

## Multiple types of somatic pain increase suicide attempts and depression: A nationwide community sample of Korean adults

Mi Jin Park<sup>a</sup>, Kwan Woo Choi<sup>a</sup>, Eun Jin Na<sup>a</sup>, Jin Pyo Hong<sup>a</sup>, Maeng Je Cho<sup>b</sup>, Maurizio Fava<sup>c</sup>, David Mischoulon<sup>c</sup>, Hong Jin Jeon<sup>a,d,e,f,\*</sup>

<sup>a</sup> Department of Psychiatry, Depression Center, Samsung Medical Center, Sungkyunkwan University School of Medicine, Seoul, Republic of Korea

<sup>b</sup> Department of Psychiatry, Seoul National University, College of Medicine, Seoul, Republic of Korea

<sup>c</sup> Depression Clinical and Research Program, Massachusetts General Hospital, Harvard Medical School, Boston, USA

<sup>d</sup> Department of Health Sciences & Technology, Samsung Advanced Institute for Health Sciences & Technology (SAIHST), Sungkyunkwan University, Seoul, Republic of Korea

<sup>e</sup> Department of Medical Device Management & Research, Samsung Advanced Institute for Health Sciences & Technology (SAIHST), Sungkyunkwan University, Seoul, Republic of Korea

<sup>f</sup> Department of Clinical Research Design & Evaluation, Samsung Advanced Institute for Health Sciences & Technology (SAIHST), Sungkyunkwan University, Seoul, Republic of Korea

### ARTICLE INFO

#### Keywords:

Multiple somatic pain  
Suicide attempt  
Major depressive disorder  
Impulsivity

### ABSTRACT

**Objective:** Somatic pain is an important risk factor for suicide and suicidal behaviors. However, the association between the number of somatic pain conditions and lifetime suicide attempts (LSA) has not been well established yet. Therefore, the objective of this study was to examine associations between LSA and multiple somatic pain (MSP), single pain, and no pain in a nationwide survey.

**Methods:** A total of 12,532 adults were randomly selected from the population using the one-person-per-household method. Each participant completed a face-to-face interview using the Korean Composite International Diagnostic Interview (K-CIDI) with Suicide Module, and the Barratt Impulsiveness Scale 11 (BIS-11). The MSP was defined as pain in two or more parts of one's body, including abdominal pain, back pain, arthralgia, arm or leg pain, chest pain, headache, menstrual pain, dysuria, genital pain, and other pain.

**Results:** Among 12,532 subjects, 858 (6.85%) had MSP. Among the three groups (MSP, single pain, and no pain) of subjects, the MSP group had higher percentages of females, those with lower education, and divorced/widowed/separated individuals. However, there were no significant differences in monthly income or residence among the three groups. The MSP group showed four times higher suicide attempts and six times higher multiple attempts than did the no pain group. The BIS total score of the MSP group was the highest among the three groups. Genital pain showed the highest odds ratio for LSA. The higher the number of somatic pain, the higher the odds ratios were for LSA, major depressive disorder (MDD), and anxiety disorders. Subjects having both MSP and MDD showed a significant association with LSA (AOR = 14.78, 95% CI 10.08–21.67,  $p < 0.001$ ) compared to those having neither somatic pain nor MDD.

**Conclusions:** MSP was significantly associated with LSA. It had greater prevalence among individuals reporting a higher number of somatic pain conditions and comorbid MDD.

© 2018 The Authors. Published by Elsevier Inc. This is an open access article under the CC BY-NC-ND license (<http://creativecommons.org/licenses/by-nc-nd/4.0/>).

### 1. Introduction

Suicide is a major public health issue that affects communities, provinces, and countries. Over 800,000 people worldwide die from suicide every year [1]. Previous studies have indicated that lifetime suicide attempts (LSA) are associated with personal factors such as depressive psychopathology and hopelessness [2,3], impulsive aggressive behavior [4], childhood trauma [5], genetic loading [6], exposure to a celebrity suicide [7], accessibility to lethal methods of suicide [8], and physical disorders with somatic pain [9]. A growing body of evidence also shows that chronic somatic pain is associated with suicidal ideation, attempts, and completed suicide [10–13].

Recent studies have investigated the relationship between types of chronic pain and suicide. Migraines and back ailments are increasingly

All authors agreed to this submission.

The material is original research. It has not been previously published or submitted for publication elsewhere while under consideration.

\* Corresponding author at: Department of Psychiatry, Depression Center, Samsung Medical Center, Sungkyunkwan University School of Medicine, Seoul, Korea; Director of the Korea Psychological Autopsy Center (KPAC); Department of Health Sciences & Technology, Department of Medical Device Management & Research, and Department of Clinical Research Design & Evaluation, Samsung Advanced Institute for Health Sciences & Technology (SAIHST), Sungkyunkwan University, #81 Irwon-ro, Gangnam-gu, Seoul 06351, South Korea.

E-mail address: [jeonhj@skku.edu](mailto:jeonhj@skku.edu) (H.J. Jeon).

associated with suicidal behaviors after adjusting for concomitant psychotic disorders [14,15]. Medically unexplained pain [16], fibromyalgia [17], and complex regional pain syndrome [18] are also associated with suicide. A positive association between pain severity and suicide has also been observed. For example, veterans with severe pain are more likely to die by suicide than are patients who have less pain [19]. Similar findings in Japanese men have been reported [20]. Thus, individuals suffering from chronic pain may benefit from screening for suicide followed by appropriate intervention [21].

