Original Article

Clinical characteristics of alexisomia in patients with incurable cancer

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Background: Alexisomia is a clinical concept that describes difficulties in the awareness and expression of bodily feelings regarding physical diseases and symptoms. The study aim was to investigate whether incurable cancer patients with alexisomia had a higher incidence of latent trigger points, higher pain intensity, and higher pain-improvement goals.

Methods: A multicenter cross-sectional survey was conducted among patients with incurable cancer referred to a palliative care service at two university hospitals in Japan. Alexisomia was evaluated using the Shitsu-Taikan-Sho Scale (STSS). All patients were manually examined on their upper trapezius to identify latent trigger points. Patients who experienced pain reported their pain numerical rating scale (PNRS) and personalized pain goal (PPG) scores.

Results: A total of 262 patients were selected as participants. Incurable cancer patients with alexisomia were observed in 30.2% of all participants [95% confidence interval (CI): 24.7–35.7]. The latent trigger points risk ratio in the alexisomic group versus the non-alexisomic group was 4.06 (95% CI: 2.24–7.37). Incurable cancer patients with alexisomia tended to have higher PNRS and PPG scores (P<0.001), but there was no significant difference in PPG achievement (P=0.641).

Conclusions: In examining incurable cancer patients with alexisomia, we must recognize that their latent trigger points risk ratio and PPGs are higher (lower symptom improvement goals) than cancer patients without alexisomia, and their rate of seeking help for pain may be low.

Keywords: Alexisomia; difficulty in identifying bodily feelings; incurable cancer; personalized pain goal (PPG); latent trigger point

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Introduction

Alexisomia is characterized by difficulties in the awareness and expression of bodily feelings (1,2). Awareness of the following bodily feelings is impaired in alexisomia: (I) bodily feelings that are necessary to maintain homeostasis (such as hunger and somnolence); (II) bodily feelings that accompany physical diseases (e.g., subjective symptoms such as pain). Individuals with alexisomia also tend to have difficulty expressing appropriate behaviors based on bodily feelings in response to social demands. For example, even if they can identify bodily sensations, they may exhibit over-adaptation

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(OA) and lack of health management (LHM) (1,2).

Alexisomia is a characteristic of psychosomatic patients and is more likely to occur under chronic psychological stress (2). Patients with cancer experience frequent, severe psychological stress and emotional distress across many cancer stages (3,4). Investigation of the clinical characteristics of alexisomia in cancer patients is important, as it could inform decision-making regarding the introduction of specialized palliative care. Specialized palliative care from an early stage contributes to improved quality of life for cancer patients by facilitating the development of coping skills for unpleasant bodily feelings (such as fatigue and pain) (5). To the best of our knowledge, there are no studies on the clinical characteristics of alexisomia in cancer patients.

Reduced awareness of bodily feelings that accompany physical diseases is a characteristic of alexisomia, and may affect physical functions (1,2). One study reported reduced gastric motility in healthy volunteers who experienced pain, even though the pain was tolerable (6). A latent trigger point (LTrP) is a tender spot caused by muscle dysfunction found on palpation and does not cause bodily feelings of spontaneous pain (7). The frequency of myofascial pain syndrome with active TrPs in patients with cancer is high: 11.9–48% (8,9). LTrPs have a small burden on patients with cancer for manual examination and significant preventive effects. One study found that healthy volunteers with alexisomia had an LTrP risk ratio of 2.30 [95% confidence interval (CI): 1.03–5.10] compared with healthy volunteers without alexisomia (10) (only the alexisomia characteristic of difficulty identifying bodily feelings (DIB) was associated with LTrP incidence).

