic changes and motor functional limitations. The precise cause of CRPS is as yet not well known, though it is clear that CRPS often induces a number of functionally debilitating effects on daily life. CRPS is classified into CRPS type 1, previously known as reflex sympathetic dystrophy without apparent nerve injury, and CRPS type 2, previously known as causalgia with apparent nerve injury. Although the symptomatology between CRPS type 1 and type 2 is known to be similar, the etiologies of respective types of CRPS are considered to be different according to presence or not of an overt nerve injury. CRPS type 2 is generally considered to be one of forms of neuropathic pain, on the basis of re-definition and the diagnostic flow-chart of neuropathic pain proposed by the Neuropathic Pain Special-Interest-Group of the International Association for the Study of Pain (IASP) [8]. On the other hand, CRPS type 1 is not included within the neuropathic pain category because the diagnosis of CRPS

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type 1 is clinically made by absence of documented nerve lesion. What is the underlying pathophysiological mechanism(s) of CRPS type 1? Some researchers have suggested that CRPS type 1 develops due to prolonged inflammation following a traumatic event and they propose that CRPS type 1 is a nociceptive/inflammatory form of pain. Clinically, understanding the pathophysiological mechanism(s) underlying pain is critical to selecting optimal treatment strategies, especially pharmacotherapy. In the present study, we aimed to elucidate whether the etiology of CRPS type 1 is nociceptive or neuropathic according to pain quality descriptors of the patients. We initially examined the discriminant validity of the classification by providing a list of distinct pain quality descriptors in the MPQ to dichotomize pain as nociceptive or neuropathic. Next, we classified pain descriptions given by patients with CRPS type 1 into nociceptive or neuropathic pain by using the MPQ.

Methods

Experiment 1

Subjects: Two hundred thirty-one patients, referred to Department of Anesthesiology and Pain Relief Center, The University of Tokyo Hospital and the Center for Pain Management (Anesthesiology) at Osaka University Medical Hospital during the period from July 2003 to January 2008, participated in this study. The inclusion criteria were: (1) suspicion (by the referring physician) of neuropathic pain and nociceptive/inflammatory pain in the extremities; (2) mean pain intensity in the past month (recorded at inclusion) >1 on an eleven-point numerical rating scale (NRS) (0=no pain, 10=worst possible pain); (3) pain duration >3 months; and (4) age >18 years. The exclusion criteria were: (1) comorbid psychiatric disorders like as schizophrenia, major depression, character disorders or other psychotic conditions according to the ICD-10 criteria and (2) inability to answer pencil-and-paper questionnaires by themselves. The enrolled patients were then divided into two groups: neuropathic pain (NeP, n=165) and nociceptive pain (NocP, n=66).The latter includes inflammatory pain as assessed by experienced pain physicians on the basis of history, local pain distribution and clinical examinations in addition to certain imaging studies. Criteria for NeP group assignment were based on those for diagnosis as redefined by the IASP Neuropathic Pain Special-Interest-Group, by experienced pain physicians: pain distribution neuroanatomically plausible, history suggesting relevant nerve lesion, negative (e.g., hypoesthesia) or positive (e.g., hyperalgesia) sensory signs confined to innervation territory of the lesioned nervous structure, and diagnostic imaging or electrophysiological tests confirming the nerve lesion [8]. CRPS type 2 patients were categorized into the NeP group. By contrast, CRPS type 1 patients were included in neither NeP nor NocP in Experiment 1. The NocP group included patients with orthopedic joint degenerative diseases or post-traumatic chronic pain syndromes involving the extremities who did not meet the criteria for CRPS type 1 in the Japanese population [9]. Patients were enrolled after providing informed consent. The study was approved by the Local Ethics Committees and adhered to the Helsinki Declaration. Demographic data were shown in Table 1.

Discriminant function analysis of pain descriptions: The MPQ, Hospital Anxiety and Depression (HAD) rating scale and the Pain Disability Assessment Scale (PDAS) were all carried out when the participants were referred to our hospital for the first time, and the data were collected. From a list of pain descriptors (78 words) in the MPQ Japanese version, the patients were asked to choose one or no descriptor, which best described their pain, from the aforementioned 20 sub-groups in a pencil-and-paper manner by themselves [10].

	NocP	NeP
N	66	165
Age (years)	47.4 ± 18.3	62.8 ± 14.3
Gender (female)	41	76
Pain duration (month)	21.3 ± 53.8	31.8 ± 45.2
NRS (pain intensity)	5.5 ± 2.5	6.6 ± 2.4
MPQ total score	22.1 ± 16.7	20.4 ± 15.6
HAD score Anxiety	8.8 ± 4.5	8.9 ± 4.9
HAD score Depression	8.9 ± 5.1	9.2 ± 5.2
PDAS score	26.7 ± 13.5	29.3 ± 16.5

Table 1: Demographic data of 231 participants.

