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Association between the number of chronic pain sites and neuropathic-like symptoms in community-dwelling older adults with chronic pain: a cross-sectional study

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ABSTRACT

Objectives We investigated the relationship between the number of chronic pain sites and the prevalence and severity of neuropathic-like symptoms in community-dwelling older Japanese adults with chronic pain.

Design Cross-sectional study.

Setting The data analysed are from a study conducted in the city of Itoshima, Japan in 2017.

Participants The study population was 988 participants (age 65–75 years) not in need of long-term care who completed questionnaires assessing sociodemographic factors, psychological factors and chronic pain.

Primary outcome measures The primary outcome was the participants' neuropathic-like symptoms evaluated by the PainDETECT Questionnaire (PD-Q). We classified the participants into mild and moderate-to-severe pain groups according to the pain intensity on the PD-Q. The number of chronic pain sites was categorised into groups with 1, 2–3 and ≥4 sites.

Results The age-adjusted and sex-adjusted prevalence of neuropathic-like symptoms was significantly higher among the participants with 2–3 or ≥4 sites compared with the single-site group. In the binomial logistic regression analyses, the multivariable-adjusted ORs and 95% CIs for neuropathic-like symptoms among the participants with 2–3 and ≥4 sites were 1.94 (1.13 to 3.33) and 3.90 (2.22 to 6.85), respectively compared with the participants with single-site pain. The ORs for moderate-to-severe neuropathic-like symptoms increased significantly with the increase in the number of chronic pain sites.

Conclusions The number of chronic pain sites was positively associated with the presence and severity of neuropathic-like symptoms in community-dwelling older Japanese adults with chronic pain.

STRENGTHS AND LIMITATIONS OF THIS STUDY

⇒ A relatively large number of participants.
⇒ Adjustment for potentially confounding factors such as physical and psychosocial factors.
⇒ A cross-sectional design.
⇒ No objective information available to suggest central sensitisation.
⇒ No medical information on diseases whose symptoms include neuropathic pain.

INTRODUCTION

The economic burden of neuropathic pain is higher than that of non-neuropathic pain, and severe pain has been reported to be significantly associated with healthcare resource use, productivity and costs.[1] A systematic review of neuropathic pain in a general population concluded that the population prevalence of pain with neuropathic characteristics is likely to be 6.9%–10%.[2]

Low back pain and pain in the knee or hip osteoarthritis have been classified as nociceptive pain, but screening tools such as the PainDETECT Questionnaire (PD-Q) suggest that some individuals with these disorders may have neuropathic-like symptoms.[3 4] Existing evidence suggests that persistent nociceptive stimulation from the periarticular area leads to plastic changes in the central nervous system, resulting in symptoms that are similar to those of neuropathic pain.[5–8] Accordingly, given the considerable overlap between neuropathic pain and nociceptive pain in terms of underlying mechanisms and treatments, it has been postulated that it might be more constructive to view these entities as different points on the same continuum.[9]

The presence of these neuropathic characteristics has been associated with central sensitisation and thus with the presence of a contributing nociplastic mechanism.[10] Central sensitisation has been found to be present in a variety of chronic musculoskeletal pain conditions.[11] In older adults, multisite pain is more prevalent than single-site pain.[12] We thus speculated that an increase in the

number of painful joints in older adults with numerous musculoskeletal pain conditions would be reflected by an increase in the number of older adults with neuropathic-like symptoms.

However, little information is available regarding the relationship between the number of chronic pain sites and neuropathic-like symptoms in community-dwelling individuals with chronic pain. In this study, we examined the relationship between the number of chronic pain sites and the prevalence and severity of neuropathic-like symptoms in community-dwelling older adults with chronic pain.

PARTICIPANTS AND METHODS

Patient and public involvement

Patients or the public were not involved in the design, or conduct, or reporting, or dissemination plans of our research.

