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The fear of dying and occurrence of posttraumatic stress symptoms after an acute coronary syndrome: A prospective observational study

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Abstract

The purpose of the study was to investigate whether experiencing fear of dying after acute coronary syndrome predicts later posttraumatic stress symptoms. We enrolled 90 patients hospitalized with main diagnosis of acute coronary syndrome and assessed baseline characteristics. One month after discharge, we collected the Posttraumatic Stress Scale. A total of 24 patients (26.7%) developed posttraumatic stress symptoms 1 month after the acute coronary syndrome event. Patients with posttraumatic stress symptoms reported significantly greater fear of dying, helplessness, avoidance-focused coping, and severe anxiety. In our prospective study, fear of dying was associated with occurrence of posttraumatic stress symptoms in patients hospitalized with acute coronary syndrome.

Keywords

anxiety, coping, coronary artery disease, depression, diagnosis

Introduction

A recent meta-analysis of 13 studies reported that about 15 percent of patients developed posttraumatic stress disorder (PTSD) after hospitalization for an acute coronary syndrome (ACS) (Gander and Von Kanel, 2006). PTSD is defined according to the fourth edition of the *Diagnostic and Statistical Manual of Mental Disorders–Fourth Edition* (DSM-IV) as an intense fear, helplessness, and horror occurring after an experienced traumatic event or life-threatening illness (American Psychiatric Association, 2000). Patients with PTSD have poorer medication-adherence and clinical outcomes after ACS; therefore, recognizing PTSD symptoms has important clinical implications (Edmondson et al., 2012; Shemesh et al., 2006). Thus, the European Society of Cardiology (ESC) guidelines on cardiovascular disease (CVD)

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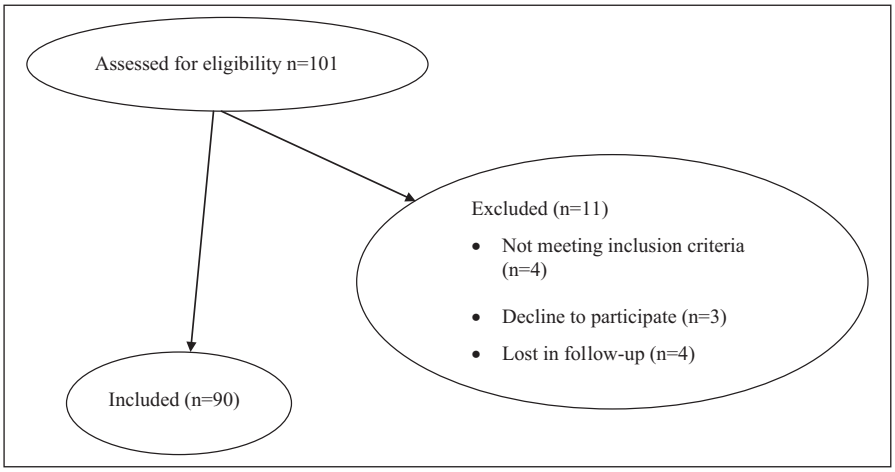

Figure 1. Flowchart of patients' enrollment from February 2012 to June 2012.

prevention in clinical practice recommend interventions to manage psychosocial stress and coping with illness (Perk et al., 2012).

Identifying patients at risk during the initial ACS hospitalization might help prevent and treat earlier the development of PTSD (Meister et al., 2013; Shemesh et al., 2006). Many patients perceived ACS as a traumatic and stressful event (Burnett et al., 1995; Gander and Von Kanel, 2006; Wikman et al., 2008). However, with the decrease of hospital length of stay (LOS), limited time is available to assess psychological conditions and identify at-risk patients, and thus, the assessment of psychological conditions must be short. Fear of dying is a good candidate for evaluating with a short question the psychological stress associated with ACS. Interestingly, the fear of dying expressed by the patients has been associated with an increased inflammation of the biological process of atherosclerosis (Steptoe et al., 2011). Few data assessed the association of fear of dying and coping responses and the occurrence of subsequent PTSD in the context of ACS (Chung et al., 2011).

This study aims at examining psychological states, such as fear of dying and helplessness, that may predict the development of subsequent posttraumatic stress (PTS) symptoms after ACS.

Materials and methods

Participants

We prospectively included 90 patients aged >18 years hospitalized with a main diagnosis of ACS in the Clinic of Cardiology ($N = 90$) of the Lithuanian University of Health Sciences Hospital, Kaunas, Lithuania from February 2012 to June 2012. ACS was defined as patients with symptoms comparable with unstable angina pectoris (chest pain, dyspnea) and at least one of the following characteristics: ST-segment elevation or depression, T inversion or dynamic electrocardiogram (ECG) changes, evidence of positive troponin, and known coronary heart disease (status after myocardial infarction (MI), bypass surgery, or percutaneous coronary intervention) (Thygesen et al., 2007). Exclusion criteria were terminal illness, being registered at Drugs and Alcohol Center for current alcohol and/or substance abuse, cognitive impairment (evaluated with Mini Mental State Examination), refusal to participate, hospital discharge before screening, or incapacities to be followed up. The flowchart of the enrollment process is described in Figure 1. The study was approved by the University Bioethics Committee (approval number VK-120), and all participants gave

written consent. The investigation conforms with the principles outlined in the Declaration of Helsinki.