Although somatic pain is known to be an important risk factor for suicide and suicidal behaviors, the association between the number of somatic pain conditions and LSA is not well established yet. Most of the previous studies have focused on specific parts of pain conditions that are strongly linked to suicidal ideation and suicide attempts [11,21]. Few studies have focused on the number of pain conditions. Although some studies were focused on chronic pain based on population data, many of them used treatment-seeking patients that might lead to selection bias and skew the data, thus limiting their generalizability. Therefore, the objective of this study was to examine associations of LSA with multiple somatic pain (MSP), single pain, and no pain in a nationwide survey.

We defined MSP as pain in two or more parts of one's body, including abdominal pain, back pain, arthralgia, arm or leg pain, chest pain, headache, menstrual pain, dysuria, genital pain, and other pain. We hypothesized that individuals with MSP would show a higher number of suicidal thoughts and behaviors than those with single or no pain. To better understand effects of MSP on LSA, we additionally hypothesized that individuals with MSP would show other comorbid psychiatric disorders such as major depressive disorder (MDD) and impulsivity in our periodic survey. Hence, we first explored the direct relationship between MSP and LSA. In addition to the assessment of LSA, we identified specific factors such as increased MDD and impulsivity with MSP that might account for a higher risk of suicide.

## 2. Methods

### 2.1. Study design and subjects

The Korean Epidemiologic Catchment Area study (KECA) is a nationwide, cross-sectional, periodic survey (typically administered every 5 years) based on a nationally representative sample of the general population. The KECA-Replication (KECA-R) was conducted from July 2006 to April 2007 [22]. The KECA-2011 was conducted from July to September 2011 using the same study design [23].

Subjects were selected using multi-stage and cluster sample techniques. This study included both populations with independent sample design based on data from the Korean Population Census [24,25]. In both KECA-R and KECA-2011, subjects were sampled across 12 catchment areas: three metropolitan districts, five districts of mid-sized cities, and four rural counties. One adult, who was 18 years or older, per household was selected randomly. Face-to-face interviews were conducted using the Korean version of Composite International Diagnostic Interview (K-CIDI) [26]. The initial sample consisted of 12,532 subjects from the KECA-R and KECA-2011 who completed the interview, with an overall response rate of 80.2%. The complete sample for analysis consisted of 2236 subjects with a history of pain (MSP or single somatic pain) in their lifetime, and 10,296 subjects without a history of somatic pain. The Institutional Review Board of Seoul National University College of Medicine approved this study. All subjects were fully informed about the aims and methods of this study prior to completing the interview. Informed consent was obtained from each subject prior to participation.

### 2.2. Interview training

A total of 160 interviewers were recruited from the 12 catchment areas, including psychiatric nurses, social workers, and medical students with experience administering psychiatric epidemiologic surveys. All interviewers

received a 5-day training with didactic sessions covering general interviewing skills and the instrument content. Mock interviews and role-playing exercises were utilized to facilitate consistent understanding of the information. In addition, live interviews with psychiatric patients and group discussions were used to determine inter-rater reliability [27,28].

### 2.3. Measures

#### 2.3.1. Assessment of DSM-IV disorders

DSM-IV diagnoses were based on the K-CIDI [29], a fully structured diagnostic interview designed to make psychiatric diagnoses [30]. The K-CIDI has been validated by Cho et al. [26], according to the World Health Organization guidelines [31]. Furthermore, clinical diagnoses with blinded clinical re-interviews using Structured Clinical Interview for DSM-IV (SCID) showed modest concordance with K-CIDI diagnoses ( $\kappa$  value: 0.50 to 1.00) [32].

#### 2.3.2. Assessment of multiple types of somatic pain

The somatoform disorder section of the K-CIDI evaluates lifetime history of somatic pain into three groups: single, multiple or none. A history of somatic pain was defined as when individuals had pain in their lifetime. According to the K-CIDI, we defined MSP as somatic pain affecting more than two parts of one's body, including abdominal pain, back pain, arthralgia, arm or leg pain, chest pain, headache, menstrual pain, dysuria, genital pain, and other pain conditions. We divided the subjects into the three following groups according to the number of their pain conditions: MSP group, single pain group, and no pain group.

#### 2.3.3. Assessment of impulsivity

Trait impulsivity was evaluated using the Barratt Impulsiveness Scale version 11 (BIS-11) [33]. A Korean version of the questionnaire was used in this study [34]. It contained 30 items. Each item was rated on a four-point Likert scale (rarely/never = 1, occasionally = 2, often = 3, and almost always/always = 4). Total score and scores for three second-order factors, namely cognitive impulsiveness (BIS-C), motor impulsiveness (BIS-M), and non-planning impulsiveness (BIS-NP), were calculated.

#### 2.3.4. Assessment of LSA

Interviewers asked all subjects about suicidal ideation, plans, and attempts in a standard and consistent manner using the following explicit questions: 'Have you ever seriously thought about committing suicide?' for suicidal ideation, 'Have you ever made a plan to commit suicide?' for suicidal plan, and 'Have you ever attempted suicide?' for suicide attempt [5,35]. Participants either responded "yes" or "no". They indicated their age at their first suicide attempt and also the number of suicide attempts. These questions showed strong validity between psychiatrists and interviewers of this study. They also showed good inter-rater and test-retest reliability, with kappa values ranging from 0.74 to 1.00. Kappa value was 0.84 for MDD in a preliminary study for the KECA-R [36]. Suicidal tendencies such as suicidal thoughts and behaviors were defined as suicidal ideation, plans, single attempt, and multiple attempts.

