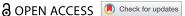




#### BASIC RESEARCH ARTICLE



# Impact of peritraumatic distress on posttraumatic stress disorder symptoms at 6 months after acute coronary syndrome: a prospective cohort study

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#### **ABSTRACT**

Background: Posttraumatic stress disorder (PTSD) symptoms are known to occur after acute coronary syndrome (ACS). Peritraumatic distress has been indicated as a risk factor for PTSD and can be measured by the Peritraumatic Distress Inventory (PDI). However, no studies have yet measured peritraumatic distress after ACS using the PDI to predict PTSD.

Objectives: This prospective cohort study examined the impact of peritraumatic distress on PTSD symptoms at 6 months after ACS.

Methods: We used the PDI to assess peritraumatic distress in patients treated for ACS at a teaching hospital in Tokyo within 7 days after percutaneous coronary intervention. They were followed up over the next 6 months and were assessed for PTSD symptoms at 6 months using the Impact of Event Scale-Revised. The association between peritraumatic distress and PTSD symptoms was examined by multiple linear regression analysis.

Results: The study enrolled 101 ACS patients, and 97 completed the follow-up assessment. PDI total score was an independent predictor of PTSD symptoms after adjustment for potential covariates (beta = 0.38; p < 0.01).

Limitations: The results were obtained from a single teaching hospital and assessment of PTSD symptoms was questionnaire based.

Conclusion: We provide the first evidence that PDI score can predict the development of PTSD symptoms in ACS patients. Assessing peritraumatic distress after ACS with the PDI may be useful for initiating early intervention against PTSD symptoms.

## Impacto del malestar peritraumàtico en los síntomas del trastorno de estrés postraumàtico, 6 meses después del síndrome coronario agudo: un estudio de cohorte prospectivo

Antecedentes: Se sabe que síntomas del trastorno de estrés postraumático (TEPT) se pueden presentar después del síndrome coronario agudo (SCA). El malestar peritraumático se ha señalado como un factor de riesgo de TEPT y puede medirse mediante el Inventario de malestar peritraumático (PDI). Sin embargo, ningún estudio ha medido todavía el malestar peritraumático después de un SCA utilizando el PDI para predecir el

Objetivos: Este estudio de cohorte prospectivo examinó el impacto del malestar peritraumático en los síntomas del TEPT a los 6 meses después del SCA.

Métodos: Utilizamos el PDI para evaluar el malestar peritraumático en pacientes tratados por SCA en un hospital universitario de Tokio dentro de los 7 días posteriores a una intervención coronaria percutánea. Fueron seguidos durante los siguientes 6 meses y se evaluaron los síntomas de TEPT a los 6 meses utilizando la Escala de Impacto de Eventos Revisada. La asociación entre malestar peritraumático y síntomas de TEPT se examinó mediante análisis de regresión lineal múltiple.

Resultados: El estudio reclutó a 101 pacientes con SCA y 97 completaron la evaluación de seguimiento. La puntuación total del PDI fue un predictor independiente de los síntomas de TEPT después del ajuste de las posibles covariables potenciales (beta = 0,38; p <0.01).

Limitaciones: Los resultados se obtuvieron de un solo hospital universitario y la evaluación de los síntomas del TEPT fueron basadas en un cuestionario.

Conclusión: Proporcionamos la primera evidencia de que la puntuación PDI puede predecir el desarrollo de síntomas de TEPT en pacientes con SCA. La evaluación del malestar peritraumático después de un SCA con el PDI puede ser útil para iniciar una intervención temprana contra los síntomas del TEPT.

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#### **KEYWORDS**

PTSD symptoms; posttraumatic stress response; peritraumatic distress; Peritraumatic Distress Inventory; acute coronary syndrome

#### **PALABRAS CLAVE**

síntomas de TEPT; respuesta al estrés postraumático; malestar peritraumático; Inventario de distrés peritraumático; síndrome coronario agudo

#### 关键词

PTSD症状; 创伤后应激反 应; 创伤性精神痛苦; 创伤 性精神痛苦量表; 急性冠 状动脉综合征

## **HIGHLIGHTS**

- Peritraumatic distress has been indicated as arisk factor for PTSD and can be measured by the Peritraumatic Distress Inventory (PDI).
- · We found the first evidence that the PDI predicts PTSD symptoms in ACS patients.

急性冠状动脉综合征6个月后创伤性精神痛苦对创伤后应激障碍症状的影 响:一项前瞻性队列研究急性冠状动脉综合征6个月后创伤性精神痛苦对创 伤后应激障碍症状的影响:一项前瞻性队列研究

背景:已知创伤后应激障碍 (PTSD) 症状会在急性冠状动脉综合征 (ACS) 之后发生。已表明 创伤性精神痛苦为PTSD风险因素,可以通过创伤性精神痛苦量表 (PDI) 进行测量。但是,尚 无研究使用PDI测量ACS后创伤性精神痛苦来预测PTSD。

目的:本前瞻性队列研究考查了在ACS后6个月时创伤性精神痛苦对PTSD症状的影响。

方法:我们使用PDI评估了在东京一所教学医院中接受ACS经皮冠状动脉介入治疗后7天内患 者的创伤性精神痛苦。在接下来的6个月中对他们进行随访, 并使用修订版事件影响量表 评估其6个月时的PTSD症状。通过多元线性回归分析考查了创伤性精神痛苦与PTSD症状之 间的关系。

结果:研究招募了101位ACS患者, 其中97位完成了随访评估。控制潜在协变量后, PDI总分是 PTSD症状的一个独立预测因子 (β= 0.38; p<0.01)

