Posttraumatic stress symptoms as predictive of prognosis after acute coronary syndrome

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Abstract

Objective: Following acute coronary syndrome (ACS), twelve percent of patients suffer from posttraumatic stress disorder (PTSD), and PTSD symptoms have been suggested as predictive of ACS prognosis. Although previous studies suggested associations between the sub-cluster symptoms of PTSD and coronary risk alterations, they included shortcomings in covariates and sample population to reinforce. In this study, we examined the associations between PTSD symptoms and ACS prognosis in a heterogeneous population from previous studies to develop the studies exploring the mechanisms underlying the link between PTSD symptoms and ACS prognosis.

Methods: The participants were 172 consecutive patients admitted to a general hospital in Tokyo with ACS diagnosis. We observed incidents of unscheduled admission due to major adverse cardiac events (MACE) and all-cause mortality (ACM). The association between PTSD symptoms and ACS prognosis was analyzed using Cox hazard models adjusted for covariates.

Results: Over the follow up period of 9.6 months on average (median 12 months), there were 3 ACM events and 27 unscheduled readmissions due to MACE. The analysis showed PTSD as significant predictive, and suggested the intrusion symptoms as most predictive.

Conclusions: On the basis of the suggested association between the intrusion symptoms and ACS prognosis, further study to elucidate the underlying mechanisms are needed.

Keywords: acute coronary syndrome, posttraumatic stress disorder, depression, prognosis, risk factor, secondary prevention

1. Introduction

Acute coronary syndrome (ACS) encompasses a group of conditions caused by reduced blood flow in the coronary arteries. They include unstable angina (UA), non-ST-elevated myocardial infarction (NSTEMI), and ST-elevated myocardial infarction (STEMI) [1]. Depression is a well-established risk factor for ACS [2], and screening for depression is recommended as a secondary strategy to prevent ACS in addition to other approaches such as quitting smoking, managing weight, engaging in physical activity, controlling blood pressure, managing diabetes mellitus (DM), managing lipids, undertaking cardiac rehabilitation, and taking medications such as antiplatelet agents and statins [3]. In addition to depression, posttraumatic stress disorder (PTSD), which develops after traumatic events [4], is reportedly associated with ACS: 12% of patients suffer from PTSD induced by ACS [5], and PTSD symptoms worsen independently ACS prognosis [5].

Although an association between PTSD and ACS prognosis has been suggested, the mechanisms by which PTSD affects ACS prognosis have not been established. Previous studies have noted that biological alterations induced by PTSD are risk factors common to ACS and atherosclerosis: hypertension [6], poor management of DM [7], poor management of lipid profile [7, 8], endothelial dysfunction [9], activated coagulation [10], neuroendocrine dysfunction [11], and inflammation-promoting factors [12, 13, 14]. Other studies have highlighted that cognition and behavior alterations induced by PTSD are also common to established risk factors: smoking [7, 15], weight gain [7, 16], low physical activity [17, 18], and low adherence to secondary preventive medication [19].

Studies have assessed whether physiological changes induced by PTSD are associated with the three PTSD symptom clusters (i.e., the intrusion symptom cluster, the avoidance symptom cluster, and the hyperarousal symptom cluster of the DSM-IV-TR [20]). Some of the reported biological alterations (e.g., hypertension) are common to sympathetic nerve symptoms that are generally considered associated with intrusion symptoms and hyperarousal symptoms. Additionally, the reported alterations in cognition and behavior are also generally considered associated with avoidance symptoms. There exist reports suggesting an association between the avoidance symptoms and ACS prognosis, and between the intrusion symptoms and ACS prognosis. Shemesh et al. [21] assumed that the avoidance symptoms would contribute to readmission through decreasing adherence to medications. They measured platelet thromboxane production as an index of aspirin adherence, and showed an association between overall PTSD symptoms, non-adherence, and readmission due to major