### 2.4. Statistical analysis

To investigate associations between MSP and higher risks for suicide, three key factors (LSA, MDD, and impulsivity) were analyzed. We compared the demographic profiles of the MSP group, the single somatic pain group, and the no-pain group. Chi-square test was performed for comparative analysis of age groups, education years, gender, marital status, monthly income, residence, and pain, including onset of pain and pain duration (two-sided). Analysis of variance (ANOVA) was used to compare differences among groups with respect to the number of suicide attempts, mental disorders, and BIS-11 score using Bonferroni correction as a post hoc method. Multivariate logistic regression analyses were performed to determine the odds ratios and 95% confidence intervals of 10 types of somatic pain for suicide attempt, after controlling for age, gender, years of education, monthly income, marital status and every other somatic symptom.

Multivariable logistic regression analyses were again performed to evaluate the effect of MDD and somatic pain (single and multiple) on LSA and lifetime multiple suicide attempts, after controlling for age, gender, years of education, and monthly income. Additionally, we analyzed the impact of MDD without pain, single somatic pain without MDD, MDD plus single somatic pain, MSP without MDD, as well as MDD plus MSP on LSA and lifetime multiple suicide attempts. All statistical analyses were performed using SPSS 18.0 for Windows.

### 3. Results

#### 3.1. Demographics profiles of MSP, single pain, and no-pain groups

Among 12,532 subjects, 858 (6.85%) had MSP and 1378 (10.99%) had single somatic pain while, 10,296 (82.16%) had no pain. As shown in Table 1, subjects in the MSP group were significantly older. The MSP group had a higher percentage of subjects with lower educational levels ( $\chi^2 = 16.66, p = 0.0023$ ), a higher percentage of females ( $\chi^2 = 190.57, p < 0.0001$ ), a higher percentage of those who had divorced/widowed/separated out-of-marital status ( $\chi^2 = 43.49, p < 0.0001$ ), and a longer duration of pain ( $t = 4.64, p < 0.0001$ ), when compared to subjects in the no-pain group. No significant differences in age, monthly income, or residence were found among the three groups. Subjects in the MSP group showed a longer duration of pain compared to those in the single somatic pain group ( $\chi^2 = 11.67, p < 0.0001$ ). However, there was no significant difference in the age of pain onset between the two pain groups (i.e., MSP and single pain group).

#### 3.2. Suicidal behaviors, mental disorders, and impulsivity

As shown in Table 2, the MSP group showed a significantly higher percentage of subjects having lifetime suicidal behaviors, including suicidal

ideation (31.1% vs. 13.4%;  $\chi^2 = 262.66, p < 0.0001$ ), plan (10.5% vs. 2.7%;  $\chi^2 = 154.27, p < 0.0001$ ), attempt (10.4% vs. 2.6%;  $\chi^2 = 155.69, p < 0.0001$ ), and multiple attempts (5.4% vs. 0.9%;  $\chi^2 = 131.60, p < 0.0001$ ) than did the no pain group. The MSP group showed four-fold higher single suicide attempts and six-fold higher multiple suicide attempts than did the no pain group. Among suicide attempters, no significant difference in total number of attempts was found. The MSP group also showed a significantly higher percentage of subjects having comorbid mental disorders, including major depressive disorder (20.5% vs. 4.8%;  $\chi^2 = 377.06, p < 0.0001$ ), anxiety disorder (28.1% vs. 6.1%;  $\chi^2 = 558.92, p < 0.0001$ ) and alcohol use disorder (18.4% vs. 11.6%;  $\chi^2 = 52.76, p < 0.0001$ ) than did the no pain group. Regarding the BIS-11 score, the MSP group showed the highest BIS-NP, BIS-M, and BIS total mean scores among the three groups.

#### 3.3. Suicide attempt with 10 types of somatic pain

As shown in Table 3, among 10 types of somatic pain, abdominal, back, arthralgia, arm or leg, chest, headache, menstrual, and genital pain were significantly associated with LSA except dysuria and other pain. Genital pain was reported as the somatic symptom that had the highest association with LSA.

#### 3.4. MDD, somatic pain, LSA, and multiple suicide attempts

As shown in Table 4, subjects with MSP were significantly associated with LSA (AOR: 4.12, 95% CI: 3.19–5.33;  $p < 0.001$ ) compared to subjects with no pain or single somatic pain. MDD and pain (especially MSP) were significantly associated with LSA and lifetime multiple suicide attempts. In multivariable logistic regression analysis for LSA, no pain with MDD showed nine-fold odds (AOR: 9.28, 95% CI: 6.96–12.38;  $p < 0.001$ ), single somatic pain without MDD showed nearly two-fold