Study population

A study was conducted in 2017 in the city of Itoshima, Japan (population: ~96 000) as an investigation of modifiable lifestyle and social factors. This study was of independent individuals aged 65–75 years who participated in the 2017 study and were not certified as requiring nursing care at that time point by Japan's National Long-term Care Insurance System. Of the approximately 10 000 older adults, we randomly selected 5000 according to their residential area, sex and age. A set of study information sheets and questionnaires was mailed to these participants, inviting them to community centres for further assessments. Of the 5000 individuals to whom questionnaires were mailed by regular post, 1589 returned questionnaires to us (within approximately 1 month). We informed residents about this survey several times through the city's newsletter and held informational meetings at each community centre in order to increase rates of participation. With those who participated at a community centre, we held face-to-face interviews about the content of the questionnaires in order to minimise the amount of missing data. In addition, residents who did not participate through a community centre were mailed or called directly to verify questions that had not been answered. In this study, we excluded the 583 individuals without chronic pain and those with missing pain-related data (n=18). All subjects participated in this study free of any and all costs associated with the study. None of the participants received compensation for their participation, and they each provided written informed consent to have their data used and published.

The number of chronic pain sites

Chronic pain was assessed using questions ascertaining the respondent's pain lasting ≥3 months in the previous 12 months.[13] Response options were 'yes' and 'no'. When answering 'yes', the respondent was asked to indicate the affected musculoskeletal sites (of a total of 14 areas; neck, shoulder(s), elbow(s), wrist/hand(s), hip(s), knee(s), foot or feet and low back) on a body diagram. We categorised the number of chronic pain sites into 1, 2–3 and ≥4 sites. The classification was made in accord with studies in which more than four pain sites was generally associated with poor health outcomes.[14–17]

Neuropathic-like symptoms

Neuropathic-like symptoms were evaluated by the PD-Q.[18] The PD-Q was developed as a self-administered psychometric questionnaire to identify the type of pain (nociceptive pain and neuropathic pain), and the Japanese version of the PD-Q has established validity and reliability.[19] It is composed of three items evaluating characteristics of the gradation of pain (seven sensory symptom items: burning, tingling/prickling, light touching, electric shock-type pain, cold/heat, numbness and slight pressure), the pain course pattern, and radiating pain, all of which contribute to an aggregate score (range: 0–38 points).

In this study, for the purpose of comparing purely nociceptive pain (PD-Q scores ≤12) with the neuropathic component, the positive components (PD-Q scores ≥19) and the unclear components (PD-Q scores 13–18) were combined with neuropathic pain score, which is referred to as neuropathic-like symptoms. This approach is consistent with earlier studies[6 20] and ensures that participants with possible neuropathic pain characteristics are included.[5] We assessed the participants' pain intensity during the prior 4 weeks on a Numerical Rating Scale (NRS). We also classified the participants' neuropathic-like symptoms into mild (NRS score ≤3) and moderate-to-severe (NRS ≥4) pain groups based on the participants' self-reported pain intensity.[13]

Covariates

The participants' sociodemographic characteristics were collected by a questionnaire: age, sex, education level (<10 vs ≥10 years), employment status (employed vs unemployed), subjective economic status (low vs high), current tobacco use (yes or no), current alcohol consumption (yes or no) and regular exercise (≥3 times/week or not). Subjective economic status was assessed by a question asking, 'How difficult or easy is your current financial status?' Response options for this question were 'very hard', 'hard', 'easy' and 'very easy'. Based on the participant's response, subjective economic status was divided into low (very hard or hard) and high (easy or very easy). Comorbidities were determined by asking the participants to state whether they had any diseases currently being treated among osteoporosis, hypertension, hyperlipidaemia, diabetes mellitus, stroke and cardiovascular disease.

The presence/absence of sleep disturbance was measured using the Pittsburgh Sleep Quality Index (PSQI), a self-administered questionnaire for assessing subjective sleep quality during the prior 30 days.[21] The PSQI consists of seven components: sleep quality, sleep latency, sleep duration, habitual sleep efficiency, sleep

disturbance, use of sleeping medication and daytime functional impairment. We rated the PSQI on a four-point scale from 0 to 3, and an overall score is calculated (range 0–21 points); the higher the overall score, the lower the respondent's subjective quality of sleep. The reliability and validity of the Japanese version of the PSQI have been confirmed,[22] and sleep disturbance was defined in this study as a total PSQI score ≥6 points. We administered the Mini-Mental State Examination (MMSE) to residents who participated at community centres. MMSE screenings were carried out by trained nurses and staff. The final scores were determined by two people.