adverse cardiac events (MACE), although sub-clusters were not evaluated. von Kanel et al. [22] assumed that intrusion symptoms contribute to readmission due to MACE. They showed that overall PTSD symptoms (HR = 1.42) and all three sub-cluster symptoms (HR = 1.27-1.33) were significantly associated with ACS prognosis. They considered the intrusion symptoms as important owing to the lack of depression evaluation, which would confound the avoidance symptoms and the hyperarousal symptoms. Regarding mechanisms, they suggested certain biological alterations as important, such as the association between hyperarousal symptoms and a clotting factor in blood samples [10], hyperarousal symptoms and hypocortisolemia [23], and intrusion symptoms, avoidance symptoms, and decreased high-density lipoprotein-cholesterol (HDL) level [8]. Edmondson et al. [24] showed that the intrusion symptoms rather than overall PTSD symptoms predicted readmissions due to MACE or all-cause mortality (ACM). However, the study suffered from shortcomings: the researchers excluded patients with low-level depression symptoms (i.e., patients who scored 0–5 on the Beck Depression Inventory) and the predictor-to-event ratio was low (i.e., 36 events per 9 covariates). Furthermore, as prior studies were limited to Israel [21], Switzerland [22], and the USA [24], findings from populations with different risk backgrounds are needed to reinforce the robustness of the association between PTSD symptoms and ACS prognosis, and would help elucidate the mechanisms underlying PTSD symptoms and ACS prognosis.

In this study, we aimed to address the shortcomings of previous studies. We explored which symptom cluster would predict ACS prognosis in a population with a different risk profile from previous studies so as to explore the mechanisms underlying the link between PTSD symptoms and ACS prognosis.

2. Methods

2.1 Study Design

The authors directly recruited consecutive adult ACS patients aged 18 or above who were admitted to the Tokyo Metropolitan Tama Medical Center from October 1, 2013 to March 31, 2015. We excluded patients who died during hospitalization, could not understand Japanese, had impaired orientation or visual/auditory disturbance, were referred to other hospitals after discharge, were missing initial records (i.e., left ventricular ejection fraction [LVEF] and laboratory data), or had no coronary artery lesion (e.g., Takotsubo cardiomyopathy).

The participants were requested to complete three self-rating questionnaires: the Patient Health Questionnaire-9 (PHQ-9) [25, 26], the State-Trait Anxiety Inventory (STAI) [27, 28], and the Impact of Event Scale-Revised (IES-R) [29, 30]. Participants were also requested to declare whether they needed unscheduled admission (e.g., for an

emergency) or not, at every outpatient follow up. We observed the incidence of MACE or ACM and statistically analyzed these data.

We obtained written informed consent from all participants. This study was approved by the institutional review board of the Tokyo Metropolitan Tama Medical Center and the Tokyo Metropolitan Institute of Medical Science.

2.2 Participants

In total, 277 patients were admitted to the center for ACS during the study period. Of these 277, 59 patients were excluded: 19 died during hospitalization, 12 had impaired orientation, 6 had visual/auditory disturbances, 2 were unable to understand Japanese, 7 were referred to other hospitals after discharge, 12 lacked initial data (i.e., 5 were lacking laboratory data and 7 were lacking LVEF data), and 1 was diagnosed with Takotsubo cardiomyopathy. Thirty-four patients refused to take part in the study, whereas 184 patients (84.4%) agreed and completed the initial assessment. Of these 184, 12 failed to complete the IES-R at the follow-up assessment. Therefore, the study sample was composed of 172 patients.

2.3 Demographic and medical covariates

Based on the established predictors of ACS prognosis, we selected the following potential medical covariates: gender (0: female, 1: male) [31], age (continuous variable) [31], marital status (0: living with spouse, 1: divorced or widowed, 2: never married) [32], smoking status (0: current non-smoker, 1: current smoker) [31], obesity (0: body mass index [BMI] < 18.5, 1: 18.5 $\leq$ BMI < 25, 2: BMI $\geq$ 25) [31], estimated glomerular filtration rate (e-GFR; continuous variable) [33], HbA1c (continuous variable) [31], total cholesterol (continuous variable) [31], Killip classification (0: mild [I or II], 1: severe [III or IV]) [34], and LVEF (0: LVEF < 40%, 1: LVEF $\geq$ 40%) [35].