**Table 1**  
Demographics of individuals with somatic pain in a nationwide sample of Korean adults.

Variables	Community adults (n = 12,532)			Statistics	
	Multiple somatic pain <sup>a</sup> (n = 858)	Single somatic pain (n = 1378)	No pain (n = 10,296)	$\chi^2$	p-Value
	N (%)	N (%)	N (%)		
Age, years (%)					
18–29	142 (16.6%)	258 (18.7%)	1681 (16.3%)	22.40	0.004
30–39	200 (23.3%)	362 (26.3%)	2453 (23.8%)		
40–49	193 (22.5%)	310 (22.5%)	2429 (23.6%)		
50–59	147 (17.1%)	252 (18.3%)	1910 (18.6%)		
≥60	176 (20.5%)	196 (14.2%)	1823 (17.7%)		
Age (mean, SD)	44.96 (14.91)	42.89 (13.85)	44.50 (14.14)	8.72	<0.0001*
Education, years (%)					
≤11	288 (33.6%)	383 (27.8%)	2802 (27.2%)	16.66	0.0023*
12	257 (30.0%)	458 (33.2%)	3505 (34.0%)		
≥13	313 (39.0%)	537 (39.0%)	3989 (38.7%)		
Education (mean, SD)	11.28 (5.25)	12.16 (6.57)	11.97 (4.65)	9.27	<0.0001*
Female gender (%)	659 (76.8%)	989 (71.8%)	5995 (58.2%)	190.57	<0.0001*
Marital status (%)					
Married	522 (61.1%)	917 (66.6%)	6988 (68.0%)	43.49	<0.0001*
Divorced/widowed/separated	172 (20.1%)	176 (12.8%)	1270 (12.4%)		
Unmarried	161 (18.8%)	284 (20.6%)	2022 (19.7%)		
Monthly income, \$ (%)					
<2000	381 (51.8%)	505 (44.3%)	3773 (44.6%)	14.24	0.007
2000–3000	164 (22.3%)	298 (26.2%)	2181 (25.8%)		
≥3000	191 (26.0%)	336 (29.5%)	2497 (29.5%)		
Residence (%)					
Urban	694 (80.9%)	1116 (81.0%)	8297 (80.6%)	0.16	0.92
Rural	164 (19.1%)	262 (19.0%)	1999 (19.4%)		
	Mean (SD)	Mean (SD)		t	p-Value
Pain					
Onset age of pain (years)	34.09 (15.49)	32.92 (14.11)	–	1.79	0.074
Duration of pain (years)	9.56 (9.85)	7.64 (9.17)	–	4.64	<0.0001*

S.D., standard deviation; Bonferroni correction (\* $p < 0.0024$ ).

<sup>a</sup> "Multiple somatic pain" was defined as pain in two or more parts of one's body, including abdominal pain, back pain, arthralgia, arm or leg pain, chest pain, headache, menstrual pain, dysuria, genital pain, and other pain.

**Table 2**  
Suicide behaviors and mental disorders among individuals with and without multiple somatic pain in a nationwide sample of Korean adults.

Variables	Community adults (n = 12,532)			Statistics	
	Multiple somatic pain <sup>a</sup> (n = 858)	Single somatic pain (n = 1378)	No pain (n = 10,296)	$\chi^2$ or F	p-Value
Suicide behaviors in lifetime	N (%)	N (%)	N (%)		
Ideation	264 (31.1%)	327 (23.9%)	1365 (13.4%)	262.66	<0.0001*
Plan	89 (10.5%)	71 (5.2%)	275 (2.7%)	154.27	<0.0001*
Attempt	88 (10.4%)	66 (4.8%)	261 (2.6%)	155.69	<0.0001*
Multiple attempt	46 (5.4%)	29 (2.1%)	89 (0.9%)	131.60	<0.0001*
	Mean (SD)	Mean (SD)	Mean (SD)		
Suicide attempters					
Total number of attempts	2.16 (1.78)	2.00 (1.85)	1.86 (2.41)	0.63	0.54
Mental disorders					
Major depressive disorder (MDD)	176 (20.5%)	157 (11.4%)	492 (4.8%)	377.06	<0.0001*
Anxiety disorders	240 (28.1%)	194 (14.1%)	624 (6.1%)	558.92	<0.0001*
Alcohol use disorder	158 (18.4%)	225 (16.3%)	1196 (11.6%)	52.76	<0.0001*
	Mean (SD)	Mean (SD)	Mean (SD)		
BIS-11					
BIS-NP (non-planning)	19.16 (4.47)	18.85 (4.13)	18.59 (4.18)	2.62	0.073
BIS-M (motor)	15.81 (2.50)	15.76 (2.59)	15.72 (2.22)	0.25	0.78
BIS-C (cognitive impulsiveness)	14.35 (2.69)	14.43 (2.79)	13.67 (2.76)	17.28	<0.0001*
BIS total	49.32 (7.49)	49.07 (7.99)	47.97 (7.42)	6.55	0.0015*

S.D., standard deviation; BIS-11, Barratt Impulsiveness Scale 11.

Bonferroni correction (\* $p < 0.0042$ ).

<sup>a</sup> "Multiple somatic pain" was defined as pain in two or more parts of one's body, including abdominal pain, back pain, arthralgia, arm or leg pain, chest pain, headache, menstrual pain, dysuria, genital pain, and other pain.

odds (AOR: 1.83, 95% CI: 1.31–2.58;  $p < 0.001$ ), and multiple somatic pain without MDD showed nearly four-fold odds (AOR: 3.67, 95% CI: 2.63–5.14;  $p < 0.001$ ) for suicide attempts. Subjects with single somatic pain and MDD showed more than eight-fold odds (AOR: 8.27, 95% CI: 5.16–13.25,  $p < 0.001$ ) and subjects with both MSP and MDD showed nearly fifteen-fold odds (AOR: 14.78, 95% CI: 10.08–21.67,  $p < 0.001$ ) for suicide attempts, when compared to subjects without both pain or MDD. Subjects with both MSP and MDD had the strongest association with LSA (AOR: 14.78, 95% CI: 10.08–21.67,  $p < 0.001$ ). Without MDD, pain was also associated with LSA (odds ratio: two- to four-fold). With MDD, the correlation of pain with suicide attempts was much stronger (odds ratio: eight-fold to >14-fold). As shown in Fig. 1, the higher the number of somatic pain areas, the higher the odds ratios were for LSA, major depressive disorder (MDD), and anxiety disorders.