Data collection

Clinical data for the included patients were collected by a trained medical doctor on standardized case report forms. Baseline data were collected during the hospital admission for ACS and follow-up performed 1 month after discharge by phone. Baseline collected data were gender, age, education status, working status, family income per person (low as "official minimum and less" versus high as "more than official minimum"), and marital status. We asked patients to answer the Hospital Anxiety and Depression (HAD) questionnaire, subjective distress experience due to ACS, and the Coping Strategies questionnaire (COPE scale). At 1 month, we asked participants to answer the PTS scale by telephone (Foa et al., 1993).

Methodology of psychological questionnaires

1. HAD scale was used to measure symptoms of anxiety (seven questions) and depression (seven questions) at baseline, each question containing four possible grades according to Likert scale (Zigmond and Snaith, 1983). After summing up the answers separately in both scales, more than 10 points indicate severe anxiety and depression symptoms, and less than 8 points indicate absence of anxiety and depression; 8–10 points indicate intermediate probability of anxiety and depression symptoms. For the present sample, scales' reliability analysis according to Cronbach's alpha was 0.726 for anxiety and 0.726 for depression subscales.
2. Patients answered four questions about subjective distress experience due to ACS, each question containing 9–10 possible answers according to Likert scale: (1) feeling fear of dying: "During my referral to the hospital, the emergency unit, or the intensive care unit, I was afraid I was dying" (1 = I did not feel the fear of dying at all; 10 = I thought I would really die); (2) feeling helplessness: "When the doctor told me I had a heart attack, I was frightened, felt helpless, and was afraid of losing the control of the situation" (1 = absolutely not true; 9 = I was really very afraid); (3) severity of chest pain: "Please indicate how strong your pain was during the heart attack" (1 = no pain at all; 10 = intolerable pain); (4) feeling dyspnea: "When you had chest pain, did you have dyspnea that made you afraid?" (1 = not at all; 9 = I was very afraid) (Guler et al., 2009). The cut-off point of dichotomization for feeling fear of dying was "I did not feel fear of dying at all" versus all other answers indicating some level of perceived fear, as done in a previous publication (Guler et al., 2009). The cut-off point of dichotomization for feeling helplessness, chest pain, and dyspnea was "moderately and more" versus "less than moderately." One question contained information on inaugural chest pain occurrence with seven probable answers and was dichotomized by more than 1 year versus 1 year and less.
3. COPE scale enables to assess the different coping with stress strategies and consists of 60 questions (Carver et al., 1989). Response choices were "I usually don't do this at all," "I usually do this a little bit," "I usually do this a medium amount," and "I usually do this a lot" (scored from 1 to 4). Based on a previous publication, we grouped 12 subscales into four categories: (1) Problem-focused coping (three subscales: active coping, planning, and suppression of competing activities) (Chung et al., 2008). Reliability of problem-focused coping scale according to Cronbach's alpha was 0.817 in the

present sample. (2) Emotion-focused coping (three subscales: seeking emotional social support, seeking instrumental social support, and focusing on and venting of emotions) with Cronbach's alpha 0.842. (3) Acceptance-focused coping (three subscales: positive interpretation and growth, restraint coping, acceptance), Cronbach's alpha 0.813. (4) Avoidance-focused coping (denial, mental disengagement, behavioral disengagement) with Cronbach's alpha 0.812. The dichotomization at the median score for each scale was performed, as done in a previous publication (Chung et al., 2008).

Measurement of the main outcome

The PTS scale assesses the presence of PTS symptoms (Foa et al., 1993). The scale was derived from the DSM-IV criteria for the diagnosis of PTSD (American Psychiatric Association, 2000). The dichotomization "yes/no" for the presence of PTS symptoms was performed according to the PTS scale evaluation method (Foa et al., 1993), as done in previous publications where Foa et al.'s PTS scale was used (Chung et al., 2007, 2008; Guler et al., 2009; Von Kanel et al., 2011). The presence of PTS symptoms was defined if all the criteria (A, B, C, D, and E) were fulfilled. A-criterion was fulfilled in case of an exposure to an extreme stressor, such as "being diagnosed with a life-threatening illness." Response choices were "Not at all or once in the last month," "Once a week or more rarely/sometimes," "2–4 times a week/often," and "5 and more times a week/almost always," scored from 1 to 4. For each question, a score of 3 or 4 was coded as a positive symptom. B-criterion was fulfilled if at least one symptom of re-experiencing the traumatic event was present. The C-criterion was fulfilled if three or more avoidance/numbing symptoms were consistently endorsed. The D-criterion was fulfilled if at least two symptoms of increased arousal were reported. In order to fulfill the E-criterion, disturbance duration had to be more than 1 month. Cronbach's alpha for re-experience scale was 0.744, for avoidance 0.783, and for arousal 0.703 in the present sample.