Alexisomia may also be associated with the awareness and recognition of pain. There are no studies on the association between alexisomia and pain in cancer patients. Alexisomia is strongly linked to alexithymia (1,2) and can aggravate symptoms, including cancer pain (11,12). Alexithymia is related to somatosensory amplification (e.g., worth pain intensity) in cancer patients (13). The use of personalized pain goals (PPGs), a new method of setting pain-improvement goals, has received attention in the field of palliative medicine (14). Introduction of PPG improves the quality of care and contributes to the medical economy (15). In patients with cancer, achieving the PPG is associated with a lower pain intensity, a lower opioid dose, less adjuvant analgesic administration, and less depression (16). A previous study on family caregivers of cancer patients showed that caregivers with chronic pain set higher PPGs owing to alexithymia (17).

We hypothesized that cancer patients with alexisomia would show higher LTrP incidence, pain intensity, and pain-improvement goals. We present the following article in accordance with the STROBE reporting checklist (available at https://dx.doi.org/10.21037/apm-21-1503).

Methods

Objective

We aimed to investigate whether incurable cancer patients with alexisomia had a higher incidence of LTrPs in the upper trapezius, higher pain intensity, and higher pain-improvement goals.

Study design

This was a cross-sectional survey of incurable cancer patients and was conducted at two university hospitals in Osaka, a city in western Japan. We collected demographic information, primary cancer site, Eastern Cooperative Oncology Group performance status (ECOG PS), and self-reported questionnaire data on alexisomia. All patients were manually examined on their upper trapezius to identify LTrPs. Patients who experienced pain reported their pain intensity and pain-improvement goals.

All dates were collected in the palliative care center of each institution and registered with the identification code to patient anonymity for each participant. The study was conducted in accordance with the Declaration of Helsinki (as revised in 2013). The study received approval from the Medical Ethics Committee of Kansai Medical University (reference number: 2019189) and informed consent was taken from all the patients. This study was registered with the University Hospital Medical Information Network Clinical Trials Registry (approval number: UMIN 000038371) on December 1, 2019.

Study participants

Patients referred to a palliative care center who met the following eligibility criteria were included in the study: (I) received a malignancy diagnosis, (II) had an incurable malignant disease, (III) were outpatients, and (IV) were aged 20 years or older. There were two exclusion criteria: patients who (I) had any comorbidity relating to psychiatric diseases or conditions that made communication difficult, such as cognitive impairment or delirium, and (II) refused to participate. Continuous registration was performed to

prevent selection bias. Patients who visited the institutions between December 2019 and June 2020 were screened, and eligible patients were enrolled in the study.

Measures

Self-report questionnaire to evaluate alexisomia

Each participant was evaluated for potential alexisomic symptoms using the Shitsu-Taikan-Sho Scale (STSS total), a self-report questionnaire consisting of 23 items rated on a scale of 1 to 5, which provides a total score ranging between 23 and 115 (2,6). The STSS total includes the scores on three subcategories: difficulty identifying bodily feelings (DIB), OA, and LHM based on bodily feelings. The DIB subcategory comprises questions about the tendency to fail to identify bodily feelings that are necessary to maintain homeostasis and act as warning signals during adaptation to external environments. The OA subcategory comprises questions on the tendency to ignore bodily warning signals that stems from prioritization of meeting social demands and adapting to external environments. The LHM subcategory contains questions on habits related to daily management of health and bodily feelings that arise from physical conditions stemming from the relaxation response.

The mean STSS total score among Japanese undergraduate students is 56.3 [standard deviation (SD): 10.2] points (18). The DIB comprises nine questions: 1, 5, 6, 10, 12, 14, 15, 18, and 19. The mean participant DIB score was 18.1 (SD: 5.6). The OA comprises six questions: 3, 7, 13, 17, 20, and 22; the mean participant OA score was 14.2 (SD: 4.5). The LHM comprises eight questions: 2, 4, 8, 9, 11, 16, 21, and 23; all questions except 23 are reverse-scored items. The average LHM score was 21.4 (SD: 3.8) (14). The STSS has previously demonstrated adequate validity and reliability in healthy volunteers, with a Cronbach's α of 0.83 (DIB, 0.84; OA, 0.83; LHM, 0.70) (18). The mean + 1 standard deviation is the cutoff value. Based on this cutoff, participants were categorized into one of two groups: non-alexisomic (score ≤66) and alexisomic (score ≥67). Subcategories were similarly generated using this cutoff value.