**Table 3**  
Multivariate logistic regression analysis of suicide attempt in individuals with 10 types of somatic pain.

Types of somatic pain	Community adults (n = 12,532)			
	Lifetime suicide attempt			
	n <sup>a</sup>	% <sup>b</sup>	AOR	(95% CI)
1. Abdominal pain	330	10.6	3.29	(2.18–4.97)***
2. Back pain	646	9.1	2.92	(2.12–4.02)***
3. Arthralgia	503	8.0	2.46	(1.68–3.61)***
4. Arm or leg pain	475	9.5	2.83	(1.96–4.07)***
5. Chest pain	419	11.5	3.21	(2.23–4.63)***
6. Headache	721	9.8	3.25	(2.41–4.39)***
7. Menstrual pain	347	9.8	2.88	(1.89–4.38)***
8. Dysuria	91	8.8	2.67	(1.26–5.68)*
9. Genital pain	36	16.7	5.60	(2.37–15.02)***
10. Other pain	142	7.0	2.27	(1.13–4.59)*

AOR: adjusted odds ratio; CI: confidence interval.

Adjusted for age, gender, years of education, monthly income, marital status, and all variables listed above.

<sup>a</sup> Numbers of subjects who have each somatic symptom among 12,532 subjects.

<sup>b</sup> Percent of subjects who experienced suicide attempt among those who had each somatic symptom.

\*  $p < 0.05$ .

\*\*\*  $p < 0.001$ .

#### 4. Discussion

To the best of our knowledge, this was the first study to investigate the association between MSP and the risk of LSA in a nationwide study. The MSP group showed four-fold higher single suicide attempts and six-fold higher multiple suicide attempts than did the no pain group. The MSP had significantly higher percentage of subjects who had comorbid mental disorders, including major depressive disorder, anxiety disorder, and alcohol use disorder than did the no pain group. The MSP group also had the highest BIS-NP, BIS-M, and BIS total mean scores reflecting impulsivity among the three groups. Subjects having both MSP and MDD showed the strongest association with LSA. The higher the number of somatic pain areas, the higher the odds ratios were for LSA, MDD, and anxiety disorders.

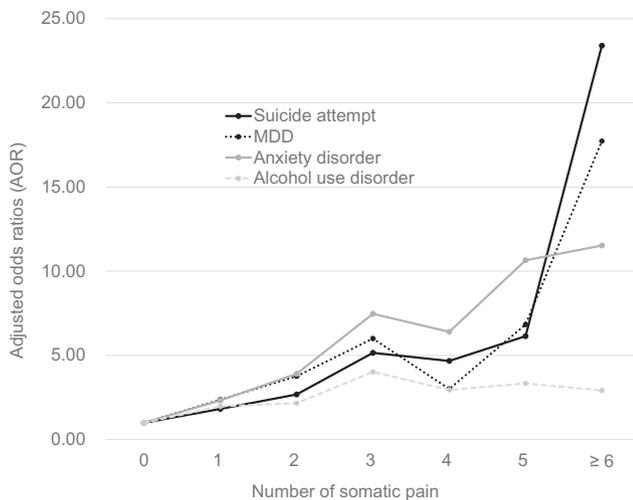
**Table 4**  
Multivariate logistic regression analysis of somatic pain and major depressive disorder (MDD) for lifetime suicide attempt (LSA) in a nationwide sample of Korean adults (n = 12,532).

Models	Community adults (n = 12,532)	
	AOR	(95% CI)
Model 1: somatic pain for LSA		
No pain	1	
Single somatic pain	1.82	(1.38–2.41)***
Multiple somatic pain	4.12	(3.19–5.33)***
Model 2: single vs. multiple somatic pain for LSA		
Single somatic pain	1	
Multiple somatic pain	1.52	(1.30–1.80)***
Model 3: single vs. multiple somatic pain, MDD, and LSA		
Neither somatic pain nor MDD	1	
No somatic pain with MDD	9.28	(6.96–12.38)***
Single somatic pain without MDD	1.83	(1.31–2.58)***
Single somatic pain with MDD	8.27	(5.16–13.25)***
Multiple somatic pain without MDD	3.67	(2.63–5.14)***
Multiple somatic pain with MDD	14.78	(10.08–21.67)***

AOR: adjusted odds ratio; CI: confidence interval.

Adjusted for age, gender, years of education, and listed in each model.

\*\*\*  $p < 0.001$ .



**Fig. 1.** Diagram for odds ratio of major depressive disorder (MDD) for lifetime suicide attempt (LSA), anxiety disorder, and alcohol use disorder for numbers of somatic pain in a nationwide sample of Korean adults ( $n = 12,532$ ). MDD, major depressive disorder. Adjusted for age, gender, years of education, and numbers of somatic pain.