2.4 Psychological measures

The PHQ-9 [25], a 9-item self-rating scale, was administered at the initial assessment during hospitalization to evaluate depressive symptoms. The frequency of depressive symptoms in the 2 weeks prior to the interview was rated as 0: “not at all,” 1: “several days,” 2: “more than half the days,” or 3: “nearly every day”. In the Japanese version of the PHQ-9 [26], patients who score 5–9 are assessed as having minimal symptoms, 10–14 as having moderate symptoms, 15–20 as having moderate to severe symptoms, and 20–27 as having severe symptoms. A cut-off score of 10 or above for the total score of the Japanese version of the PHQ-9 has shown good sensitivity (0.84) and specificity (0.95) for screening for major depressive disorder [26]. Respondents who scored 10 or above were defined as “depressive.”

The STAI [27], a 40-item self-rating scale consisting of 20 anxiety state items

(STAI-S) and 20 anxiety trait items (STAI-T), was administered at the initial assessment during hospitalization to evaluate present anxiety symptoms and inherent trait anxiety as confounding variables. In the STAI-S, the intensity of anxiety was rated as 1: “not at all,” 2: “somewhat,” 3: “moderately so,” or 4: “very much so” and the frequency of anxiety was rated as 1: “almost never,” 2: “sometimes,” 3: “often,” or 4: “almost always” in the STAI-T. The Japanese version of the STAI [28] was used; it is considered a reliable questionnaire and has been validated by Spielberger, who constructed the original version of the test.

The IES-R [30], a 22-item self-rating scale consisting of 8 intrusion symptoms, 8 avoidance symptoms, and 6 hyperarousal symptoms, was used to evaluate PTSD symptoms in the week prior to the assessment. The IES-R was completed at the follow-up assessment after discharge with the instruction to describe the ACS attack that led to the last admission. The mean and median duration between the date of admission and that of the IES-R assessment were 35.0 (SD = 18.2) and 30 (Q1 = 25, Q3 = 38) days, respectively. The intensity of the PTSD symptoms was rated as 0: “None,” 1: “A little,” 2: “Moderate,” 3: “Quite a bit,” or 4: “Extremely” in the IES-R. A cut-off score of 25 or above for the total score of the Japanese version of the IES-R [29] has shown good sensitivity (0.75–0.89) and specificity (0.71–0.93) for identifying PTSD and partial PTSD. We used a cut-off score of 33 or above to decrease the incidence of patients with partial PTSD, with reference to the original version [30]. Respondents who scored 33 or above on the IES-R were defined as “PTSD positive.”

2.5 Primary endpoint

The primary endpoint was defined as ACM or an unscheduled readmission due to MACE in the observational period. The participants were requested to select whether they needed emergency admission due to MACE or not at every outpatient follow up, and we collated these data with medical records. In cases of missing or suspicious replies (i.e., inconsistent with medical records), we telephoned the individual and ascertained their condition. MACE was defined as recurrent ACS, heart failure, arrhythmia, stroke, and peripheral vessel disease (e.g., deep vein thrombosis).

2.6 Statistical analysis

We used the chi-square test for categorical variables and Student’s t-test for continuous variables when comparing the characteristics of 2 groups. Mean substitution was used for missing data, because the proportion of missing data was less than 5%.

In the log-rank test to compare the survival curve of 2 groups concerning overall PTSD symptoms and the 3 sub-clusters, we divided our participants into high and low PTSD categories.

We generated Cox hazard models to adjust for covariates. Although numerous covariates were considered based on established predictors, we limited the number of covariates to maintain an adequate predictor-to-event ratio. Therefore, we added covariates using a forward-selection method. We selected age, gender, and PHQ-9 a priori; then, LVEF emerged in the forward-selection procedure from additional covariates (i.e., marital status, smoking status, BMI, type of ACS, e-GFR, HbA1c, total cholesterol, and Killip classification). Each of the symptom clusters was analyzed separately. Model 1 did not adjust for covariates. Model 2 adjusted for demographic factors (age and gender), model 3 for demographic factors and severity (LVEF), and model 4 for demographic factors, severity, and psychological factors (PHQ-9 score). Total scores and the scores of the 3 clusters of the IES-R were treated as dichotomous, using high and low categories, because these categories are more useful than a continuous variable as an indicator in daily clinical practice, the distributions of the total score and the 3 cluster scores of the IES-R were skewed, and appeared to have distinct thresholds. The cut-off scores used both in the log-rank test and Cox hazard models for the total score and for each subscale were 33 or above, and 11 or above, respectively, similar to previous studies [21, 24]. As a secondary analysis, we analyzed IES-R as a continuous variable.