Statistical analysis

To assess the relationship between the participants' characteristics and the number of chronic pain sites, we conducted an analysis of covariance and a logistic regression analysis to estimate age-adjusted and sex-adjusted mean values and frequencies, and to test their differences between groups, respectively. The trends in age-adjusted and sex-adjusted means and frequencies across groups were tested by a linear regression analysis and a logistic regression analysis, respectively. The relationship between the number of chronic pain sites and the age-adjusted and sex-adjusted prevalence of neuropathic-like symptoms was examined by a direct method for both the entire population of participants and the pain-intensity subgroups.

We performed multivariable-adjusted binomial logistic regression analyses to investigate the association between the number of chronic pain sites and neuropathic-like symptoms. The following covariates were adjusted: age, sex, education level, employment status, subjective economic status, osteoporosis, hypertension, hyperlipidaemia, diabetes mellitus, stroke, cardiovascular disease, current tobacco use, current alcohol consumption, regular exercise and sleep disturbance. We also examined the association between the number of chronic pain sites and subgroups of the seven sensory symptoms (ie, burning, tingling/prickling, light touching, electric shock-type pain, cold/heat, numbness and slight pressure).

We used a multinomial logistic regression model to examine the associations between the number of chronic pain sites and both mild and moderate-to-severe neuropathic-like symptoms. A sensitivity analysis was performed excluding the participants with diabetes mellitus or stroke: the analysis was done for the 776 participants with chronic pain (after the exclusion of the 181 individuals with diabetes mellitus and the 31 participants with stroke). We performed an additional sensitivity analysis excluding the participants with an MMSE score ≤23 points[23]; the analysis was thus conducted for the 579 participants with chronic pain (after the exclusion of the 9 participants with suspected cognitive impairment or dementia from among the 588 individuals with chronic pain who completed the MMSE).

We calculated the ORs and 95% CIs, using the group with single-site pain as the reference group. The data were processed using SAS software V.9.4 (SAS Institute). Statistical significance was defined as a two-tailed p<0.05.

RESULTS

Overall, 988 participants with a mean age of 70.7 years (men: n=488, 49.4%; women: n=500, 50.6%) were included in the study. The median value of the number of chronic pain sites was 2 (IQR 1–3), and the majority of the participants reported two or more chronic pain sites; 35.3% had a single site, 41.2% had 2–3 sites and 23.5% had ≥4 sites. The most frequent chronic pain sites were in the low back (52.5%), shoulders (42.9%) and knees (40.7%). The age-adjusted and sex-adjusted characteristics of the study population according to the number of chronic pain sites are summarised in table 1.

The frequencies of women, education level <10 years, hyperlipidaemia and sleep disturbance each increased significantly with the increase in the number of chronic pain sites, whereas the frequency of regular exercise decreased significantly with the increase in the number of chronic pain sites. The PD-Q scores and the pain intensity each increased significantly with the increase in the number of chronic pain sites; there were also significant differences in these two variables between the 2–3 sites or ≥4 sites group and the single-site group.

Overall, 15.6% (n=154) of the participants were classified as having neuropathic-like symptoms. Among them, 82.5% reported moderate-to-severe neuropathic-like symptoms. As shown in figure 1, the age-adjusted and sex-adjusted prevalence of neuropathic-like symptoms were significantly increased in the groups with 2–3 and ≥4 sites compared with the single-site group. The age-adjusted and sex-adjusted prevalence of moderate-to-severe neuropathic-like symptoms was also significantly increased among the participants with 2–3 or ≥4 sites compared with the single-site group, while there was no evidence of a significant association between 2–3 and ≥4 sites and the prevalence of mild neuropathic-like symptoms.