Our results agree with previous studies showing that chronic somatic pain is associated with LSA [9]. The unique finding of the present study was that MSP was associated with LSA more strongly than was single somatic pain. Compared to single-site pain, multi-site musculoskeletal pain has been reported to have a greater negative impact on patients' functioning, disability, and depressive and anxiety disorders [37], which is consistent with results of the present study. We found that the MSP group showed greater rates of comorbid depression. In addition, the MSP group had sociodemographic characteristics associated with MDD such as higher percentages of females and divorced/widowed/separated individuals.

Multiple pain conditions may induce impulsivity, anger, and catastrophic thinking. Findings of the present study showed higher impulsivity in the MSP group. In the literature, anger has been more frequently reported in patients with chronic pain compared to that in other groups [38]. Overt aggression, in particular verbal and auto-aggression, is more frequent in patients with chronic pain compared to that in the control group [39]. Another study has reported that there is a potential relationship between impulsivity and risk for opioid analgesic misuse in patients with chronic lower-back pain [40]. Pain is correlated with endogenous opioid system dysfunction as well as genetic polymorphisms affecting opioid, serotonergic, and adrenergic systems. Altered metabolism of serotonin, noradrenergic, and dopaminergic activities can also play an important role in impulsive behaviors. These results suggest that impulsivity, overt aggression, and pain share a common biological and structural core [39].

Among psychosocial factors, pain catastrophizing is a key psychosocial factor consistently associated with pain-related negative outcomes in people with chronic pain [41]. Multiple pain may induce helplessness in patients and increase their risk of suicidality. Furthermore, perceived burdensomeness for patients with chronic pain has been shown to be a predictor for suicidal ideation after controlling for other well-established risk factors such as age, gender, depressive symptoms, and pain severity [42]. With an increasing number of pain areas, the degree of perceived burdensomeness might increase accordingly.

Although this study does not consider data on drug treatment or psychotherapies, the increase in suicidal behaviors depending on the number of pain areas can be explained by mechanisms such as substance dependence. In the present study, the MSP group also showed higher comorbidity of alcohol use disorder. Patients with multiple pain conditions may increase their use of opioid or pain-killer medication, resulting in chronic substance abuse. Increased dispensation of potent opioids such as oxycodone, hydromorphone, and fentanyl over time has been strongly correlated with increased opioid mortality.

Utilization of opioid at high doses is associated with an increased risk of mortality. Furthermore, drug interactions involving opioids and other central nervous system depressants also appear to increase the risk of opioid toxicity and mortality [43].

Inflammatory responses have been linked to suicidal behaviors, with evidence using blood samples suggesting a link between inflammation and suicidality in the central nervous system and peripheral tissues [44]. The hypothalamic-pituitary-adrenal (HPA) axis is a key regulator of cortisol release and stress response. In one study, hypocortisolemia and a blunted diurnal cortisol slope have been found in subjects with chronic multi-site musculoskeletal pain [37], in line with other studies reporting a hypoactive HPA-axis under chronic pain conditions [45,46]. The HPA stress axis has also been extensively characterized in relation to suicide risk [2]. In the present study, multiple pain and comorbid depression showed significant and powerful association with LSA. As depression is a known powerful predictor of suicidal behavior, the combination of multiple pain and comorbid depression might have a synergistic impact on suicidality. Recent studies have also indicated that MDD is associated with inflammation [47] and dysfunction in the HPA axis [48], similarly to chronic pain conditions.

This study has several limitations. First, this was a cross-sectional survey, in which information about somatic pain, LSA, depressive symptom, and their diagnosis was based on retrospective reports. Therefore, a recall bias might have affected the accuracy of the data. Our results showed association rather than causality between MSP and LSA. Second, false negative responses in questionnaires may result in underestimation of the real prevalence of MSP or LSA. Third, non-responsiveness to the interview might have impacted the results. It has been reported previously that non-respondents have higher rates of mental disorders compared to respondents [49]. Fourth, more detailed information on somatic pain, treatments, and detailed drug interactions would be useful in future studies. Causes of somatic pain or specific number of pain areas were not fully evaluated in this study. Fifth, BIS-11 tends to measure trait impulsivity, not state impulsivity. There is growing evidence showing that state impulsivity is associated with acute suicidal behavior [50,51].

In conclusion, MSP was more strongly associated with LSA compared to single somatic pain or no pain. LSA was greater in individuals with a higher number of somatic pain areas and comorbid MDD. This study showed that MSP was an important and strong risk factor for LSA in a community population. Thus, careful screening of suicide risk in patients with MSP and comorbid mental disorders is needed. Integrated services that can reduce somatic pains and prevent suicide attempts are needed.

#### Acknowledgements

The authors wish to express their gratitude to 12 local investigators and 120 interviewers. This study was funded by the Korean Ministry of Health and Welfare. This study was also supported by the Original Technology Research Program for Brain Science through the National Research Foundation of Korea (NRF) funded by the Ministry of Science and ICT (No. NRF-2016M3C7A1947307; PI HJJ), and the Bio & Medical Technology Development Program of the NRF sponsored by the Korean government, MSIP (No. NRF-2017M3A9F1027323; PI HJJ).

#### Role of funding source

The Korean Ministry of Health & Welfare and the National Research Foundation of Korea had no role in study design, data collection, data analysis, data interpretation, writing of the paper, or the decision to submit the paper for publication.

#### Conflict of interest disclosures

None.