局限性:结果由一所教学医院获得, PTSD症状的评估基于问卷。

结论:我们首次为PDI评分可以预测ACS患者PTSD症状的发展提供了证据。使用PDI评估 ACS 后的创伤性精神痛苦可能有助于开始针对PTSD症状的早期干预。

## 1. Introduction<sup>1</sup>

Cardiovascular disease is a major cause of death globally. In Japan, a registration study on acute myocardial infarction (AMI) conducted in Miyagi Prefecture (Takii et al., 2010) reported that prevalence (per 100,000 population) increased from 7.4 in 1979 to 27.0 in 2008, which is approximately a 4-fold increase over about 30 years. Despite increasing survival rates for cardiovascular disease, it is still perceived by the public as a major threat to life. Individuals who have cardiovascular events consequently experience intense emotional reactions such as fear and anxiety (over dying or recurrence), anger, sadness, and grief as well as posttraumatic stress disorder (PTSD). In light of the association of PTSD and PTSD symptoms with heart disease, Kutz et al. (Kutz, Shabtai, Solomon, Neumann, & David, 1994) proposed the concept of cardiac-disease-induced posttraumatic stress disorder (CDI-PTSD).

Acute coronary events such as acute coronary syndrome (ACS) occur in the case of suddenly reduced blood flow to the heart. ACS is often accompanied by severe chest pain, shortness of breath or lightheadedness, which can be a traumatic event. A systematic review of PTSD after ACS (Vilchinsky, Ginzburg, Fait, & Foa, 2017) reported rates of PTSD within 3 to 18 months after ACS ranging from 3% to 21%. A meta-analytic review of PTSD in patients with ACS (ST-segment elevation myocardial infarction, non-ST -segment elevation myocardial infarction, or unstable angina) found a prevalence of 12% (Edmondson et al., 2012). Survivors of ACS who develop PTSD experience emotional symptoms distress impaired functioning, they are also at risk of medication non-adherence (Husain, Edmondson, Kautz, Umland, & Kronish, 2018; Kronish, Edmondson, Goldfinger, Fei, & Horowitz, 2012; Kronish, Edmondson, Li, & Cohen, 2012), and have almost a 2-fold increased risk of recurrent cardiovascular events and mortality (Kronish et al., 2012, 2012). As the survival rate after ACS has steadily increased, preventing PTSD symptoms after ACS has become vitally important.

The risk factors for PTSD are younger age (Bennett & Brooke, 1999; Rocha et al., 2008), objective severity of ACS (Guler et al., 2009; Von Känel, Baumert, Kolb, Cho, & Ladwig, 2011; Whitehead, 2006), illness perception such as consequences, identity, concern, and emotion (Oflaz et al., 2014), depression (Dinenberg, McCaslin, Bates, & Cohen, 2014; Whitehead, 2006), neuroticism (Chung, Dennis, Berger, Jones, & Rudd, 2011), and attachment anxiety and difficulties in identifying feelings (Gao, Zhao, Li, & Cao, 2015). To explain the development of comorbidities with PTSD, Ginzburg et al. (Ginzburg, Ein-Dor, & Solomon, 2010) describe four competing models, which have all received support in the literature: the first model suggests that preexisting psychiatric disorders such as depression and anxiety increase the risk for PTSD; the second model suggests the opposite causality where PTSD is a causal risk factor for anxiety and depression; the third model suggests that PTSD, anxiety, and depression develop independently but occur together due to shared risk factors; and the fourth model suggests that the comorbidity found among PTSD, anxiety, and depression is an artefact caused by symptom overlap.

On the other hand, the risk factors for PTSD after ACS are identified as objective severity of ACS, perceived severity of ACS, illness representations, distress during myocardial infarction or hospitalization, and previous psychological vulnerability in a systematic review (Vilchinsky et al., 2017). 'Distress during myocardial infarction or hospitalization' is a form of 'peritraumatic distress', which is a group of physiological, emotional, and cognitive responses occurring during and immediately after the time of trauma (Brunet et al., 2001).

Elevated threat perception has been found to predict posttraumatic psychopathology after evaluation for ACS, but most research has measured threat retrospectively. In regard to predicting PTSD symptoms based on peritraumatic distress assessed immediately after ACS, there have been no studies conducted in Japan and just four studies conducted in Western countries. Three found that acute stress disorder symptoms immediately after ACS predicted PTSD symptoms at 1 month (Roberge, Dupuis, & Marchand, 2010) or 3 months (Bennett, Owen, Koutsakis, & Bisson, 2002; Whitehead, 2006), and the fourth study found that peritraumatic distress during angiography predicted PTSD at 1 and 6 months (Marke & Bennett, 2013). The degree of peritraumatic distress can be measured by the Peritraumatic Distress Inventory (PDI) (Brunet et al., 2001), a widely used self-report measure. PDI scores have been used to predict PTSD severity following motor vehicle accidents (Guardia et al., 2013), physical trauma such as sustained in vehicular collisions and falls (Bunnell, Davidson, & Ruggiero, 2018), and physical illness such as stroke (Favrole et al., 2013), Stevens-Johnson syndrome, and toxic epidermal necrolysis (Hefez et al., 2019). Despite studies have reported that peritraumatic distress during heart attack is associated with PTSD symptoms (Bennett et al., 2002; Marke & Bennett, 2013), peritraumatic distress measured in those studies was measured using non-standardized scales.

In this study, we examined whether the degree of peritraumatic distress during myocardial infarction in ACS patients, as assessed using the standardized PDI, can predict the development of PTSD symptoms 6 months later. Establishing such a means of prediction would help clinicians initiate early intervention against PTSD symptoms.