3. Results

3.1 Characteristics of the participants

The mean age of the 172 participants was 67 years (SD = 12.6, range 35–92 years). Forty-nine patients (28.5%) were women. All but one were Japanese. Thirty-one patients (18.0%) were divorced or widowed, and 25 (14.5%) were unmarried. Thirty-nine patients (22.7%) were current smokers, 51 (29.7%) were obese (BMI $\geq$25), and 10 (5.8%) were underweight (BMI < 18.5; Table 1). There were no significant differences observed between the patients who completed the IES-R follow-up and those who did not.

3.2 Medical status of the participants

Of the 172 patients, 107 (62.2%) were diagnosed with STEMI; 20 (11.6%), NSTEMI; 45 (26.2%), UA; 20 (11.6%), coronary spastic ACS; 37 (21.5%), severe symptoms (Killip III or IV); and 18 (10.5%), low LVEF (< 40%). The mean values of e-GFR, HbA1c, and total cholesterol were 66.0 ml/min/1.73m^2 (SD = 24.1), 6.2% (SD = 1.3), and 193.4 mg/dl (SD = 55.8), respectively (Table 1). There were no significant differences in medical status except for LVEF between the participants who had completed the IES-R and those who had not. Significantly fewer patients who completed the IES-R had low LVEF.

Table 1				
Base line characteristics of 172 participants.				N=172
demographic characteristics				
	age mean, (SD)			67.0 (12.6)
	female n, (%)			49 (28.5%)
	marital status			
		living with spouse n, (%)		116 (67.4%)
		divorce or widowed n, (%)		31 (18.0%)
		not married n, (%)		25 (14.5%)
	current smoker, n (%)			39 (22.7%)
	BMI, mean (SD)			23.2 (3.6)
		BMI ≥25, n (%)		51 (29.7%)
		25>BMI ≥18.5, n (%)		111 (64.5%)
		18.5>BMI, n (%)		10 (5.8%)
psychological variables				
	PHQ-9 score			
		total, mean (SD)		3.7 (3.8)
		total score≥10, n (%)		14 (8.1%)
	STAI score			
		STAI-S score, mean (SD)		38.9 (11.0)
		STAI-T score, mean (SD)		37.9 (9.9)
	IES-R score			
		total, mean (SD)		14.0 (13.5)
		total score≥33, n (%)		16 (9.3%)
		intrusion, mean (SD)		5.0 (5.3)
		intrusion score≥11, n (%)		20 (11.6%)
		avoidance, mean (SD)		5.0 (5.1)
		avoidance score≥11, n (%)		29 (16.9%)
		hyperarousal, mean (SD)		4.0 (4.2)
		hyperarousal score≥11, n (%)		13 (7.6%)
medical characteristics				
	type of ACS			
		STEMI, n (%)		107 (62.2%)
		NSTMI ACS, n (%)		20 (11.6%)
		UA, n (%)		45 (26.2%)
	etiology			
		thromboembolic ACS, n (%)		152 (88.4%)
		coronary spastic ACS, n (%)		20 (11.6%)
	e-GFR, mean (SD)			66.0 (24.1)
	HbA1c, mean (SD)			6.2 (1.3)
	total cholesterol, mean (SD)			193.4 (55.8
	Killip score≥3, n (%)			37 (21.5%)
	LVEF <40, n (%)			18 (10.5%)

note. ACS:acute coronary syndrome, BMI: body mass index, e-GFR: estimated-glomerular filtration rate, IES-R: Impact of Event Scale-Revised, LVEF: left ventricular ejection fraction, NSTEMI: non ST elevated myocardinal infarction, PHQ-9: Patient Health Questionnaire-9, STAI-S: State-Trait Anxiety Inventory-Stait, STAI-T: State-Trait Anxiety Inventory-Trait, STEMI: ST elaveted myocardinal infarction, UA: unstable angina