Numerical values indicate means ± SD. Statistical analyses were performed using the Mann-Whitney test. NocP indicates nociceptive pain; NeP indicates neuropathic pain; NRS indicates numerical rating scale of pain intensity.

	CRPS type 1	NocP subgroup	NeP subgroup	*Pvalue*
N	36	17	19	-
Age (years)	48.1 ± 16.9	51.9 ± 15.2	44.7 ± 18.0	*0.21*
Gender (female)	22	9	13	*<0.01*
Pain duration (month)	441.0 ± 234.0	378.9 ± 248.3	496.6 ± 211.4	*0.72*
NRS (pain intensity)	6.4 ± 1.8	6.2 ± 1.6	6.5 ± 2.8	*0.64*
MPQ total score	21.5 ± 14.2	22.9 ± 14.8	20.2 ± 13.9	*0.58*
HAD score Anxiety	8.6 ± 4.1	8.0 ± 4.2	9.2 ± 4.2	*0.43*
HAD score Depression	9.6 ± 5.8	11.3 ± 7.0	8.2 ± 4.2	*0.15*
PDAS score	26.0 ± 14.3	27.9 ± 15.1	24.4 ± 13.9	*0.50*

Table 2: Demographic data of 36 CRPS type 1 patients, 19 neuropathic pain and 17 nociceptive pain subgroups.

CRPS type 1 patients were divided into neuropathic pain and nociceptive pain subgroups on the basis of the discriminant function which is obtained in Experiment 1. Numerical values indicate means ± SD. Statistical analyses were performed using the Mann-Whitney test.NocP indicates nociceptive pain; NeP indicates neuropathic pain; NRS indicates numerical rating scale of pain intensity.

The discriminant function analysis is similar to a regression analysis. The discriminant function analysis builds a predictive model for group membership, and the model is composed of a discriminant function based on linear combinations of predictor variables. The discriminant function analysis assesses how well the independent variables separate the groups: the analysis defines a coefficient of each independent variable. A discriminant score can be calculated based on the weighted combination of the independent variables. In the present study, we used the discriminant function analysis to define a coefficient of each descriptor in the MPQ and maximize the difference between the discriminant scores in NocP and NeP groups. The resultant discriminant function was applied to NocP and NeP groups and then we evaluate the probability for whole of the participants and respective groups. By applying this function to each patient's MPQ responses, we were able to classify the responses as NeP, if the numerical value of the discriminant function was >1, or NocP if it was <1.The chi-square test was used to validate the robustness of the discriminant function. Significance was accepted at the 5% level. Each analysis was performed using Dr. SPSS (Statistical Package for the Social Sciences, USA).

Experiment 2

Subjects: The study was also approved by the Local Ethics Committees and adhered to the Helsinki Declaration.

Thirty-six CRPS type 1 patients (age, 48.1 ± 16.9 years; pain duration, 21.4 ± 20.7 months; female, 21; affected limb, upper 11, lower 14, both 2; affected side, left 20, right 13, both 3; NRS, 6.4 ± 1.8; HAD

anxiety 8.6 ± 4.2, depression 9.6 ± 5.8; PDAS 26.0 ± 14.3), referred to the two hospitals during the period from July 2003 to January 2008, were eligible for participation in this study (Table 2). All met the Japanese diagnostic criteria for CRPS, but did not have any apparent nerve injuries which are evaluated by experienced pain physicians. The patients answered the same set of pencil-and-paper questionnaires (the MPQ and so on) by themselves. The patients were enrolled after providing informed consent.

Discrimination of descriptions of CRPS type 1, by applying the discriminant function between neuropathic pain and nociceptive pain: On the basis of the discriminant function developed in Experiment 1, CRPS type 1 patients' responses to the MPQ were classified as NeP or NocP. Then, we compared demographic data of the NeP and NocP subgroups in CRPS type 1 patients by using the Mann-Whitney test and the chi-square test.

Results

Experiment 1

Coefficients for pain descriptors in the MPQ and discriminant probability

The distribution of pain descriptors chosen from the list of the MPQ and coefficients for each pain descriptor to classify pain as NocP or NeP dichotomously are shown in Table 3. We set the coefficients for each word and the constant term, to discriminate the two groups most efficiently, by using the discriminant function analysis. Among 78 pain descriptors, "annoying" and "tearing" were discarded: their coefficient was set as 0. On the other hand, "gnawing", "smarting" and "frightful" were characterized as neuropathic descriptions because their coefficients were more than 3. "Cruel" and "troublesome" were characterized as nociceptive/inflammatory descriptions but their contribution to categorize patients' pain response to the MPQ into NocP was relatively small because their absolute value of coefficient is around 1.6 at most.