Table 2 provides the ORs and 95% CIs of the presence of neuropathic-like symptoms according to the number of chronic pain sites. In the binomial logistic regression analyses, the age-adjusted and sex-adjusted ORs and 95% CIs for the presence of neuropathic-like symptoms among the participants with 2–3 and ≥4 sites were 1.93 (1.22 to 3.07) and 3.92 (2.43 to 6.32), respectively compared with the single-site group (P for trend<0.001, per 1-site increment: OR 1.37, 95% CI 1.26 to 1.49, p<0.001). This association did not materially change after adjustment for potential confounding factors.

Table 3 presents the multivariable-adjusted ORs and 95% CIs of the presence of burning, tingling/prickling, light touching, electric shock-type pain, cold/heat, numbness and slight pressure symptoms, each of which was significantly increased among the participants

Table 1 Age-adjusted and sex-adjusted characteristics of the study population according to the number of chronic pain sites

Variable	No of chronic pain sites			P for trend
	1 site n=349	2–3 sites n=407	≥4 sites n=232	
Age, years, mean (SE)	70.9 (0.2)	70.5 (0.2)	70.7 (0.2)	0.192
Women, %	44.6	51.2	58.6**	0.001
Educational level, <10 years, %	11.7	15.3	18.1	0.030
Employment, employed, %	35.2	34.3	37.3	0.688
Subjective economic status, low, %	55.0	54.1	63.2	0.081
Osteoporosis, %	7.4	6.2	5.0	0.158
Hypertension, %	41.8	45.9	45.6	0.318
Hyperlipidaemia, %	30.0	33.1	38.7	0.037
Diabetes mellitus, %	17.7	17.0	16.8	0.779
Stroke, %	3.9	4.6	4.6	0.648
Cardiovascular disease, %	12.9	12.1	12.8	0.919
Current tobacco use, %	6.0	7.8	7.6	0.369
Current alcohol consumption, %	48.7	51.7	52.0	0.442
Regular exercise, ≥3 times/week, %	70.3	62.9	60.6*	0.013
Sleep disturbance, %	25.4	28.9	36.9*	0.009
PD-Q, score, mean (SE)	6.3 (0.2)	7.4 (0.2)*	9.9 (0.3)**	<0.001
Pain intensity, mean (SE)	3.5 (0.1)	4.5 (0.1)**	5.3 (0.2)**	<0.001

An analysis of covariance and a logistic regression analysis were respectively used to estimate age-adjusted and sex-adjusted means values and frequencies, and to test their differences between groups. The trends in age-adjusted and sex-adjusted means and frequencies across groups were tested by a linear regression analysis and a logistic regression analysis, respectively. Age was sex adjusted; female sex was age adjusted.
*p<0.05, **p<0.01 vs 1-site group.
PD-Q, PainDETECT Questionnaire.

with 2–3 sites and ≥4 sites compared with the single-site group. There was no evidence of a significant association between 2 and 3 pain sites and the presence of burning, light touching or cold/heat symptoms.

Table 4 presents the ORs and 95% CIs for the subgroups of pain intensity according to the number of chronic pain sites. In the multinomial logistic regression analyses, the participants with 2–3 and ≥4 sites had a higher OR for moderate-to-severe neuropathic-like symptoms compared with the single-site group (2–3 sites: OR 2.12, 95% CI 1.26 to 3.54, ≥4 sites: OR 4.31, 95% CI 2.54 to 7.31, P for trend <0.001; per 1-site increment: OR 1.39, 95% CI 1.27 to 1.52, p<0.001), while there was no evidence of a significant association between 2–3 and ≥4 sites and the prevalence of mild neuropathic-like symptoms. This association did not materially change after adjustment for potential confounding factors.

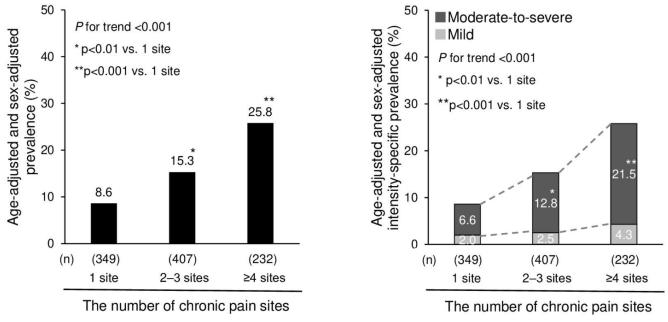

Figure 1 Age-adjusted and sex-adjusted prevalence of neuropathic-like symptoms and subgroups of pain intensity according to the number of chronic pain sites.