#### 2. Materials and methods

## 2.1. Participants and procedure

We previously conducted a prospective cohort study called 'CONPAC (Cohort with Nutritional Aspect for Psychiatric Disorder after Acute Coronary Syndrome)'. From that study, we have previously reported the association between polyunsaturated fatty acids and psychiatric disorder at 3 months (Yamashita et al., 2017) and 6 months (Noguchi et al., 2019) after ACS. We analysed the same patients in the present study, but here our focus was prediction of PTSD symptoms after ACS using the PDI. Participants were consecutively admitted to the National Disaster Medical Centre, Tokyo, Japan for ACS between 1 March 2014 and 8 February 2017. ACS was diagnosed if new-onset chest pain occurred with ischaemic electrocardiogram changes (Thygesen, Alpert, & White, 2007).

The inclusion criteria were as follows: age ≥20 years; native Japanese speaker; able to contact us within 7 days of percutaneous coronary intervention (PCI); confirmed not to be in a life-threatening condition by a cardiologist and thus be in a stable enough condition to be interviewed; and able to understand the scope of the study and give written consent for study participation. Exclusion criteria were as follows: score on the Mini-Mental State Examination (Folstein, Folstein, & McHugh, 1975) <24; residing >90 min from the medical centre by train or car; a serious psychiatric condition such as hallucination, delusion, suicidalideation, or self-harm behaviour; currently undergoing treatment for a psychiatric disorder; and end-stage cancer. Researchers conducted bedside interviews during hospitalization to confirm the inclusion criteria and explained about the study to those who met the criteria, including that participation was entirely voluntary. Those who consented to participate were asked to fill out the PDI (see 2.2. Assessment) before they were discharged. For follow-up, we conducted an interview in a meeting room in our laboratory on the day the patient was visiting the outpatient clinic.

The Ethics Committee of the National Disaster Medical Centre (2013-42) approved the study protocol. Written informed consent for study participation was obtained within 7 days of PCI. From the medical records and the questionnaire we asked participants to answer, we extracted baseline demographic and medical characteristics such as age, sex, highest educational attainment, psychiatric history, psychiatric family history, and Killip class indicating ACS severity. Peritraumatic distress was assessed using the standardized PDI within 7 days after PCI. We then performed follow-up over the next 3 and 6 months and assessed posttraumatic stress response (PTSD symptoms) using the standardized Impact of Event Scale-Revised (IES-R) at 3 and 6 months after PCI. The study conformed to the Strengthening the Reporting of Observational Studies in Epidemiology (STROBE) guidelines (von Elm et al., 2007).

## 2.2. Assessments

Peritraumatic distress was assessed using the Japanese version of the 13-item PDI (Brunet et al., 2001). Total score ranges from 0 to 52, with each item scored on a 5-point Likert scale (0 = not at all, 1 = slightly true, 2 =somewhat true, 3 =very true, and 4 =extremely true). Internal consistency, concurrent validity, and test-retest reliability have been confirmed for the Japanese version of the PDI (Nishi et al., 2009).

PTSD symptoms were assessed using the IES-R (Weiss, 2004). Total score ranges from 0 to 88. This self-report questionnaire investigates the occurrence

PTSD symptoms experienced in the previous week and comprises 22 items regarding re-experiencing, avoidance, and hyperarousal (i.e., the three most common PTSD symptoms according to the Diagnostic and Statistical Manual of Mental Disorders, fourth edition [DSM-IV]). The validity and reliability of the Japanese version of the IES-R has been confirmed (Asukai et al., 2002).

## 2.3. Statistical analysis

To examine the association between the PDI and PTSD symptoms, we used multiple linear regression analysis with IES-R total score as the dependent variable and PDI total score as the independent variable. We adjusted for the following potential covariates that have been previously identified as risk factors for PTSD: age, sex, psychiatric history, Psychiatric family history, highest educational attainment (Epstein, Fullerton, & Ursano, 1998; Schlenger et al., 2002), and Killip class. In addition, bivariate regression analysis was conducted to determine the relationship of PTSD symptoms with PDI total score and with PDI individual item scores.

Relationships between the dependent and independent variables were expressed as a regression coefficient (beta weight) with 95% confidence interval (95% CI). A p-value of less than 0.05 was considered to indicate statistical significance. SPSS statistical software version 25 for Windows (SPSS, Tokyo, Japan) was used for all data analyses.

#### 3. Results

PCI was used to assess 280 patients, 104 of whom did not meet the inclusion criteria. Of 176 patients approached to participate in the CONPAC study, 100 participated, 71 declined, and 4 withdrew consent. At the follow-up, three participants did not respond. Thus, we enrolled 101 ACS patients, with 97 completing the follow-up assessment (Figure 1). Demographic characteristics of these 97 patients are shown in Table 1. Mean age was  $63.4 \pm 11.1$  (range, 36-87) years and 84 were men (85.7%).

Severity of heart disease was assessed as Killip class grade 1 in 91 (92.9%). PDI was administered 4.0 days (SD = 2.1) after ACS, with an average score of 14.1 (standard deviation [SD] = 9.7, 0-39). The IES-R was

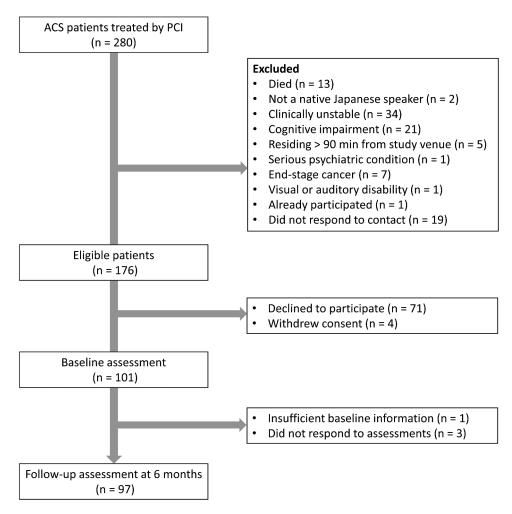


Figure 1. Enrolment flowchart of the CONPAC study. ACS, acute coronary syndrome; PCI, percutaneous coronary intervention.