The probability of this discriminant function was 81.0%

Group	Sub-group	Descriptor	Coefficients
1 sensory	1 temporal	flickering	1.12
		quivering	0.18
		pulsing	-0.20
		throbbing	1.20
	2 spatial	beating	0.44
		pounding	-1.32
		jumping	0.70
		flashing	0.41
		shooting	0.51
	3 punctate pressure	pricking	0.00
		boring	1.62
		drilling	-0.37
		stabbing	1.30
	4 inciseve pressure	lancinating	0.23
		sharp	-0.47
		cutting	1.28
		lacerating	-0.41
	5 constructive pressure	pinching	-1.44
		pressing	-0.34
		gnawing	3.62
		cramping	-0.30
	6 traction pressure	crushing	0.17
		tugging	0.83
		pulling	1.24
		wrenching	-0.56
	7 thermal	hot	0.13
		burning	0.27
		scalding	0.00
		searing	2.94
	8 brightness	tingling	-1.10
		Itchy	-0.79
		smarting	3.41
		stinging	-0.55
	9 dullness	dull	0.34
		sore	1.30
		hurting	-0.77
		aching	1.05
		heavy	0.95
		tender	-0.34
	10 sensory miscellaneous 1	taut	0.68
		rasping	1.13
		splitting	-0.62
2 effective	11 tension	tiring	-0.94
		exhausting	0.37
	12 Autonomic	sickening	-0.84
		suffocating	-0.76
	13 fear	fearful	-0.63
		frightful	3.14
		terrifying	0.16
	14 punishment	punishing	-0.27
		grueling	-0.29
		cruel	-1.64
		vicious	1.30
		killing	0.88
	15 affective miscellaneous	wretched	0.41
		blinding	0.16
		annoying	0.00
3 evaluative	16 evaluative	troublesome	-1.57
		miserable	0.07
		intense	-1.07
	17 sensory miscellaneous 2	unbearable	-1.83
		spreading	0.19
		radiating	0.93
		penetrating	-1.07
4 sensory miscellaneous 2	18 sensory miscellaneous 2	piercing	-0.50
		tight	0.86
		numb	-0.14
		drawing	-1.17
		squeezing	-1.1
	19 sensory	tearing	0.00
		cool	0.35
		cold	0.25
		freezing	0.
		nagging	-0.24
5 affective miscellaneous	20 affective-evaluative miscellaneous	nauseating	0.94
		agonizing	0.05
		dreadful	1.35
		torturing	0.07
		Constant term	-0.49

Table 3: Coefficients for 58 pain descriptors in the MPQ and a constant term in the discriminant function between neuropathic pain and nociceptive pain.

(Wilks'slambda, 0.64; chi-square test, p=0.24). The probabilities of the function for NocP and NeP were 80.3% and 81.2%, respectively.

Experiment 2

CRPS type 1 patient's complaints of their pain characteristics

Applying the discriminant function developed in Experiment 1, 19 CRPS type 1 patients' descriptions based on the MPQ were classified into NocP (47.2%) and 17 were classified into NeP (52.8%). Demographic data of NocP and NeP subgroups of CRPS type 1 patients were almost similar, except for gender (Table 2).