The sensitivity analysis showed that excluding diabetes mellitus or stroke, which are associated with neuropathic pain, had no relevant effect on the results: OR 2.27, 95% CI 1.19 to 4.33 for 2–3 sites and OR 5.06, 95% CI 2.60 to 9.85 for ≥4 sites, P for trend <0.001; per 1-site increment: OR 1.42, 95% CI 1.27 to 1.59, p<0.001 (online supplemental table S1).

The sensitivity analysis excluding participants with suspected cognitive impairment or dementia also showed no relevant impact of cognitive function on the results: OR 2.84, 95% CI 1.29 to 6.25 for 2–3 sites and OR 5.32, 95% CI 2.31 to 12.25 for ≥4 sites, P for trend <0.001; per 1-site increment: OR 1.45, 95% CI 1.25 to 1.68, p<0.001 (online supplemental table S2).

DISCUSSION

The results of the present analyses demonstrated that the number of chronic pain sites was significantly associated with a higher risk of the presence of neuropathic-like symptoms in a population of older community-dwelling

Table 2 The ORs and 95% CIs of the presence of neuropathic-like symptoms according to the number of chronic pain sites

No of chronic pain sites	Participants, n	Participants with neuropathic-like symptoms, n	Age-adjusted and sex-adjusted OR (95% CI)	Multivariable-adjusted OR (95% CI)*
One site	349	30	1.00 (ref.)	1.00 (ref.)
2–3 sites	407	62	1.93 (1.22 to 3.07)	1.94 (1.13 to 3.33)
≥4 sites	232	62	3.92 (2.43 to 6.32)	3.90 (2.22 to 6.85)
P for trend			<0.001	0.001
Per 1-site increment			1.37 (1.26 to 1.49)	1.35 (1.22 to 1.49)
P value			<0.001	<0.001

Binomial logistic regression analyses were used to estimate ORs and 95% CIs for the presence of neuropathic-like symptoms according to the number of chronic pain sites.
*The multivariable model was adjusted for age, sex, education level, employment status, subjective economic status, osteoporosis, hypertension, hyperlipidaemia, diabetes mellitus, stroke, cardiovascular disease, current tobacco use, current alcohol consumption, regular exercise and sleep disturbance.

Japanese adults with chronic pain. The subgroup analysis showed that burning, tingling/prickling, light touching, electric shock-type pain, cold/heat, numbness and slight pressure symptoms were significantly increased among the participants with 2–3 sites and ≥4 sites compared with the single-site group, while burning, light touching and cold/heat symptoms were associated only with the ≥4 sites group. In addition, the ORs for moderate-to-severe neuropathic-like symptoms increased significantly with the increase in the number of chronic pain sites.

We were unable to find any study that examined the number of chronic pain sites and the prevalence of neuropathic-like symptoms in community-dwelling older individuals with chronic pain. The overall prevalence of neuropathic-like symptoms among the participants with chronic pain in this study was 15.6%, which is lower than other reports, for example, 20.1% among subjects with musculoskeletal pain,[20] 47% among subjects with low-back pain[3] and 20%–40% among subjects with knee pain.[4] This may be due to differences in the target populations, such as the sample size and specific disease cohorts, as well as differences in the definition of neuropathic-like symptoms. Our present analyses revealed that the age-djusted and sex-adjusted prevalence of neuropathic-like symptoms increased significantly with the increase in the number of chronic pain sites, especially in the participants with moderate-to-severe pain.

Although there are apparently no prior studies of the association between the number of chronic pain sites and neuropathic-like symptoms, we found a single investigation of risk factors potentially associated with neuropathic-like symptoms that used the modified PD-Q; the subjects were patients with knee osteoarthritis[7]; its results are consistent with our present observation that the number of paint sites was an independent possible risk factor for neuropathic-like symptoms. Our analyses also revealed that the presence of burning, tingling/prickling, light touching, electric shock-type pain, cold/heat, numbness and slight pressure symptoms increased significantly with the increase in the number of chronic pain sites.