Table 1. Demographic, medical, and psychiatric characteristics of acute coronary syndrome survivors who participated in a follow-up study (n = 97).

Variables	n	%	Mean	SD	Median	Range
Peritraumatic Distress Inventory	97		14.2	9.7	13.0	0–39
Age (years)	-	-	63.4	11.1	64.0	36-87
Sex, male	83	85.6	-	-	-	-
History of psychiatric illness	7	7.2	-	-	-	-
Family history of psychopathology	15	15.5	-	-	-	-
Highest educational attainment						
Junior high school	14	14.4	-	-	-	-
High school	42	43.3	-	-	-	-
Junior or technical college	16	16.5	-	-	-	-
University or higher	25	25.8	-	-	-	-
Killip class						
1	91	93.8	-	-	-	-
2	3	3.1	-	-	-	-
3	1	1.0	-	-	-	-
4	2	2.1	-	-	-	-
Outcome						
IES-R at 6 months	97	-	6.5	9.3	3.0	0-44

IES-R, Impact of Event Scale - Revised; SD, standard deviation

administered 3.8 days (SD = 2.1) after ACS, with an average IES-R score of 6.5 (SD = 9.2, 0-44) 6 months after ACS.

PDI total score was an independent predictor for PTSD symptoms after adjustment for covariates (beta = 0.38, 95% CI, 0.19–0.57; p < 0.01; Table 2). The value of R-squared for the multiple linear regression model was 0.22 at 6 months.

The results of bivariate regression analysis are shown in Table 3 for each of the 13 PDI items. At

Table 2. Results of multiple linear regression analysis with PDI at 6 months as the dependent variable (n = 97).

	Beta (95% CI)	p value
PDI per 1 point	0.38 (0.19, 0.57)	≤.001
Covariates		
Age per 1 year	-0.11 (-0.28, 0.07)	.23
Women	1.09 (-5.02, 7.20)	.72
History of psychiatric illness	-1.23 (-8.22, 5.75)	.73
Family history of psychopathology	-0.03 (-0.21, 0.15)	.77
Highest educational attainment		
0 (junior high school)	Reference	
1 (high school)	-4.29 (-9.86, 1.29)	.13
2 (junior or technical college)	-4.49 (-11.03, 2.04)	.18
3 (university or more)	-0.79 (-6.69, 5.11)	.79
Killip	5.06 (.887, 9.23)	.18
2 2		

 $R^2 = 0.22$ ,  $R^2$  change = 0.22

the follow-up assessment, significant predictors of PTSD symptoms were item 1 (beta = 2.80, 95% CI = 1.23-4.37; p = 0.001), item 4 (beta = 2.95, 95%, 1.52–4.38;  $p \le 0.001$ ), item 5 (beta = 2.42, 95%) CI, 0.86-3.99; p = 0.003), item 6 (beta = 2.16, 95%CI = 0.26-4.07; p = 0.026), item 8 (beta = 3.36, 95%) CI, 1.27-5.45; p = 0.002), and item 10 (beta = 1.63, 95% CI, 0.36–2.89; p = 0.012).

## 4. Discussion

This is the first study to show that PTSD symptoms can be predicted by measuring peritraumatic stress immediately after ACS in Japanese subjects. To our knowledge, this is also the first study to predict later PTSD symptoms in ACS using the standardized PDI, with 6 of the 13 PDI items helping to predict such symptoms at 6 months after ACS.

We confirmed here that PTSD symptoms related to a life-threatening physical condition could be predicted, as could PTSD symptoms in individuals who had experienced a vehicular accident (Nishi et al., 2010) and in disaster rescue medical workers (Kawashima et al., 2016; Nishi et al., 2012). The PDI

**Table 3.** Results of univariate regression analysis (n = 97).

Item description	Mean (±SD, range)	Beta (95% CI)	R square	p value
1. I felt helpless to do more	0.97 (±1.1, 0-4)	2.80 (1.23, 4.37)	.12	≤.001
2. I felt sadness and grief	1.33 (±1.2, 0-4)	1.18 (-0.35, 2.70)	.02	.129
3. I felt frustrated or angry I could not do more	1.03 (±1.2, 0-4)	0.58 (-0.94, 2.10)	.01	.450
4. I felt afraid for my safety	1.43 (±1.2, 0-4)	2.95 (1.52, 4.38)	.15	.000
5. I felt guilt that more was not done	0.93 (±1.2, 0-4)	2.42 (0.86, 3.99)	.09	.003
6. I felt ashamed of my emotional reactions	0.67 (±1.0, 0-4)	2.16 (0.26, 4.07)	.05	.026
7. I felt worried about the safety of others	1.33 (±1.3, 0-4)	0.60 (-0.84, 2.04)	.01	.407
8. I had the feeling I was about to lose control of my emotions	0.63 (±0.9, 0-3)	3.36 (1.27, 5.45)	.10	.002
9. I had difficulty controlling my bowel and bladder	0.21 (±0.7, 0-4)	2.40 (-0.14, 5.22)	.03	.093
10. I was horrified by what happened	1.7 (±1.4, 0-4)	1.63 (0.36, 2.89)	.06	.012
11. I had physical reactions like sweating, shaking, and pounding heart	1.57 (±1.5, 0-4)	0.81 (-0.41, 2.03)	.02	.190
12. I felt I might pass out	0.97 (±1.3, 0-4)	0.37 (-1.05, 1.78)	.00	.610
13. I felt I might die	1.43 (±1.4, 0-4)	1.04 (-0.25, 2.34)	.03	.111
Total	14.14 (±9.7, 0-39)	0.30 (0.12, 0.48)	.10	.002

CI, confidential interval.