Discussion

Pathophysiological mechanisms underlying CRPS type 1 are as yet poorly understood. Some researchers have suggested that CRPS type 1 is nociceptive and inflammatory pain, based on the following concepts and observations: the axonal reflex and retrograde secretion of neurotransmitters from peripheral nerve endings into peripheral tissues can induce dilation and hyper permeability of small vessels, resulting in skin erythema, edema and temperature elevation, and peripheral nerve sensitization results in allodynia, hyperalgesia and severe pain inappropriate to the initiating event [11]. Furthermore, pro-inflammatory cytokines, mainly Tumor Necrosis Factor alpha (TNF-alpha) and Interleukin-6 (IL-6), are reportedly elevated in CRPS-affected limbs but not in CRPS-unaffected limbs [12]. On the other hand, other researchers have suggested that CRPS type 1 is neuropathic pain based on direct evidence of nerve injury. Oaklander et al. demonstrated loss of axons in the CRPS-affected limb by means of skin biopsy, indicating hypoesthesia of CRPS-affected limbs; and Blaes et al. reported autoantibodies to the surface of peripheral autonomic neurons in sera from CRPS type 1 patients, which produced sympathetic dysfunction in CRPS-affected limbs [13,14]. Thus, the controversy as to whether CRPS type 1 is primarily neuropathic or nociceptive has raged for more than two decades. Clinically, understanding the underlying pathophysiological mechanism(s) of pain is critical to selecting appropriate treatment strategies, especially pharmacotherapy. However, in human pain patients, it is very difficult and often impossible to define the mechanism(s). Instead, we usually infer the mechanism(s) from characteristic pain descriptions, in combination with physical and imaging examinations. One of the most exciting features of the MPQ is its potential value as an aid in the differential diagnosis of various pain syndromes [1]. To support this critical understanding in clinical settings, we developed a discriminant function based on MPQ descriptions and found that moderate probability could be demonstrated. In the present study, by applying the discriminant function to pain descriptions of CRPS type 1, we classified about a half of our CRPS type 1 patients as NocP and the other half asNeP. Therefore, our findings suggest that the underlying pathophysiological mechanism(s) of CRPS type 1 is in a gray zone between NeP and NocP. Recently. The mixed pain condition has been proposed to be the pathophysiological mechanism underlying chronic pain in clinical settings. With a prolonged nociceptive and inflammatory state, for example, neuronal hyper-excitability can occur in the spinal dorsal horn. Neuronal hyper-excitability is also observed with NeP. Furthermore, the actions of inflammatory mediators originating from peripheral tissue and proliferation of lymphocytes in peripheral nerves can induce neuronal inflammation and inflammatory-neuropathic pain [15]. Supporting evidence comes from Freynhagen et al. study showing that chronic low back pain, which has been considered to be due to mechanical and inflammatory nociception, includes a neuropathic component as revealed by using a neuropathic pain screening tool [16]. Thus, based on such observations, the participation of nociceptive as well as neuropathic mechanisms has been confirmed in chronic pain states, and is thus proposed to be a mixed pain condition [17]. In the present study, the discriminant function apparently showed moderately-high probability (more than 80%). However, the function was not sufficiently robust nor was the results statistically significant. This might be due to ambiguity caused by NeP and NocP group participants in Experiment 1 having both neuropathic and nociceptive components, namely mixed pain. Considering that a cohort of CRPS type 1 patients would have both neuropathic and nociceptive mechanisms and CRPS type 1 might well be a mixed pain disorder, it would be not be surprising for CRPS type 1 to be dichotomously classifiable as neither NeP nor NocP based on such an ambiguous function. Our findings would be helpful to select optimal treatment strategies for CRPS type 1.

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Ⅰ．基礎／臨床研究

2．臨床研究

2）運動器慢性疼痛の疫学調査

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要　旨
我が国における運動器の慢性疼痛の実態と問題点を明らかにするために疫学調査を施行した．その結果，運動器の慢性疼痛は長期の治療にもかかわらず，その改善は必ずしも得られず，患者自身の身体及び精神的健康，さらには社会生活に悪影響を与え，日常生活において介助を要する機会が増加するために周囲に与える影響も少なくない実態が明らかになった．運動器の慢性疼痛に対する治療法と治療体系の早急な見直しが必要である．

（ペインクリニック 34：S62-S66，2013）
キーワード：疫学，慢性疼痛，筋骨格系

はじめに

わが国の国民が現在どんな症状に苦しんでいるかを示すデータとして，国民生活基礎調査がある．これによると，頻度の高い自覚症状として，腰痛，肩こり，関節痛，頭痛といった痛みの症状が上位を占めている[1]．しかし，これら慢性的な疼痛の問題は，致死的でない，各科に跨る領域である，実態がよくわからない等々の理由により，個別の行政施策があまり行われなかった領域であった．しかし，米国では1998～1999年に大規模な疫学調査が行われ，程度の高い慢性疼痛に悩む患者が成人人口の9％を上回ること，無効な治療やドクターショッピングなどにより医療資源が浪費されていること，疼痛のための就労困難などによる社会的損失が年間650億ドルに上ることなどが明らかになり，この慢性疼痛が医学，公衆衛生学的問題としてクローズアップされるに至った[2]．