LTrP palpation procedure

Each participant was individually evaluated for LTrPs, non-spontaneous tender spots in the muscles, by palpation with the thumb. TrP diagnosis requires careful manual examination and reliability estimates were generally higher for subjective signs such as tenderness (19). Based on a previous study, palpation was performed when each participant was in a relaxed prone position lying on a bed (6,20). The palpation area was approximately 3 cm wide (horizontal) and 2 cm high (vertical). The palpation target area was limited to both sides of the upper trapezius and did not include other scapular muscle groups such as the lower trapezius, supraspinatus, serratus anterior, and rhomboideus. The most commonly tested muscle is the upper trapezius because of the high prevalence of TrPs in that muscle and the ease of access to the taut band (21,22). All palpation examinations were performed by one of two expert clinicians (H.H. and K.S.) who each have over 10 years of experience in the specific diagnosis and treatment of TrPs.

Pain intensity

Patients evaluated their average pain intensity during the previous 24 hours using an 11-point pain numerical rating scale (PNRS) ranging from 0 (no pain) to 10 (worst possible pain) (23). PNRS scores of 1–4 were considered to indicate mild pain intensity, 5–6 moderate pain intensity, and 7–10 severe pain intensity (24). The reliability and validity of this scale has been established (25).

Pain-improvement goal

One way of ensuring that pain-improvement goals are tailored to individual needs is to use a PPG, which relies on participants' own criteria for meaningful pain relief. The PPG is assessed in a similar way to pain intensity (14). PPGs were assessed by asking participants "What is the maximum level of pain that you would feel comfortable with?" Participants indicated their responses using an 11-point NRS ranging from 0 (I feel comfortable and at ease at the NRS of 0 points) to 10 (I feel comfortable even at the NRS of 10 points). The median PPG for cancer patients is 3 (14). The PPG does not vary daily, and does not change during follow-up periods (16).

PPG achievement

The achievement of PPG was defined as achieving an average pain intensity lower than or equal to the PPG in the previous 24 hours (16,26). The reported PPG achievement among cancer patients with pain is 30% to 45% (14,16).

Outcomes

The primary outcome was an LTrP incidence with or

without alexisomia. The secondary outcomes were the proportion of patients with alexisomia among those with incurable cancer, PNRS and PPG scores with and without alexisomia in participants with pain, and correlation between the PPG score and LTrP incidence.

Sample size calculation

Because previous studies on cancer patients are limited, the sample size calculation was based on studies of healthy volunteers (8). We assumed an LTrP incidence with and without alexisomia of 65% and 45%, respectively. The sample size required to achieve 90% statistical power at a 5% two-sided significance level was 122 patients per group, which was calculated using a chi-square test.

Statistical analysis

Data are reported as means and standard deviations, medians with interquartile ranges, or frequencies (%), as appropriate. When participants provided missing data, we used the worst scores in the data. We estimated the proportion of incurable cancer patients with alexisomia among all patients and calculated 95% CIs. Participants were categorized into an alexisomic and a non-alexisomic group using the aforementioned cutoff score. Unpaired *t*-tests were used to compare age between the two groups. Chi-square tests were used to analyze the dependent variables of sex, ECOG PS, LTrP incidence, and pain. Participants were then categorized into a pain alexisomic group and a pain non-alexisomic group according to the presence or absence of pain. Mann-Whitney U tests were used to compare PNRS score and PPG score between the two groups. Chi-square tests were used to analyze PPG achievement. Spearman's rank correlation coefficients were calculated to assess associations between STSS total score, STSS subscale scores, PNRS score, PPG score, PPG achievement, and LTrP incidence.