CI, confidence interval; IES-R, Impact of Event Scale - Revised; PDI, Peritraumatic Distress Inventory.

 $R^2$ , coefficient of multiple correlation, index of goodness in the model.

was originally designed to explore PTSD Criterion A2 in DSM-IV, which requires fear, helplessness, or horror at the time of the event. Absence of peritraumatic distress has been shown to be a strong indicator of absence of PTSD (Nishi et al., 2009). In a metaanalysis by Thomas et al. (Thomas, Saumier, & Brunet, 2012), peritraumatic distress was significantly correlated with PTSD symptoms in 18 studies. These previous studies and our results indicate a strong association between peritraumatic distress PTSD symptoms in patients who have experienced a traumatic event, including those caused by physical illness. To clarify this, further studies are required.

We administered the PDI at 3.9 days (SD =  $\pm 2.1$ , 1-10) after ACS. The meta-analysis of PDI and the course of PTSD symptoms (Thomas et al., 2012) showed that regression slopes decreased (numerically or significantly) for separate meta-regressions on results of studies that administered the PDI within or after 1 month of a traumatic event. Recall and memory bias becomes worse as time passes after a traumatic event, so it becomes more difficult to recall emotions accurately. Therefore, it seems important that the PDI be administered as soon after a traumatic event as possible.

One study found that almost 25% of participants who developed PTSD (criteria B-F) did not experience fear, helplessness, or horror but experienced other intense peritraumatic distress experiences such as worry about others, frustration, and physical symptoms during or just after injury (O'Donnell, Creamer, McFarlane, Silove, & Bryant, 2010). Furthermore, it was suggested that removing Criterion A2 from DSM-IV (American Psychiatric Association, 1994) would make diagnosing PTSD easier without a substantial increase in the number of qualified diagnoses (Karam et al., 2010). Criterion subsequently omitted from DSM-5 was (American Psychiatric Association, 2013). However, peritraumatic distress remains an important risk factor for PTSD and being able to assess such distress immediately after a traumatic event is clinically

meaningful. Because the prevalence of meeting diagnostic thresholds based on other criteria is significantly higher in the presence of Criterion A2 than in its absence, it has been suggested that A2 be reconceptualized as a risk factor for PTSD (Karam et al., 2010). The advantage of the PDI that explores A2 is that it can be completed quickly and soon after a traumatic event. Also, those who develop PTSD without meeting A2 include individuals amnestic to their peritraumatic emotional experience (O'Donnell et al., 2010). Amnesia can occur after traumatic brain injury due to physical injury or dissociation due to physical and sexual violence, but amnesia is unlikely to occur after ACS. Therefore, assessing degree of peritraumatic distress using the PDI would be helpful for identifying ACS patients at risk of developing PTSD symptoms.

The following PDI items helped to predict later PTSD symptoms: "1. I felt helpless to do more", '4. I felt afraid for my safety', '5. I felt guilt that more was not done', '6. I felt ashamed of my emotional reactions', '8. I had the feeling I was about to lose control of my emotions', and '10. I was horrified by what happened'. Three previous studies (Bunnell et al., 2018; Nishi et al., 2012, 2010) have examined which PDI items contribute to predicting PTSD symptoms (Table 4), and in all three studies and the present study, items 1, 6, and 8 were significant predictors of PTSD symptoms. Previous studies have reported that cognitive state such as total helplessness during the event (Başoglu, Şalcioglu, & Livanou, 2002) and loss control (Simeon, Greenberg, Schmeidler, & Hollander, 2003) during the peritraumatic period predict later PTSD symptoms. Based on these results, helplessness and difficulty in controlling emotions during traumatic events are thought to be strong predictors of PTSD symptoms. It has been reported that early intervention such as traumafocused cognitive-behavioural therapy (CBT-T), cognitive therapy without exposure and eye movement desensitization and reprocessing (EMDR)) for people with PTSD symptoms after psychological trauma is

Table 4. Comparison between the CONPAC study and previous studies regarding the prediction of posttraumatic stress disorder symptoms using the Peritraumatic Distress Inventory items.

Item description	CONPAC	Nishi 2010	Nishi 2012	Bunnell 2018
1. I felt helpless to do more	✓	✓	✓	✓
2. I felt sadness and grief	-	✓	✓	✓
3. I felt frustrated or angry I could not do more	-	✓	✓	✓
4. I felt afraid for my safety	✓	✓	-	✓
5. I felt guilt that more was not done	✓	-	✓	-
6. I felt ashamed of my emotional reactions	✓	✓	✓	✓
7. I felt worried about the safety of others	-	✓	✓	✓
8. I had the feeling I was about to lose control of my emotions	✓	✓	✓	✓
9. I had difficulty controlling my bowel and bladder	-	-	-	-
10. I was horrified by what happened	✓	✓	-	✓
11. I had physical reactions like sweating, shaking, and pounding heart	-	✓	✓	✓
12. I felt I might pass out	-	✓	-	✓
13. I felt I might die	-	✓	✓	✓

CONPAC, Cohort with Nutritional Aspect for Psychiatric Disorder after Acute Coronary Syndrome.

effective in alleviating the symptoms (Roberts et al., 2019). The result of this study might be useful for earlier screening.