Table 3 The ORs and 95% CIs of the presence of seven sensory symptoms according to the number of chronic pain sites

No of chronic pain sites	Burning	Tingling/ prickling	Light touching	Electric shock-type pain	Cold/heat	Numbness	Slight pressure
One site	1.00 (ref.)	1.00 (ref.)	1.00 (ref.)	1.00 (ref.)	1.00 (ref.)	1.00 (ref.)	1.00 (ref.)
2–3 sites	1.40 (0.96 to 2.04)	1.44 (1.02 to 2.04)	1.33 (0.79 to 2.21)	1.97 (1.18 to 3.28)	2.78 (0.88 to 8.76)	1.81 (1.23 to 2.67)	1.79 (1.29 to 2.49)
≥4 sites	2.99 (1.97 to 4.55)	2.55 (1.71 to 3.79)	2.19 (1.27 to 3.78)	3.40 (1.97 to 5.86)	5.26 (1.65 to 16.78)	4.33 (2.81 to 6.67)	3.32 (2.23 to 4.92)
P for trend	<0.001	<0.001	0.005	<0.001	0.003	<0.001	<0.001
Per 1-site increment	1.28 (1.17 to 1.39)	1.23 (1.13 to 1.33)	1.20 (1.09 to 1.32)	1.22 (1.11 to 1.34)	1.32 (1.14 to 1.53)	1.38 (1.27 to 1.51)	1.30 (1.19 to 1.41)
P value	<0.001	<0.001	<0.001	<0.001	<0.001	<0.001	<0.001

Binomial logistic regression analyses were used to estimate the ORs and 95% CIs for the presence of seven sensory symptoms according to the number of chronic pain sites. The multivariable model was adjusted for age, sex, education level, employment status, subjective economic status, osteoporosis, hypertension, hyperlipidaemia, diabetes mellitus, stroke, cardiovascular disease, current tobacco use, current alcohol consumption, regular exercise and sleep disturbance.

Table 4 The ORs and 95% CIs of subgroups of pain intensity according to the number of chronic pain sites

No of chronic pain sites	Participants, n	Participants with neuropathic-like symptoms, n		Age-adjusted and sex-adjusted OR (95% CI)		Multivariable-adjusted OR (95% CI)*	
		Mild	Moderate to severe	Mild	Moderate to severe	Mild	Moderate to severe
One site	349	7	23	1.00 (ref.)	1.00 (ref.)	1.00 (ref.)	1.00 (ref.)
2–3 sites	407	10	52	1.33 (0.50 to 3.54)	2.12 (1.26 to 3.54)	1.61 (0.47 to 5.54)	2.03 (1.12 to 3.66)
≥4 sites	232	10	52	2.65 (0.99 to 7.14)	4.31 (2.54 to 7.31)	3.23 (0.91 to 11.48)	4.07 (2.21 to 7.52)
P for trend				0.05	<0.001	0.06	<0.001
Per 1-site increment				1.26 (1.06 to 1.50)	1.39 (1.27 to 1.52)	1.25 (1.01 to 1.54)	1.37 (1.23 to 1.52)
P value				0.01	<0.001	0.04	<0.001

Multinomial logistic regression analyses were performed to examine the association of the number of chronic pain sites with the severity of neuropathic-like symptoms.
*The multivariable model was adjusted for age, sex, education level, employment status, subjective economic status, osteoporosis, hypertension, hyperlipidaemia, diabetes mellitus, stroke, cardiovascular disease, current tobacco use, current alcohol consumption, regular exercise and sleep disturbance.