## References

- [1] World Health Organization. Suicide prevention (SUPRE) - the WHO worldwide initiative for the prevention of suicide. Geneva: World Health Organization; 2013.
- [2] Lutz PE, Mechawar N, Turecki G. Neuropathology of suicide: recent findings and future directions. *Mol Psychiatry* 2017;22:1395–412.
- [3] Jeon HJ, Park JI, Fava M, Mischoulon D, Sohn JH, Seong S, et al. Feelings of worthlessness, traumatic experience, and their comorbidity in relation to lifetime suicide attempt in community adults with major depressive disorder. *J Affect Disord* 2014; 166:206–12.
- [4] Turecki G. The molecular bases of the suicidal brain. *Nat Rev Neurosci* 2014;15: 802–16.
- [5] Jeon HJ, Roh MS, Kim KH, Lee JR, Lee D, Yoon SC, et al. Early trauma and lifetime suicidal behavior in a nationwide sample of Korean medical students. *J Affect Disord* 2009;119:210–4.
- [6] Brent DA, Mann JJ. Family genetic studies, suicide, and suicidal behavior. *Am J Med Genet C Semin Med Genet* 2005;133C:13–24.
- [7] Myung W, Won HH, Fava M, Mischoulon D, Yeung A, Lee D, et al. Celebrity suicides and their differential influence on suicides in the general population: a national population-based study in Korea. *Psychiatry Investig* 2015;12:204–11.
- [8] Myung W, Lee GH, Won HH, Fava M, Mischoulon D, Nyer M, et al. Paraquat prohibition and change in the suicide rate and methods in South Korea. *PLoS One* 2015;10: e0128980.
- [9] Hawton K, van Heeringen K. Suicide. *Lancet* 2009;373:1372–81.
- [10] Tang NK, Crane C. Suicidality in chronic pain: a review of the prevalence, risk factors and psychological links. *Psychol Med* 2006;36:575–86.
- [11] Braden JB, Sullivan MD. Suicidal thoughts and behavior among adults with self-reported pain conditions in the national comorbidity survey replication. *J Pain* 2008;9:1106–15.
- [12] Hassett AL, Aquino JK, Ilgen MA. The risk of suicide mortality in chronic pain patients. *Curr Pain Headache Rep* 2014;18:436.
- [13] Calati R, Laglaoui Bakhiyi C, Artero S, Ilgen M, Courtet P. The impact of physical pain on suicidal thoughts and behaviors: meta-analyses. *J Psychiatr Res* 2015;71:16–32.
- [14] Ratcliffe GE, Enns MW, Belik SL, Sareen J. Chronic pain conditions and suicidal ideation and suicide attempts: an epidemiologic perspective. *Clin J Pain* 2008;24:204–10.
- [15] Ilgen MA, Kleinberg F, Ignacio RV, Bohnert AS, Valenstein M, McCarthy JF, et al. Noncancer pain conditions and risk of suicide. *JAMA Psychiatr* 2013;70:692–7.
- [16] Park S, Cho MJ, Seong S, Shin SY, Sohn J, Hahm BJ, et al. Psychiatric morbidities, sleep disturbances, suicidality, and quality-of-life in a community population with medically unexplained pain in Korea. *Psychiatry Res* 2012;198:509–15.
- [17] Trinanès Y, Gonzalez-Villar A, Gomez-Perretta C, Carrillo-de-la-Pena MT. Suicidality in chronic pain: predictors of suicidal ideation in fibromyalgia. *Pain Pract* 2015;15: 323–32.
- [18] Lee DH, Noh EC, Kim YC, Hwang JY, Kim SN, Jang JH, et al. Risk factors for suicidal ideation among patients with complex regional pain syndrome. *Psychiatry Investig* 2014;11:32–8.
- [19] Ilgen MA, Zivin K, Austin KL, Bohnert AS, Czyz EK, Valenstein M, et al. Severe pain predicts greater likelihood of subsequent suicide. *Suicide Life Threat Behav* 2010; 40:597–608.
- [20] Kikuchi N, Ohmori-Matsuda K, Shimazu T, Sone T, Kakizaki M, Nakaya N, et al. Pain and risk of completed suicide in Japanese men: a population-based cohort study in Japan (Ohsaki Cohort Study). *J Pain Symptom Manage* 2009;37:316–24.
- [21] Ilgen MA, Zivin K, McCammon RJ, Valenstein M. Pain and suicidal thoughts, plans and attempts in the United States. *Gen Hosp Psychiatry* 2008;30:521–7.
- [22] Cho MJ, Chang SM, Lee YM, Bae A, Ahn JH, Son J, et al. Prevalence of DSM-IV major mental disorders among Korean adults: a 2006 National Epidemiologic Survey (KECA-R). *Asian J Psychiatr* 2010;3:26–30.
- [23] Seoul National University College of Medicine. The epidemiological survey of mental disorders in Korea. Seoul: Korea Ministry of Health and Welfare; 2011.
- [24] Korea National Statistical Office. 2005 Population and housing census report. Daejeon: Korea National Statistical Office; 2006.
- [25] Korea National Statistical Office. 2010 Death and cause of death in Korea. Daejeon: Korea National Statistical Office; 2011.
- [26] Cho MJ, Hahm BJ, Bae JN, Suh TW, Lee DW, Cho SJ, et al. Development of the Korean version of composite international diagnostic interview. Annual meeting of the Korean Neuropsychiatric Association. Seoul, Korea: Korean Neuropsychiatric Association; 1999.
- [27] World Health Organization. CIDI, core version 2.1 interviewer's manual. Geneva: World Health Organization; 1997; 1–114.