## 5. Limitations

Although our study presents new findings, there are some limitations. First, because this study was conducted at a single hospital in Tokyo, multicenter studies are also required to confirm generalizability. Second, participants in our study included mostly males with Killip class 1. Therefore, the prevalence of PTSD and the prediction of PTSD symptoms by PDI in more severe ACS patients may differ from these results. Third, 'being diagnosed with a life-threatening illness' such as ACS was included in DSM-IV as Criterion A2 but is no longer included in DSM-5. This raises the question of whether the PTSD symptoms detected of this study can be referred to as 'PTSD' symptoms when following DSM-5 criteria. However, because experts vary in their opinions of PTSD Criterion A2 (Friedman, 2013; Roberts et al., 2019), whether physical diseases will be included in any reestablished Criterion A2 depends on how the DSM will be revised in future. Therefore, screening for peritraumatic distress and preventing PTSD symptoms after ACS would be beneficial to patients. In addition, PTSD symptoms were assessed using the self-administered IES-R in this study, which raises concerns about the accuracy of symptom assessments. However, the reliability and validity of the Japanese version of the IES-R for evaluating PTSD symptoms is reported to be comparable to that of the Clinician-Administered PTSD Scale for DSM-IV (Asukai et al., 2002). To generalize our findings, it will be necessary to conduct a large-scale study with a larger number of facilities and participants.

### 6. Conclusion

We examined for the first time worldwide the use of the PDI to predict PTSD in patients with ACS. We confirmed that PTSD symptoms could be predicted by PDI score after adjusting for covariates. PDI items 1, 4, 5, 6, 8, and 10 were significant predictors of PTSD symptoms at 6 months. We also suggest that to predict PTSD symptoms, it may be important that PDI measurements be made within 7 days of the traumatic event. Based on these findings, evaluating peritraumatic distress using PDI at an early stage after an ACS episode is expected to contribute to early detection of PTSD symptoms and early intervention.

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#### Note

1. Abbreviations: ACS, acute coronary syndrome; AMI, acute myocardial infarction; CDI-PTSD, cardiacdisease-induced posttraumatic stress disorder; DSM-IV, Diagnostic and Statistical Manual of Mental Disorders; IES-R, Impact of Event Scale-Revised; PCI, percutaneous coronary intervention; PDI, Peritraumatic Distress Inventory; PTSD, posttraumatic stress disorder.

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## **Author contributions**

YJM conceived and managed the entire research project. TN, HN, AY and YJM collected baseline and follow-up data. TN, DN, RO, HN and YJM analyzed and interpreted the data. TN drafted the manuscript. DN, RO, HN, KH, and YJM critically revised the manuscript for important intellectual content. YJM obtained funding. All authors read and approved the final manuscript.

## **Conflict of interest**

Dr Matsuoka received speaker fees from Suntory, Pfizer, Mochida, Eli Lilly, Morinaga Milk and NTT Data and is conducting collaborative research with SUSMED. The other authors have no conflicts of interest to declare.

## **Data availability statement**

The data that support the findings of this study are available on request from the corresponding author. The data are not publicly available due to privacy or ethical restrictions.

## **Disclosure statement**

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## References

- American Psychiatric Association. (1994). Diagnostic and statistical manual of mental disorders (4th ed.). Washington, DC: American Psyschiatric Association.
- American Psychiatric Association. (2013). Diagnostic and statistical manual of mental disorders (5th ed.). Washington, DC: Author.
- Asukai, N., Kato, H., Kawamura, N., Kim, Y., Yamamoto, K., Kishimoto, J., Miyake, Y., & Nishizono-Maher, A. (2002). Reliability and validity of the Japanese-language version of the impact of event scale-revised (IES-R-J): Four studies of different traumatic events. The Journal of Nervous and Mental Disease, 190(3), 175–182.
- Başoglu, M., Şalcioglu, E., & Livanou, M. (2002). Traumatic stress responses in earthquake survivors in Turkey. Journal of Traumatic Stress, 15(4), 269-276.
- Bennett, P., & Brooke, S. (1999). Intrusive memories, post-traumatic stress disorder and myocardial infarction. British Journal of Clinical Psychology, 38(4), 411-416.
- Bennett, P., Owen, R. L., Koutsakis, S., & Bisson, J. (2002). Personality, social context and cognitive predictors of post-traumatic stress disorder in myocardial infarction patients. Psychology & Health, 17(4), 489-500.
- Brunet, A., Weiss, D. S., Metzler, T. J., Best, S. R., Neylan, T. C., Rogers, C., Fagan, J., & Marmar, C. R. (2001). The peritraumatic distress inventory: A proposed measure of PTSD criterion A2. American Journal of Psychiatry, 158 (9), 1480-1485.
- Bunnell, B. E., Davidson, T. M., & Ruggiero, K. J. (2018). The peritraumatic distress inventory: Factor structure and predictive validity in traumatically injured patients admitted through a Level I trauma center. Journal of Anxiety Disorders, 55, 8-13.
- Chung, M. C., Dennis, I., Berger, Z., Jones, R., & Rudd, H. (2011). Posttraumatic stress disorder following myocardial infarction: Personality, coping, and trauma exposure