3.3 Psychological measures

The mean scores of the PHQ-9, STAI-S, STAI-T, and IES-R were 3.7 (SD = 3.8), 38.9 (SD = 11.0), 37.9 (SD = 9.9), and 14.0 (SD = 13.5), respectively. Fourteen (8.1%) participants screened positive for depressive symptoms on the PHQ-9. Sixteen patients (9.3%) screened positive for PTSD on the IES-R. Regarding the PTSD symptom clusters, the mean scores for intrusion, avoidance, and hyperarousal were 5.0 (SD = 5.3), 5.0 (SD = 5.1), and 4.0 (SD = 4.2), respectively (Table 1). The number of participants who scored 11 or above for the 3 sub-scales was 20 (11.6%) for the intrusion symptom cluster, 29 (16.9%) for the avoidance symptom cluster, and 13 (7.6%) for the hyperarousal symptom cluster.

3.4 Incidence of primary end point

In the study period, we observed our participants for 9.6 months on average (median 12 months). Three participants (1.7%) died and 27 participants (15.7%) experienced unscheduled readmission due to MACE.

3.5 Association between each PTSD symptom cluster and prognosis

In the log-rank test, total scores for the IES-R ($p < 0.01$; Fig. 1), the intrusion symptoms ($p < 0.01$; Fig. 2), and the hyperarousal symptoms ($p = 0.03$) were significantly associated with ACM or MACE. In contrast, the avoidance symptoms ($p = 0.40$) were not significantly associated with ACM or MACE.

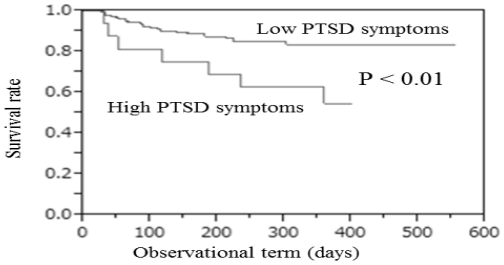

Fig. 1
The difference between the patients with high PTSD symptoms and those without (log-rank test).
Note. The lower line shows the survival rate of the patients with high PTSD symptoms (scored 33 or above in the Impact of Event Scale-Revised). The upper line shows that of the patients with low PTSD symptoms. The log-rank test showed a significant difference between the two groups.

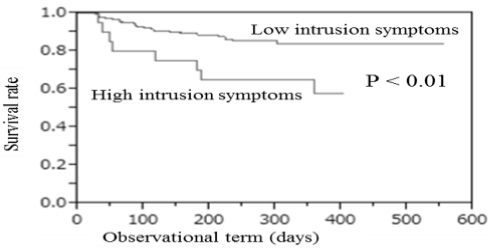

Fig. 2
The difference between the patients with high intrusion symptoms and those without (log-rank test).
Note. The lower line shows the survival rate of the patients with high intrusion symptoms (scored 11 or above in intrusion symptom items of the Impact of Event Scale-Revised). The upper line shows that of the patients with low intrusion symptoms. The log-rank test showed a significant difference between the two groups.

3.6 Risk-adjusted association between three symptom clusters and prognosis

In the Cox hazard models, without adjustment for covariates, total scores on the IES-R (HR = 3.1, 95% CI 1.2–6.8, p = 0.02) and the intrusion symptom cluster (HR = 2.9, 95% CI 1.2–6.3, p = 0.02) significantly predicted ACS prognosis, whereas neither the avoidance symptom cluster (HR = 1.4, 95% CI 0.6–3.2, p = 0.42) nor the hyperarousal symptom cluster (HR = 2.7, 95% CI 0.9–6.5, p = 0.07) were significant predictors. The intrusion symptoms cluster was insignificant in the final model, which adjusted for the PHQ-9 (HR = 2.6, 95% CI 0.96–6.41, p = 0.06), whereas overall PTSD symptoms remained significant (HR = 3.2, 95% CI 1.1–7.9, p = 0.03; Table 2).