- [28] World Health Organization. CIDI, core version 2.1 trainer's manual. Geneva: World Health Organization; 1997; 1–244.
- [29] World Health Organization. Composite international diagnostic interview (CIDI), version 1.0. Geneva, Switzerland: World Health Organization; 1990.
- [30] American Psychiatric Association. Diagnostic and statistical manual of mental disorders. 4th ed. Washington (DC): American Psychiatric Press; 1994.
- [31] World Health Organization. Procedures for the development of new language versions of the WHO Composite International Diagnostic Interview (WHO-CIDI). Geneva, Switzerland: World Health Organization; 1997.
- [32] Cho MJ, Hahm BJ, Suh DW, Hong JP, Bae JN, Kim JK, et al. Development of Korean version of the composite international diagnostic interview (K-CIDI). *J Korean Neuropsychiatr Assoc* 2002;41:123–37.
- [33] Patton JH, Stanford MS, Barratt ES. Factor structure of the Barratt impulsiveness scale. *J Clin Psychol* 1995;51:768–74.
- [34] Lee SR, Lee WH, Park JS, Kim SM, Kim JW. The study on Reliability and Validity of Korean Version of the Barratt Impulsiveness Scale-11-revised in nonclinical adult subjects. *J Korean Neuropsychiatr Assoc* 2012;51:1–9.
- [35] Lee S, Fung SC, Tsang A, Liu ZR, Huang YQ, He YL, et al. Lifetime prevalence of suicide ideation, plan, and attempt in metropolitan China. *Acta Psychiatr Scand* 2007;116: 429–37.
- [36] Cho MJ, Hahm BJ, Suh DW, Hong JP, Bae JN, Cho SJ, et al. A preliminary study for the 2006 National Survey of Psychiatric Illness. Seoul: Seoul National University; 2005.
- [37] Generaal E, Vogelzangs N, Macfarlane GJ, Geenen R, Smit JH, Penninx BW, et al. Reduced hypothalamic-pituitary-adrenal axis activity in chronic multi-site musculoskeletal pain: partly masked by depressive and anxiety disorders. *BMC Musculoskelet Disord* 2014;15:227.
- [38] Fishbain DA, Lewis JE, Bruns D, Disorbo JM, Gao J, Meyer LJ. Exploration of anger constructs in acute and chronic pain patients vs. community patients. *Pain Pract* 2011;11:240–51.
- [39] Margari F, Lorusso M, Matera E, Pastore A, Zagaria G, Bruno F, et al. Aggression, impulsivity, and suicide risk in benign chronic pain patients – a cross-sectional study. *Neuropsychiatr Dis Treat* 2014;10:1613–20.
- [40] Marino EN, Rosen KD, Gutierrez A, Eckmann M, Ramamurthy S, Potter JS. Impulsivity but not sensation seeking is associated with opioid analgesic misuse risk in patients with chronic pain. *Addict Behav* 2013;38:2154–7.
- [41] Racine M. Chronic pain and suicide risk: a comprehensive review. *Prog Neuropsychopharmacol Biol Psychiatry* 2018;87:269–80.
- [42] Kanzler KE, Bryan CJ, McGeary DD, Morrow CE. Suicidal ideation and perceived burdensomeness in patients with chronic pain. *Pain Pract* 2012;12:602–9.
- [43] Madadi P, Persaud N. Suicide by means of opioid overdose in patients with chronic pain. *Curr Pain Headache Rep* 2014;18:460.
- [44] Black C, Miller BJ. Meta-analysis of cytokines and chemokines in suicidality: distinguishing suicidal versus nonsuicidal patients. *Biol Psychiatry* 2015;78:28–37.
- [45] Reason CL, Miller AH. When not enough is too much: the role of insufficient glucocorticoid signaling in the pathophysiology of stress-related disorders. *Am J Psychiatry* 2003;160:1554–65.
- [46] McBeth J, Silman AJ, Gupta A, Chiu YH, Ray D, Morriss R, et al. Moderation of psychosocial risk factors through dysfunction of the hypothalamic-pituitary-adrenal stress axis in the onset of chronic widespread musculoskeletal pain: findings of a population-based prospective cohort study. *Arthritis Rheum* 2007;56:360–71.
- [47] Kiecolt-Glaser JK, Derry HM, Fagundes CP. Inflammation: depression fans the flames and feasts on the heat. *Am J Psychiatry* 2015;172:1075–91.
- [48] Muhtz C, Rodriguez-Raecke R, Hinkelmann K, Moeller-Bertram T, Kiefer F, Wiedemann K, et al. Cortisol response to experimental pain in patients with chronic low back pain and patients with major depression. *Pain Med* 2013;14:498–503.
- [49] de Graaf R, Bijl RV, Smit F, Ravelli A, Vollebergh WA. Psychiatric and sociodemographic predictors of attrition in a longitudinal study: the Netherlands Mental Health Survey and Incidence Study (NEMESIS). *Am J Epidemiol* 2000;152: 1039–47.
- [50] Westheide J, Quednow BB, Kuhn KU, Hoppe C, Cooper-Mahkorn D, Hawellek B, et al. Executive performance of depressed suicide attempters: the role of suicidal ideation. *Eur Arch Psychiatry Clin Neurosci* 2008;258:414–21.
- [51] Caceda R, Moskoviak T, Prendes-Alvarez S, Wojas J, Engel A, Wilker SH, et al. Gender-specific effects of depression and suicidal ideation in prosocial behaviors. *PLoS One* 2014;9:e108733.