- characteristics. The International Journal of Psychiatry in Medicine, 42(4), 393-419.
- Dinenberg, R. E., McCaslin, S. E., Bates, M. N., & Cohen, B. E. (2014). Social support may protect against development of posttraumatic stress disorder: Findings from the heart and soul study. American Journal of Health Promotion, 28(5), 294-297.
- Edmondson, D., Richardson, S., Falzon, L., Davidson, K. W., Mills, M. A., & Neria, Y. (2012). Posttraumatic stress disorder prevalence and risk of recurrence in acute coronary syndrome patients: A meta-analytic review. PLoS One, 7 (6), e38915.
- Epstein, R. S., Fullerton, C. S., & Ursano, R. J. (1998). Posttraumatic stress disorder following an air disaster: A prospective study. American Journal of Psychiatry, 155, 934-938.
- Favrole, P., Jehel, L., Levy, P., Descombes, S., Muresan, I.-P., Manifacier, M.-J., & Alamowitch, S. (2013). Frequency and predictors of post-traumatic stress disorder after stroke: A pilot study. Journal of the Neurological Sciences, 327(1-2), 35-40.
- Folstein, M. F., Folstein, S. E., & McHugh, P. R. (1975). "Mini-mental state": A practical method for grading the cognitive state of patients for the clinician. Journal of Psychiatric Research, 12(3), 189-198.
- Friedman, M. J. (2013). Finalizing PTSD in DSM-5: Getting here from there and where to go next. Journal of Traumatic Stress, 26(5), 548-556.
- Friedman, M. J., Resick, P. A., Bryant, R. A., & Brewin, C. R. (2011). Considering PTSD for DSM-5. Depression and Anxiety, 28(9), 750-769.
- Gao, W., Zhao, J., Li, Y., & Cao, F.-L. (2015). Post-traumatic stress disorder symptoms in first-time myocardial infarction patients: Roles of attachment and alexithymia. Journal of Advanced Nursing, 71(11), 2575-2584.
- Ginzburg, K., Ein-Dor, T., & Solomon, Z. (2010). Comorbidity of posttraumatic stress disorder, anxiety and depression: A 20-year longitudinal study of war veterans. Journal of Affective Disorders, 123(1-3), 249-257.
- Guardia, D., Brunet, A., Duhamel, A., Ducrocq, F., Demarty, A. L., & Vaiva, G. (2013). Prediction of trauma-related disorders: A proposed cutoff score for the peritraumatic distress inventory. The Primary Care Companion to CNS Disorders, 15. https://doi.org10.4088/ PCC.12l01406
- Guler, E., Schmid, J.-P., Wiedemar, L., Saner, H., Schnyder, U., & Känel, R. V. (2009). Clinical diagnosis of posttraumatic stress disorder after myocardial infarction. Clinical Cardiology, 32(3), 125-129.
- Hefez, L., Zaghbib, K., Sbidian, E., Valeyrie-Allanore, L., Allain, M., Duong, T. A., Colin, A., Bellivier, F., Romano, H., De Prost, N., Chazelas, K., Chosidow, O., Wolkenstein, P., & Ingen-Housz-Oro, S. (2019). Posttraumatic stress disorder in Stevens-Johnson syndrome and toxic epidermal necrolysis: Prevalence and risk factors. A prospective study of 31 patients. British Journal of Dermatology, 180(5), 1206-1213.
- Husain, S. A., Edmondson, D., Kautz, M., Umland, R., & Kronish, I. M. (2018). Posttraumatic stress disorder due to acute cardiac events and aversive cognitions towards cardiovascular medications. Journal of Behavioral Medicine, 41(2), 261-268.
- Karam, E. G., Andrews, G., Bromet, E., Petukhova, M., Ruscio, A. M., Salamoun, M., Sampson, N., Stein, D. J., Alonso, J., Andrade, L. H., Angermeyer, M., Demyttenaere, K., De Girolamo, G., De Graaf, R., Florescu, S., Gureje, O., Kaminer, D., Kotov, R., Lee, S.,