A value of $P<0.05$ was considered statistically significant. Statistical analyses were performed using SPSS version 25.0 and Amos version 25.0 for Macintosh (SPSS, Inc., IBM, Chicago, IL, USA).

Results

Number of registered patients

A total of 573 patients were referred to the palliative care service and 301 patients met the eligibility criteria. Of these 301 patients, 262 were selected as participants, after excluding 39 patients who met the exclusion criteria: (I) any comorbidity relating to psychiatric diseases or conditions that made communication difficult (n=23), and (II) patient refusal to participate (n=16).

Demographic characteristics

The demographics, clinical characteristics, LTrP incidence, and STSS scores of all participants are shown in *Table 1*. No missing data were provided in the data of 320 caregivers. LTrPs in the upper trapezius were observed in 60.3% of participants (95% CI: 54.4–66.2). Alexisomia accounted for 30.2% of all participants with incurable cancer (95% CI: 24.7–35.7). All participants were categorized into an alexisomic group (n=79) and a non-alexisomic group (n=183). There were significant between-group differences in all STSS subcategory scores ($P<0.001$).

Relationship between alexisomia and LTrP for all participants

Table 2 shows the demographics, ECOG PS, LTrP incidence, and the number of participants with pain for both groups. A test of independence between STSS total and LTrP incidence resulted in a chi-square of 34.54 ($P<0.001$), indicating a correlation between the two factors. The LTrP risk ratio in the alexisomic group versus the non-alexisomic group was 4.06 (95% CI: 2.24–7.37). The analysis of the STSS DIB and STSS OA scores showed a similar result, with chi-squares of 26.9 ($P<0.001$) and 20.1 ($P<0.001$), respectively. The LTrP risk ratio was 3.70 (95% CI: 1.98–6.91) for STSS DIB and 3.15 (95% CI: 1.85–5.23) for STSS OA. In contrast, analysis of STSS LHM produced a chi-square of 2.476 ($P=0.143$), indicating no correlation between LTrP incidence and STSS LHM scores.

Relationship between alexisomia and pain intensity and pain-improvement goals in participants with pain

Of all participants, 77.1% (95% CI: 74.4–79.9) experienced pain. They were categorized into a pain alexisomic group (n=64) and a pain non-alexisomic group (n=138). *Table 3* shows PNRS and PPG scores, PPG achievement, clinical characteristics of pain, and LTrP incidence for both groups. Incurable cancer patients with alexisomia tended to have

Table 1 Demographic and clinical characteristics of study participants and patients

Variable	Total
Age (years), mean (SD)	66.0 (12.2)
Sex, n (%)	
Male	113 (43.1)
Female	149 (56.9)
Primary cancer site, n (%)	
Lung	11 (4.2)
Gastrointestinal	80 (30.5)
Liver, pancreas, biliary system	44 (16.8)
Breast	49 (18.7)
Gynecological	38 (14.5)
Urological	16 (6.1)
Head and neck	19 (7.3)
Others	5 (1.9)
ECOG PS, n (%)	
0	67 (25.6)
1	80 (30.5)
2	52 (19.8)
3	49 (18.7)
4	14 (5.3)
LTrP incidence, n (%)	158 (60.3)
STSS total score, mean (SD)	57.7 (14.1)
DIB score	23.8 (8.4)
OA score	16.1 (5.3)
LHM score	17.7 (5.6)

ECOG PS, Eastern Cooperative Oncology Group performances status; LTrP, latent trigger point; STSS, Shitsu-Taikan-Sho Scale; DIB, difficulty of identifying bodily feelings; OA, over-adaptation; LHM, lack of health management based on bodily feelings; SD, standard deviation.

higher PNRS and PPG scores than other participants (P<0.001), but there was no difference in the frequencies of PPG achievement (P=0.641). There were correlations between STSS total score, STSS subscale scores, PNRS score, PPG score, and LTrP incidence (*Table 4*). The partial correlation coefficient between PPG score and LTrP incidence with STSS total score as the control variable was 0.335.