しかし，わが国においては，慢性疼痛の対策を立案するにあたり，その基礎的情報すら不足しているのが現状であった．一方，欧米各国では全国レベルの疫学調査がすでに実施され，対象とする集団や使用した質問票の相違，慢性疼痛の基準の違いなどによりばらつきはあるものの，慢性疼痛の有症率は23～35％と報告されている[3-5]．また近年では，アジアでも香港，シンガポールで調査が実施され，有症率は9～11％とかなり欧米と比較して低い結果であった[6,7]．これに対し，日本では服部ら[8]が疫学調査を行い，慢性疼痛の有症率は13.4％と報告された．しかし，この調査はインターネット調査であり，慢性疼痛有症者や60歳代以降の年代の者にとっては，インターネットのハードルは低くないと予想され，アクセスできる者が限定

Epidemiologic study of musculoskeletal chronic pain in Japan
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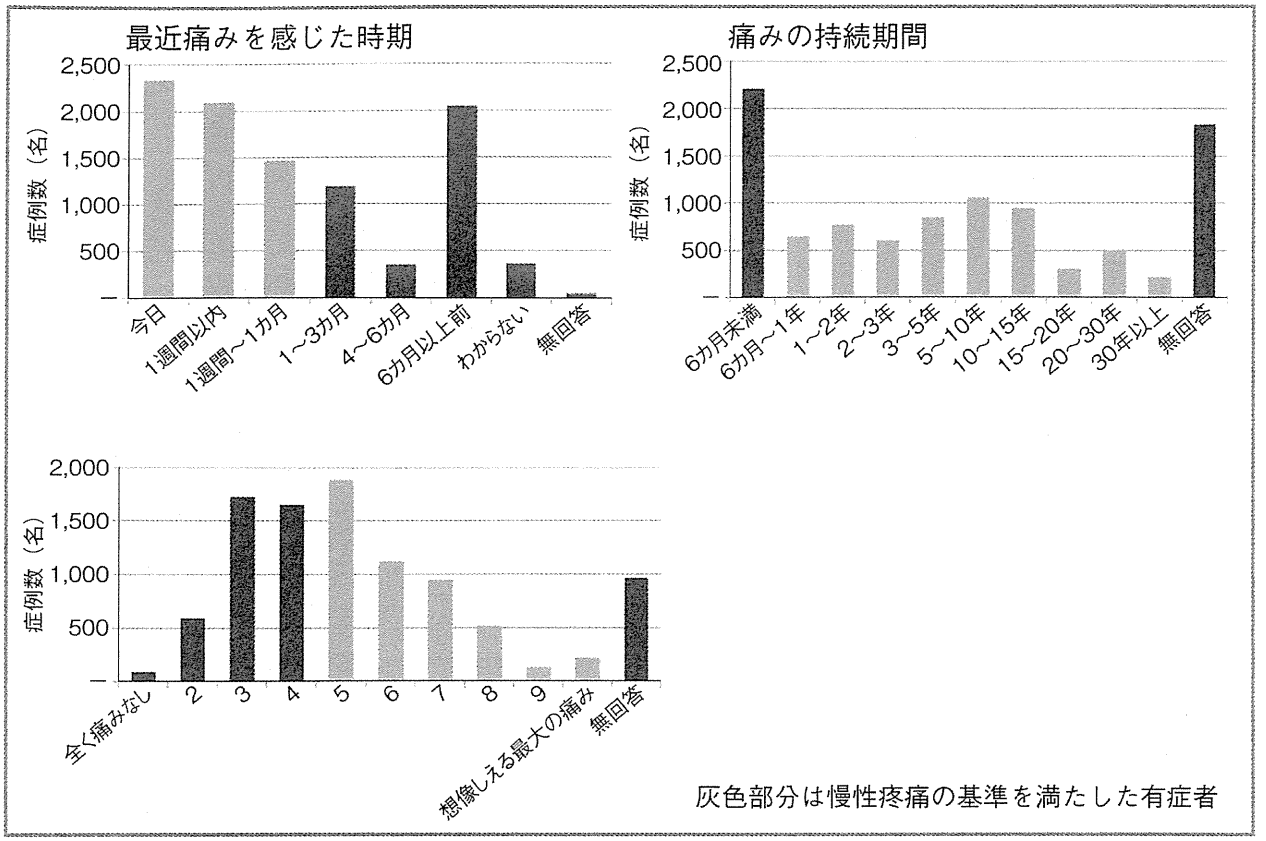

図1　筋骨格系の疼痛の出現時期，持続期間，程度（visual analogue scale）（文献9より引用改変）

されるという点に注意が必要である．さらに，この調査における慢性疼痛には，頭痛，生理痛，顔面神経痛，帯状疱疹後神経痛なども含まれており，運動器における慢性疼痛の実態の詳細な検討はされなかった．