In the secondary analysis, which considered IES-R as a continuous variable, total scores (HR = 1.02, 95% CI 0.99–1.64, p = 0.14; Table 2) did not significantly predict ACS prognosis.

Table 2

Cox hazard models adjusterd for covariates

factors	model 1		model 2		model 3		model 4	
	B (SE)	HR (95% CI)	B (SE)	HR (95% CI)	B (SE)	HR (95% CI)	B (SE)	HR (95% CI)
IES-R (dichotomous)	0.56 (0.22)	3.1 (1.22-6.80)†	0.60 (0.22)	3.3 (1.32-7.44)†	0.57 (0.22)	3.1 (1.23-7.09)†	0.58 (0.24)	3.2 (1.13-7.88)†
age			-0.04 (0.02)	1.04 (1.01-1.08)†	-0.04 (0.02)	1.04 (1.01-1.08)†	-0.04 (0.02)	1.04 (1.01-1.08)†
female			0.15 (0.21)	0.7 (0.30-1.62)	0.13 (0.21)	0.8 (0.32-1.73)	0.13 (0.21)	0.8 (0.32-1.73)
LVEF<40					-0.22 (0.25)	1.6 (0.51-3.85)	-0.22 (0.25)	1.6 (0.51-3.86)
PHQ-9							0.005 (0.05)	1.0 (0.90-1.08)
intrusion	0.53 (0.21)	2.9 (1.22-6.29)†	0.48 (0.21)	2.6 (1.08-5.67)†	0.47 (0.21)	2.6 (1.07-5.64)†	0.48 (0.24)	2.6 (0.96-6.41)
age			-0.04 (0.02)	1.04 (1.00-1.07)†	-0.04 (0.02)	1.03 (1.00-1.07)†	-0.04 (0.02)	1.04 (1.00-1.07)†
female			0.13 (0.21)	0.8 (0.32-1.70)	0.10 (0.21)	0.8 (0.33-1.81)	0.10 (0.21)	0.8 (0.33-1.81)
LVEF<40					-0.29 (0.25)	1.8 (0.60-4.36)	-0.29 (0.25)	1.8 (0.60-4.38)
PHQ-9							0.004 (0.05)	1.0 (0.90-1.09)
IES-R (continuous)	0.02 (0.01)	1.02 (0.99-1.04)	0.02 (0.01)	1.02 (0.99-1.04)	0.02 (0.01)	1.02 (0.99-1.04)	0.02 (0.01)	1.02 (0.99-1.04)
age			0.04 (0.02)	1.04 (1.00-1.08)†	0.04 (0.02)	1.04 (1.01-1.08)†	0.04 (0.02)	1.04 (1.00-1.08)†
female			-0.15 (0.21)	0.74 (0.31-1.62)	-0.12 (0.21)	0.78 (0.32-1.73)	-0.12 (0.21)	0.79 (0.32-1.75)
LVEF<40					0.26 (0.25)	1.67 (0.55-4.14)	0.26 (0.25)	1.68 (0.55-4.16)
PHQ-9							0.01 (0.05)	1.01 (0.90-1.11)

note. IES-R: Impact of Event Scale-Revised, LVEF: left ventricular ejection fraction, PHQ-9: Patient Health Questionnaire-9

†: $p < 0.05$

4. Discussion

In this study, we examined which PTSD symptom cluster would be most predictive of ACS prognosis, so as to provide a basis for exploring the mechanisms underlying the link between PTSD symptoms and ACS prognosis. We showed that overall PTSD symptoms were significantly predictive, with a HR of 3.2 in the final model, consistent

with previous studies [21, 22, 24], and the intrusion symptom cluster was suggested as most predictive, consistent with a previous study [24]. However, overall PTSD symptoms were not significantly predictive when they were treated as a continuous variable in the secondary analysis. The discrepancy between the results of the primary analysis and secondary analysis suggests the existence of a threshold effect in the association between PTSD symptoms and ACS prognosis.