Table 2 Latent trigger point incidence and sociodemographic information for the alexisomic and non-alexisomic groups

Variable	Alexisomic group (n=79)	Non-alexisomic group (n=183)	P value
Age, years, mean (SD)	65.2 (11.8)	66.4 (12.4)	0.482
Sex, n (%)			
Male	30 (38.0)	83 (45.4)	0.280
Female	49 (62.0)	100 (54.6)	
ECOG PS, n (%)			
0–2	60 (75.9)	139 (76.0)	1
3–4	19 (24.1)	44 (24.0)	
LTrP incidence, n (%)	69 (87.3)	89 (48.6)	<0.001
Participants with pain, n (%)	64 (81.0)	137 (74.9)	0.340

ECOG PS, Eastern Cooperative Oncology Group performances status; LTrP, latent trigger point; SD, standard deviation.

Discussion

To the best of our knowledge, this is the first report to suggest a possible association between alexisomia and LTrP incidence, pain intensity, and pain-improvement goals in patients with incurable cancer.

The first important finding of this study is the possible association between alexisomia and LTrP incidence in the upper trapezius of patients with incurable cancer. DIB score showed the strongest association with LTrP incidence. The reduced awareness of bodily feelings may lead to an inability to recognize physical muscle tension as a subjective bodily feeling. A previous study that identified alexisomia in a psychosomatic patient group found a substantial negative correlation between objective and subjective physical tension in response to stress load (27). We hypothesized that DIB would make cancer patients more prone to LTrP incidence owing to their inability to physically relax their muscles (e.g., by stretching). However, as this was a cross-sectional survey, it is difficult to assess causal relationships.

The present findings of an association between DIB and LTrP incidence are similar to those in a previous study of healthy volunteers (10). However, incurable cancer patients with alexisomia had a higher LTrP risk ratio than healthy volunteers with alexisomia, and LTrP risk was associated with both DIB and OA. The STSS total score of patients with incurable cancer was similar to that of healthy

Table 3 Pain characteristics of the pain alexisomic and pain non-alexisomic groups

Variable	Pain alexisomic group (n=64)	Pain non-alexisomic group (n=138)	P value
PNRS score, median [IQR]	7 [5–9]	6 [3–8]	<0.001
PPG score, median [IQR]	5 [4–7]	3 [2–4]	<0.001
PPG achievement, n (%)	25 (39.1)	49 (35.5)	0.641
Site of the pain, n (%)			
Chest	7 (10.9)	14 (10.1)	
Abdomen	13 (20.3)	34 (24.6)	
Head	9 (14.1)	15 (10.9)	
Upper back	16 (25)	33 (23.9)	
Lower back	10 (15.6)	24 (17.4)	
Extremities	9 (14.1)	18 (13.1)	
Analgesic drug use, n (%)	50 (78.1)	110 (79.7)	0.853
Opioid drug use	27 (42.2)	57 (41.3)	1.000
Dose (mg/day)[a], median [IQR]	30 [20–60]	30 [20–60]	0.977
LTrP incidence, n (%)	58 (90.6)	74 (53.6)	<0.001

[a], dose of opioids is expressed as oral dose level of morphine (mg/dL). For conversion: parenteral morphine: oral morphine =1:2, parenteral, oxycodone: oral morphine =1:2, oral oxycodone: oral morphine =2:3, fentanyl: morphine =1:100, oral methadone: oral morphine =1:8. PNRS, pain numerical rating scale; PPG, personalized pain goal; LTrP, latent trigger point; IQR, interquartile range.