そこで，運動器の慢性疼痛に焦点をあて，その対策立案に不可欠な情報を，臨床医学，公衆衛生，行政施策の観点から浮き彫りにするために，極力バイアスの除去に配慮したデザインにより，全国ランダム抽出サンプルに対する疫学調査を実施した[9]．サンプリングは，住所台帳に基づく無作為抽出サンプルを基盤とし，性，年齢分布が国勢調査の分布に近くなるように配慮した．1万超のサンプルを得るために回答率を55％と推定して，19,198名の対象者に調査票を郵送し，有効回答数は11,507名（女性6,365名，男性5,142名）で，回収率は59.9％であった．質問票の内容は，基礎情報（性別，年齢，在住地，職業など），筋骨格系の慢性疼痛の実態に関する設問（疼痛の程度・部位・期間，治療の有無，治療を受けた機関，治療内容，治療期間，費用，治療効果，満足度），日常生活・QOLに関する設問（Katz ADL scale，Lawton instrumental ADL scale，SF-36），社会的損失に関する質問（休業，転職，退職その他）である．

1．運動器慢性疼痛の実態と背景因子

「これまでに，頸（くび）の痛み・肩こり・腰痛・手足の痛みなど，骨や筋肉，関節・神経に起因すると思われる痛みを経験したことがありますか」という質問に対して，「ある」と回答した者は86％（9,891名）であった．これらの中で

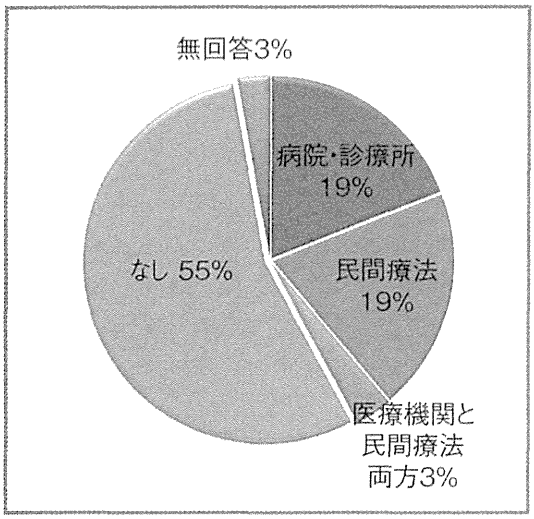

図2　筋骨格系の慢性疼痛有症者の治療機関
（文献9より引用改変）

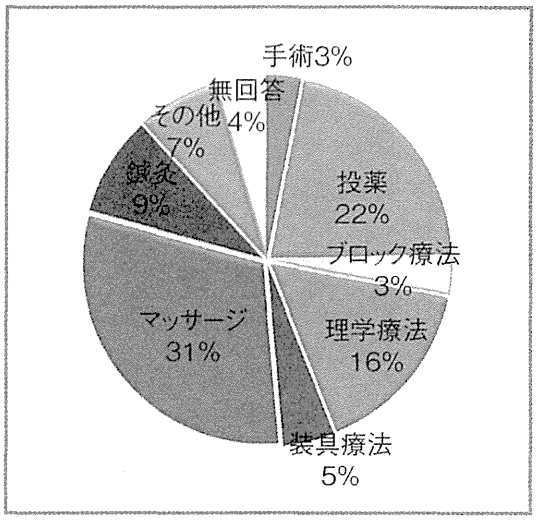

図3　筋骨格系の慢性疼痛の治療内容
（文献9より引用改変）

慢性疼痛を，①現在から1カ月以内に症状が存在し，②持続期間が6カ月以上で，③ visual analogue scale（VAS）が5以上と定義すると[8]，有症率は15.4%（1,770名）であった（図1）．慢性疼痛有症者の背景因子として，性別では女性の有症率が高く（男性13.6% vs 女性16.8%），服部らと同様の結果であった．年代別の有症率は，服部らの報告では，50歳以上の中高齢層で有症率は高く，30～40歳代，30歳未満と順に低下していたが，今回の検討では30～50歳代のいわゆる就業年齢層で17～19%と他の年齢層より有意に高いことが明らかになった．この結果は，大都市圏が郡部よりも有症率が高いこと，職種でも専門職，事務・技術，パート・アルバイト，労務・技能で高く，無職，農林水産業で低かった結果と一致していた．これらの相違の要因としては，全身を含む慢性疼痛と運動器の慢性疼痛の違いによるものが考えられるが，疼痛部位は両調査とも上位は，腰，頸，肩，膝と一致していたことから，前述したサンプリングの違いによる可能性が高いと考えられる．