An association between the PD-Q score and quantitative sensory testing (QST) has been reported.[20 24 25] QST indirectly suggests the possibility of the sensitisation of nociceptive neurons and is increasingly used in studies of musculoskeletal pain[26] as well as in patients with features of neuropathic pain.[27] A hospital-based study of patients with chronic pain demonstrated that self-reported neuropathic features identified by the Neuropathic Pain Symptom Inventory are correlated with brush-evoked pain, pressure-evoked pain and cold-evoked pain examined by QST.[24] A study of patients with fibromyalgia demonstrated that pain pressure thresholds were correlated with the PD-Q score.[25] Soni *et al* demonstrated that heat pain thresholds and mechanical pain sensitivity in a general population were significantly associated with likely neuropathic symptoms identified by the PD-Q; in addition, one-third of the subjects with musculoskeletal pain showed increased sensitivity to both heat and suprathreshold mechanical stimuli.[20] In this study, light touching and cold/heat symptoms were associated with the participants with ≥4 pain sites, suggesting that central sensitisation might be partially involved.

Evaluations of the number of pain sites have indicated that an increase in the number of pain sites is associated with non-musculoskeletal symptoms, overall health, psychological health, daily and social activities, physical performance, pain-related disability and depressive symptoms or anxiety.[17 28–32] The present analyses obtained a new finding, that is, the number of chronic pain sites is associated with a higher risk of the presence of and with the severity of neuropathic-like symptoms. Future longitudinal studies should examine whether an increase in the number of chronic pain sites leads to long-term potentiation due to cumulative nociceptive input to the central nociceptive system, resulting in severe neuropathy-like symptoms from peripheral and central sensitisation.[33]

The strengths of our study are as follows. This is the first study to examine the relationship between the number of chronic pain sites and the presence and severity of neuropathic-like symptoms in a general population, and the information was obtained from a relatively large number of participants (n=988). The ORs were calculated in detail with adjustment for potentially confounding factors. However, when interpreting the results of this study, some limitations must be considered. (1) The cross-sectional design does not allow conclusions about the direction of causality of these associations. (2) The association between the number of chronic pain sites and the presence of neuropathic-like symptoms may simply reflect the influence of radiating pain. However, this association did not materially change after adjustment for radiating pain (data not shown). (3) We have no objective information available to suggest central sensitisation because we did not use QST. (4) We were unable to obtain medical information on diseases that include symptoms of neuropathic pain and thus could not examine their association with the number of chronic pain sites by causative disease. However, we confirmed that excluding individuals with diabetes mellitus or stroke (which are associated with neuropathic pain) and individuals with suspected cognitive impairment or dementia had no relevant impact on the results. (5) We cannot rule out the possibility of bias due to residual confounding effects such as a family history of pain and psychological, emotional, sexual or physical abuse.[10] (6) There are limitations in the generalisability of these findings to other populations with different cultures and lifestyles, as this study was conducted in a single region of Japan.

CONCLUSION

The results of this study demonstrated that the number of chronic pain sites was significantly associated with a higher risk of the presence and severity of neuropathic-like symptoms in a population of older community-dwelling Japanese adults with chronic pain. In addition, the burning, tingling/prickling, light touching, electric shock-type pain, cold/heat, numbness and slight pressure symptoms increased significantly with the increase in the number of chronic pain sites. Although mechanism-based pain treatment is optimal, identifying the mechanisms behind the pain can be challenging or impossible in clinical practice, so clinicians should therefore be aware that an evaluation of the number of a patient's chronic pain sites might be necessary in order to prevent or manage neuropathic-like symptoms. Further prospective and interventional studies are needed to develop a multidisciplinary approach based on a biopsychosocial framework of chronic pain that includes physical therapy, pharmacotherapy, procedural interventions, cognitive behavioural therapy, and complementary and integrative therapies.

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Contributors TS and HK were involved in the study design and conceptualisation. TS, TC, HY, TC, XL and HK were involved in the measurements and dataset creation. TS and HK were involved in the statistical analyses and interpretation of the results. TS, TC, HY, TC, XL and HK were involved in the drafting and revising of the manuscript. All authors have reviewed the manuscript and approved its final version. HK is responsible for the overall content as the guarantor.

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Competing interests None declared.

Patient and public involvement Patients and/or the public were not involved in the design, or conduct, or reporting, or dissemination plans of this research.

Patient consent for publication Not applicable.

Ethics approval This study involves human participants and was approved by the Institutional Review Board of Kyushu University (Approval number: 201708). Participants gave informed consent to participate in the study before taking part.

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