Table 4 Correlations between Shitsu-Taikan-Sho Scale scores, pain characteristics, and latent trigger point incidence

Variable	Total	DIB	OA	LHM	PNRS	PPG score	PPG achievement
STSS total score							
STSS DIB score	0.859***						
STSS OA score	0.704***	0.556***					
STSS LHM score	0.517***	0.169*	0.037				
PNRS score	0.202**	0.185**	0.040	0.154*			
PPG score	0.506***	0.441***	0.448***	0.162*	0.154*		
PPG achievement	0.044	−0.019	0.141*	0.015	−0.681***	0.243***	
LTrP incidence	0.458***	0.345***	0.306***	0.250***	0.175*	0.330***	0.035

*, P<0.05; **, P<0.01; ***, P<0.001. STSS, Shitsu-Taikan-Sho Scale; DIB, difficulty of identifying bodily feelings; OA, over-adaptation; LHM, lack of health management based on bodily feelings; PNRS, pain numerical rating scale; PPG, personalized pain goal; LTrP, latent trigger point.

volunteers, whereas the DIB and OA scores were higher than those of healthy volunteers. DIB is a characteristic of patients with psychosomatic disorders, and cancer patients have a high rate of psychosomatic disorders associated with myofascial pain (57.1%) (2,8). There are no reports on OA in cancer patients. Patients with incurable cancer over-adapt to changing cancer stages and cancer treatment, which increases the likelihood that they will ignore warning signals of physical muscle tension. Given the suggested association between OA and autonomic nervous system activities (28), physical muscle tension associated with the sympathetic nervous system may be more likely to lead to

LTrP incidence. In contrast, cancer patients showed a low LHM score. Most patients in this study had good ECOG PS and so may have been more aware of the need for health management.

The second important finding of this study is that although incurable cancer patients with alexisomia had higher PNRS scores, their PPG achievement rate did not significantly differ from that of cancer patients without alexisomia. This could be explained by the significantly higher PPG scores of incurable cancer patients with alexisomia. All three alexisomia subcategories were correlated with PPG scores, particularly DIB and OA scores. Incurable cancer patients with high STSS DIB scores unconsciously experience difficulties in the awareness and expression of bodily feelings of pain, and this lack of awareness may have resulted in their setting high PPGs. Incurable cancer patients with high STSS OA scores over-adapt to changing cancer stages and cancer treatment, and may ignore warning signals of physical muscle tension.

Because they set high PPGs (lower goals for symptom improvement), incurable cancer patients with alexisomia may seek help only at a more severe stage. Chronic anxiety patients with alexithymia show lower help-seeking behavior and lower hospital visit rates (29). In this study, the partial correlation between PPG score and LTrP incidence was relatively high when alexisomia was used as a control variable. If long-term physical muscle tension is untreated, LTrPs eventually become active TrPs (30). It is likely that cancer patients with alexisomia have a high frequency of severe myofascial pain syndrome.

The limitations of this study include the following. First, no standardized method for assessing alexisomia has been established. The STSS has demonstrated reliability and validity and a positive correlation with alexisomia, but has no standardized cutoff values. In this study, 30.2% of patients with incurable cancer had alexisomia. In a previous study conducted in the same two centers, 22.7% of healthy volunteers had alexisomia (10). Second, this study was an exploratory study and no association between alexisomia and other psychological factors was investigated. Other psychological factors might be potential biases. Finally, this study focused on incurable cancer patients referred to a palliative care service, and so the findings may not generalize to other cancer patients.

Conclusions

In examining incurable cancer patients with alexisomia, we must recognize that their latent trigger points risk ratio and PPGs are higher (lower symptom improvement goals) than cancer patients without alexisomia, and their rate of seeking help for pain may be low.

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Footnote

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Ethical Statement: The authors are accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved. The study was conducted in accordance with the Declaration of Helsinki (as revised in 2013). The study received approval from the Medical Ethics Committee of Kansai Medical University (reference number: 2019189) and informed consent was taken from all the patients.

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