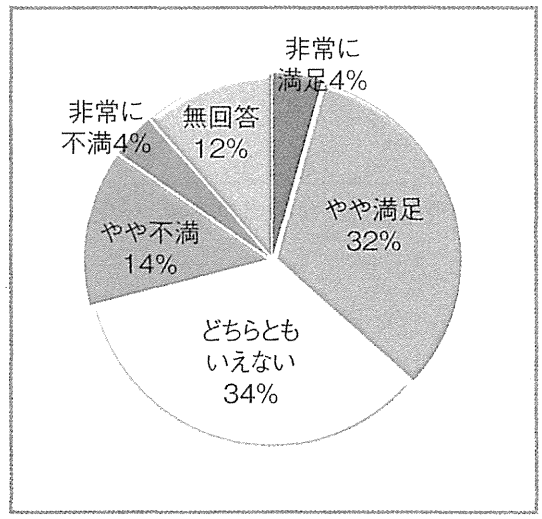

図4　筋骨格系の慢性疼痛の治療に対する満足度
（文献9より引用改変）

2．慢性疼痛に対する治療の実態からみた問題点

慢性疼痛有症者の42%が調査時に治療を受けており，その治療機関は，病院・診療所などの医療機関が19%，民間療法が20%，その両方が3%であり，医療機関と民間療法でほぼ同程度に治療を受けていることが明らかになった

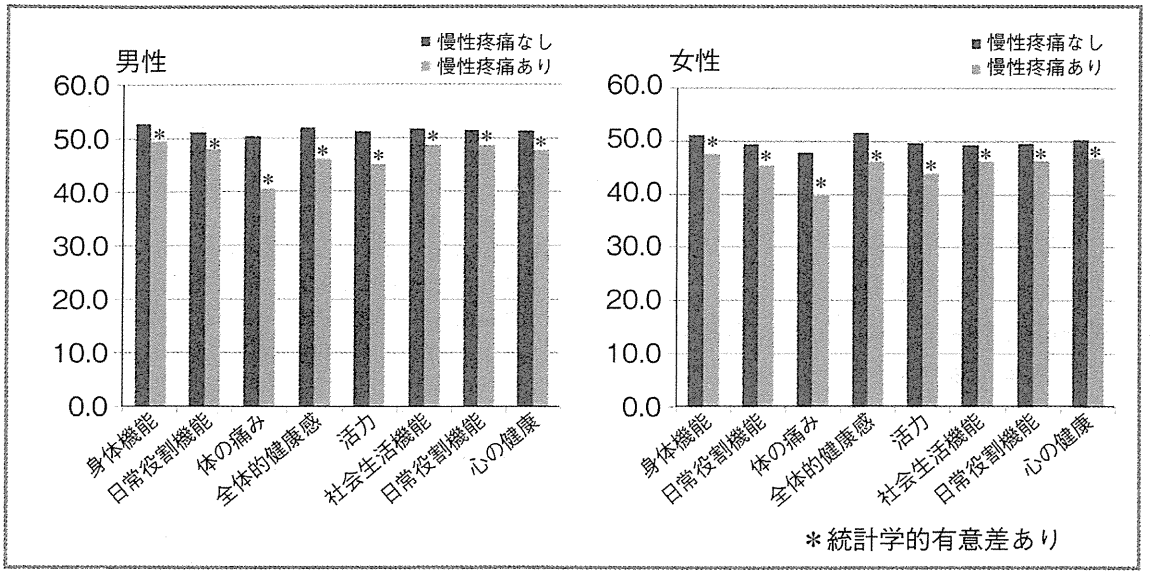

図５　筋骨格系の慢性疼痛の有無による SF-36 の比較（文献９より引用改変）

（**図２**）．これを反映して，治療内容もマッサージと鍼灸で４割を占め，次いで投薬が 22%，理学療法が 16%，装具療法が 5%であった（**図３**）．治療の頻度は２週間に１回以下が最多で 35%，次いで週１回が 25%，週数回と２週に１回が 15%であり，その治療期間は１年以上が全体の７割を占め，治療が長期化している実態が浮き彫りになった．また，治療に対する満足度は低く（「どちらともいえない」が 34%，「やや不満」14%，「非常に不満」が 4%）（**図４**），治療機関の変更も約半数の有症者にみられた．その理由として「前の治療に満足できなかった」が４割と最多であったことから，運動器の慢性疼痛に対する現行の治療では十分な効果が得られず，治療機関を変える，いわゆるドクターショッピングを行っている実態が明らかになった．

さらに，これらの治療に要する費用（自己負担額，入院や手術の一時金は除く）は，月額 3,000 円代と 5,000 円代がいずれも 11%と最多で，特筆すべきは月額 10,000～15,000 円が約 8%存在したことである．治療期間が長期化している状況を勘案すると，運動器の慢性疼痛に対する治療費が高額に上り，医療経済に大きな影響を与えていることが本調査により明らかになった．