- Lépine, J.-P., Medina-Mora, M. E., Oakley Browne, M. A., Posada-Villa, J., Sagar, R., Shalev, A. Y., Takeshima, T., Tomov, T., & Kessler, R. C. (2010). The role of criterion A2 in the DSM-IV diagnosis of posttraumatic stress disorder. Biological Psychiatry, 68(5), 465-473.
- Kawashima, Y., Nishi, D., Noguchi, H., Usuki, M., Yamashita, A., Koido, Y., Okubo, Y., & Matsuoka, Y. J. (2016). Posttraumatic stress symptoms and burnout among medical rescue workers 4 years after the great east Japan earthquake: A longitudinal study. Disaster Medicine and Public Health Preparedness, 10(6), 848-853.
- Kronish, I. M., Edmondson, D., Goldfinger, J. Z., Fei, K., & Horowitz, C. R. (2012). Posttraumatic stress disorder and adherence to medications in survivors of strokes and transient ischemic attacks. Stroke, 43(8), 2192-2197.
- Kronish, I. M., Edmondson, D., Li, Y., & Cohen, B. E. (2012). Post-traumatic stress disorder and medication adherence: Results from the mind your heart study. Journal of Psychiatric Research, 46(12), 1595–1599.
- Kutz, I., Shabtai, H., Solomon, Z., Neumann, M., & David, D. (1994). Post-traumatic stress disorder in myocardial infarction patients: Prevalence study. The Israel Journal of Psychiatry and Related Sciences, 31, 48-56.
- Marke, V., & Bennett, P. (2013). Predicting post-traumatic stress disorder following first onset acute coronary syndrome: Testing a theoretical model. British Journal of Clinical Psychology, 52(1), 70-81.
- Nishi, D., Koido, Y., Nakaya, N., Sone, T., Noguchi, H., Hamazaki, K., Hamazaki, T., & Matsuoka, Y. (2012). Peritraumatic distress, watching television, and posttraumatic stress symptoms among rescue workers after the great east Japan earthquake. PLoS One, 7(4), e35248.
- Nishi, D., Matsuoka, Y., Noguchi, H., Sakuma, K., Yonemoto, N., Yanagita, T., Homma, M., Kanba, S., & Kim, Y. (2009). Reliability and validity of the Japanese version of the peritraumatic distress inventory. General Hospital Psychiatry, 31(1), 75-79.
- Nishi, D., Matsuoka, Y., Yonemoto, N., Noguchi, H., Kim, Y., & Kanba, S. (2010). Peritraumatic Distress Inventory as a predictor of post-traumatic stress disorder after a severe motor vehicle accident. Psychiatry and Clinical Neurosciences, 64(2), 149-156.
- Noguchi, H., Okubo, R., Hamazaki, K., Yamashita, A., Narisawa, T., & Matsuoka, Y. J. (2019). Serum polyunsaturated fatty acids and risk of psychiatric disorder at 6 months after acute coronary syndrome: A prospective cohort study. Prostaglandins, Leukotrienes and Essential Fatty Acids, 149, 18-23.
- O'Donnell, M. L., Creamer, M., McFarlane, A. C., Silove, D., & Bryant, R. A. (2010). Should A2 be a diagnostic requirement for posttraumatic stress disorder in DSM-V? Psychiatry Research, 176(2-3), 257-260.
- Oflaz, S., Yüksel, S., Şen, F., Özdemiroğlu, F., Kurt, R., Oflaz, H., & Kaşikcioğlu, E. (2014). Does illness perception predict posttraumatic stress disorder in patients with myocardial infarction? Nöro Psikiyatri Arşivi, 51(2), 103–109.
- Roberge, M.-A., Dupuis, G., & Marchand, A. (2010). Posttraumatic stress disorder following myocardial infarction: Prevalence and risk factors. Canadian Journal of Cardiology, 26(5), e170-5.
- Roberts, N. P., Kichuner, N. J., Kenardy, J., Lewis, C. E., & Bisson, J. I. (2019). Early psychological intervention

- following recent trauma: A systematic review and meta-analysis. European Journal of Psychotraumatology, 10(1), 1695486.
- Rocha, L. P., Peterson, J. C., Meyers, B., Boutin-Foster, C., Charlson, M. E., Jayasinghe, N., & Bruce, M. L. (2008). Incidence of posttraumatic stress disorder (PTSD) after myocardial infarction (MI) and predictors of PTSD symptoms post-MI-a brief report. The International Journal of Psychiatry in Medicine, 38(3), 297-306.
- Schlenger, W. E., Caddell, J. M., Ebert, L., Jordan, B. K., Rourke, K. M., Wilson, D., Thalji, L., Dennis, J. M., Fairbank, J. A., & Kulka, R. A. (2002). Psychological reactions to terrorist attacks. JAMA, 288, 581.
- Simeon, D., Greenberg, J., Knutelska, M., Schmeidler, J., & Hollander, E. (2003). Peritraumatic reactions associated with the world trade center disaster. American Journal of Psychiatry, 160(9), 1702-1705.
- Takii, T., Yasuda, S., Takahashi, J., Ito, K., Shiba, N., Shirato, K., Shimokawa, H., & On Behalf of the Miyagi-Ami Study, I. (2010). MIYAGI-AMI study investigators. Trends in acute myocardial infarction incidence and mortality over 30 years in Japan. Circulation Journal, 74(1), 93-100.
- Thomas, É., Saumier, D., & Brunet, A. (2012). Peritraumatic distress and the course of posttraumatic stress disorder symptoms: A meta-analysis. The Canadian Journal of Psychiatry, 57(2), 122-129.
- Thygesen, K., Alpert, J. S., & White, H. D. (2007). Joint ESC/ACCF/AHA/WHF task force for the redefinition of myocardial infarction. Universal definition of myocardial infarction. Journal of the American College of Cardiology, 50(22), 2173-2195.
- Vilchinsky, N., Ginzburg, K., Fait, K., & Foa, E. B. (2017). Cardiac-disease-induced PTSD (CDI-PTSD): A systematic review. Clinical Psychology Review, 55, 92-106.
- von Elm, E., Altman, D. G., Egger, M., Pocock, S. J., Gotzsche, P. C., Vandenbroucke, J. P., & Initiative, S. (2007). The strengthening the reporting of observational studies in epidemiology (STROBE) statement: Guidelines for reporting observational studies. Annals of Internal Medicine, 147 (8), 573-577.
- Von Känel, R., Baumert, J., Kolb, C., Cho, E. Y. N., & Ladwig, K.-H. (2011). Chronic posttraumatic stress and its predictors in patients living with an implantable cardioverter defibrillator. Journal of Affective Disorders, 131(1-3), 344-352.
- Weiss, D. S. (2004). The impact of event scale-revised. In J. P. Wilson & T. M. Keane (Eds.), Assessing psychological trauma and PTSD: A practitioner's handbook (2nd ed., pp. 168-189). New York: Guilford Press.
- Whitehead, D. L. (2006). Post-traumatic stress disorder in patients with cardiac disease: Predicting vulnerability from emotional responses during admission for acute coronary syndromes. *Heart*, 92(9), 1225–1229.
- Yamashita, A., Noguchi, H., Hamazaki, K., Sato, Y., Narisawa, T., Kawashima, Y., Usuki, M., Nishi, D., Yoshimasu, H., Horikawa, N., & Matsuoka, Y. J. (2017). Serum polyunsaturated fatty acids and risk of psychiatric disorder after acute coronary syndrome: A prospective cohort study. Journal of Affective Disorders, 218, 306-312.