We showed comparable results to previous studies [21, 22, 24] in our predominately Japanese patient sample; this population has reported differences from people living in Western countries in the incidence of AMI [36], obesity or individual physical activity [37], diet [36, 38], and vulnerability to glucose intolerance [39]. Indeed, when comparing the characteristics of our participants to those of previous studies, our mean reported age of 67 years old is higher than that of previous studies (e.g., 53 years old [21], 61 years old [22], and 60 years old [24]). Our mean population BMI of 23.2 is smaller than that previously reported 28.5-29.0 [24] and our percentage of patients with DM (21.5%) is less than the value of 31.2% reported previously [24]. Our results are thus valuable in reinforcing the robustness of the association between PTSD and ACS prognosis. Although the intrusion symptom cluster was insignificant only in the final model, which adjusted for depressive symptoms, limited power would have likely impacted our results.

Regarding mechanisms, and complimenting previous work addressing the link between intrusion symptoms and decreased HDL level [8], we note a suggestive case: this female individual scored 42 on the IES-R at the initial assessment and she was later readmitted due to acute heart failure. When she found that her blood pressure was elevated at a regular checkup, she was reminded of her initial ACS attack. Then, she could not control her fear that she might experience another ACS attack. The consequent increased sympathetic nerve function, shown as tachycardia and high blood pressure, would have contributed to the heart failure. It is clinically plausible to assume a causal relationship between intrusion symptoms, increased sympathetic nerve function, and readmission. This case was also suggestive with respect to intervention methods: After treatment with psychoeducation and a sertraline prescription, the patient stated that her elevated blood pressure was no longer a source of stress. Given that she did not need a third admission, at least during this study period, an intervention that includes psychoeducation and medication appears safe and effective for preventing readmission due to MACE. Although there are no established intervention methods, Shemesh et al. [40] suggested the potential for cognitive behavioral therapy, consisting of relaxation, exposure, and cognitive reprocessing, to improve PTSD symptoms and

adherence in patients with post-threshold PTSD. Shemesh et al. [41] also examined and illustrated the safety of imaginal exposure in a randomized control trial. A trial has also been reported (MI-SPRINT) [42] that aimed to prevent development of PTSD symptoms by trauma-focused psychological counseling. To improve secondary preventive strategies for ACS, further data are needed.

There are several limitations in our study. First, because participants were recruited from only one hospital, selection bias may have affected our results. However, the prevalence of PTSD was comparable to that of a previous meta-analysis [5]. Second, the 34 patients who refused to respond to the IES-R at their outpatient follow-up would likely have reported greater PTSD symptoms, especially avoidance symptoms, than those who responded. However, the response rate was very high, with 93.5% of the participants completing the IES-R. This illustrates the representativeness of the participants who completed the study. Third, because we checked PTSD symptoms and MACEs via self-administered questionnaires, there exist concerns about accuracy. Indeed, some patients corrected their responses when we confirmed the details of MACE. However, we checked medical records and confirmed information as needed, to decrease the incidence of such mistakes. Because, the IES-R was sometimes assessed within 30 days of an index attack, the prevalence of PTSD was not accurate. Fourth, we did not assess some known predictive factors such as hypertension, alcohol consumption, and physical activity because it was difficult to conduct these assessments in our study plan. Fifth, we used a forward-selection method, in order to keep a favorable predictor-to-event ratio. Therefore, we could not adjust for some known risk factors. Future studies with large sample sizes are thus desirable.

Notwithstanding these limitations, our results reinforced the evidence of links between PTSD symptoms and ACS prognosis as the first study from Asia. This is valuable to reinforce a sound basis for further study to elucidate the mechanisms underlying the link between PTSD symptoms and ACS prognosis.

5. Conclusion

We suggest that PTSD symptoms, particularly the intrusion symptoms, predict ACS prognosis. Development of intervention strategies for ACS secondary prevention are needed, which will require future studies to elucidate the mechanisms underlying the link between PTSD symptoms and ACS prognosis.

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Disclosure

Conflicts of interest: none.

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