３．運動器の慢性疼痛が日常・社会生活に及ぼす影響からみた問題点

SF-36 を用いた身体および精神面の健康度を慢性疼痛の有無で比較すると，すべてのスコアにおいて慢性疼痛有症者は無症者よりも有意に低かったことから，運動器の慢性疼痛が身体機能や日常役割機能（身体）など肉体面での影響のみならず，心の健康，日常生活（精神）にも大きな影響をあたえていることがわかった（**図５**）．次に，運動器の慢性疼痛が社会生活に及ぼす影響を明らかにするために，失職・退学，休職・休学，転職，仕事の内容変更のいずれかがあった者を「仕事への影響あり」として，慢性疼痛の有無で比較すると，女性では 14.6% vs 7.2%，男性では 17.6% vs 7.4%となり，慢性疼痛有症者で社会生活により大きな影響をきたしていることがも明らかになった．さらに，慢性疼痛が基本日常生活動作に及ぼす影響を調

べると，女性では排泄，男性では入浴，身支度，トイレ，排泄，食事において影響がみられた．以上の結果より，運動器の慢性疼痛は有症者の社会生活活動に大きな影響を与えるのみならず，日常生活における要介護度が増加することにより，その周囲の人々の社会生活にも大きな影響を与えている実態が明らかになった．

今回の調査結果を踏まえて，今後，医療側として運動器の慢性疼痛に対してどのように対処していくのか，さらには行政としてどのような施策を行っていくべきか，極めて重要な時期にきているといえる．

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※　　※　　※

4. 抗けいれん薬，抗うつ薬

Antiepileptics and antidepressants

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key words

プレガバリン
三環系抗うつ薬
デュロキセチン
侵害受容性疼痛
神経障害性疼痛

骨・関節疾患が継続し痛みが慢性的に持続する状況では，痛みの治療だけでなく慢性疼痛と併発する不眠や意欲の低下，食欲不振，不安，抑うつ症状，日常生活動作（ADL）の制限なども治療し，ADL と QOL を改善することが目標となる．骨・関節疾患に起因する侵害受容性（炎症性）疼痛に対する薬物療法としては抗うつ薬，抗けいれん薬は EBM に基づく治療指針では推奨されていないが，実臨床ではこれら薬剤が果たす役割は大きい．

はじめに

骨・関節疾患が継続し痛みが慢性的に持続する状況では，痛みに対する考え方や性格傾向が歪曲し，不眠や食欲不振，意欲の低下，日中の眠気などが現れ，それに続いて患者が過度な安静を保とうとする結果，関節機能障害や廃用症候群，活動範囲の極端な低下から抑うつ的になり，痛みの認知がさらに歪められ増悪していく悪循環（図）[1]が考えられる．骨・関節疾患に起因する慢性疼痛治療では，手術療法や理学療法以外に，このような悪循環を念頭に置いた適切な薬物療法の選択が必要である．

骨・関節疾患に起因する侵害受容性（炎症性）疼痛を対象とした薬物療法では，EBM（evidence-based medicine）に基づく治療指針に抗けいれん薬や抗うつ薬が挙げられていないが，実臨床ではこれら薬剤が果たす役割は極めて大きい．さらに，骨・関節疾患であっても痛みの病態が神経障害性疼痛の場合には，抗うつ薬や抗けいれん薬は一躍，第一選択薬として名乗りを挙げることになる．本稿では，骨・関節疾患の薬物療法として，NSAIDs や選択的 COX-2 阻害薬以外の選択肢としての抗けいれん薬と抗うつ薬の役割について概説する．

神経障害性疼痛薬物療法アルゴリズム

神経障害性疼痛は“体性感覚神経系に対する病変や疾患によって引き起こされる疼痛”と定義され[2]，国際疼痛学会をはじめとした欧米諸国に加え，わが国でも日本ペインクリニック学会から EBM の考えに則りつつ日常診療に即した神経障害性疼痛薬物療法の治療指針や推奨が提案されている[3)-5)]．いずれの治療指針でも第一選択薬として Ca^{2+}チャネル α2δ リガンドであるプレガバリンとガバペンチン，三環系抗うつ薬（主にノルトリプチリンとアミトリプチリン）が挙げられている．

プレガバリン

Ca^{2+}チャネル α2δ リガンドのうち，ガバペンチンはわが国ではてんかんを適応症とする抗けいれん薬として承認販売されているが，プレガバリンは末