Statistical analyses

We used the SPSS 22.0 statistical software package for statistical analysis. We presented baseline categorical variables as frequencies and continuous variables as mean and standard deviation. We calculated crude odds ratios (OR) and their 95 percent confidence intervals (CIs) of the association between psychological factors and PTS symptoms. A two-sided p-value < 0.05 was considered significant. To assess the quality of fear of dying to predict PTS symptoms, we computed sensitivity, specificity, and predictive values with their associated 95 percent CIs. All collected variables were available without missing values.

Results

Patient characteristics

Participants were primarily male ($n = 73$, 81.1%) with a mean age of 61.21 ± 9.0 years. In all, 40.0 percent ($n = 36$) patients were diagnosed with unstable angina, 43.3 percent ($n = 39$) patients with ST-segment elevation MI, and 16.7 percent ($n = 15$) patients with non ST-segment elevation MI.

PTS symptoms

The prevalence of PTS symptoms 1 month after the ACS in the present sample was 26.7 percent ($n = 24$). Participants who screened positive for PTS symptoms did not differ from those who screened negative on gender, age, revascularization treatment option, employment, education level, marital status, and income (Table 1).

Table 2 presents the OR of the associations between PTS symptoms and psychological and clinical variables. Fear of dying (OR: 3.74, 95% CI: 1.39–10.05), helplessness (OR: 4.50, 95%

Table 1. Sociodemographic and clinical characteristics according to the presence of posttraumatic stress symptoms ($N = 90$).

Variables	Total population	PTS symptoms present ($n = 24$)	PTS symptoms absent ($n = 66$)	*p*-value
	n (%)	*n* (%)	*n* (%)	
Age (mean ± SD)	61.21 ± 9.0	62.67 ± 9.47	60.68 ± 8.84	0.277
⩽65 years	57 (63.3)	13 (54.2)	44 (66.7)	
>65 years	33 (36.7)	11 (45.8)	22 (33.3)	
Women	17 (18.9)	6 (25.0)	11 (16.7)	0.372
Revascularization treatment				
PCI	59 (65.6)	13 (54.2)	46 (69.8)	0.286
CABG	14 (15.5)	4 (16.6)	10 (15.1)	
Conservative	17 (18.9)	7 (29.2)	10 (15.1)	
Self-reported working status				
Working (full/part time)	45 (50)	8 (33.3)	37 (56.1)	0.057
No employment/retired	45 (50)	16 (66.7)	29 (43.9)	
Self-reported education status				
University graduation	26 (28.9)	9 (37.5)	17 (25.8)	0.277
Others (vocational school or lower, high school graduation)	64 (71.1)	15 (62.5)	49 (74.2)	
Self-reported marital status				
Married/partnership	77 (85.6)	20 (83.3)	57 (86.4)	0.718
Single/divorced/widow	13 (14.4)	4 (16.7)	9 (13.6)	
Self-reported income per person				
High	25 (27.8)	4 (16.7)	21 (31.8)	0.156
Low	65 (72.2)	20 (83.3)	45 (68.2)	

PTS: posttraumatic stress; PCI: percutaneous coronary intervention; CABG: coronary artery bypass graft; SD: standard deviation.

CI: 1.63–12.43), and avoidance-focused coping strategy (OR: 4.33, 95% CI: 1.52–12.34) during the hospitalization predicted the presence of PTS symptoms. Problem-focused and acceptance-focused coping showed a potentially protective effect against PTS symptoms (OR: 0.41, 95% CI: 0.15–1.12; OR: 0.71, 95% CI: 0.28–1.84, respectively).

Table 3 presents the number of patients who indicated the presence or absence of fear of dying, as well as the presence or absence of PTS symptoms. Fear of dying, as a screening question to predict later PTS symptoms, had a sensitivity of 66.7 percent (95% CI: 44.7–84.4) and a specificity of 65.2 percent (95% CI: 52.4–76.5). Its positive predictive value (PPV) was 41.0 percent, (95% CI: 25.6–57.9) and its negative predictive value (NPV) was 84.3 percent (95% CI: 71.4–93.0).

Discussion

We conducted this study among ACS survivors investigating the presence of PTS symptoms 1 month after the hospitalization and found that 26.7 percent of patients with ACS developed PTS symptoms. We found that feeling fear of dying, feeling of helplessness, severe anxiety, and avoidance-focused coping predicted the occurrence of PTS symptoms 1 month after ACS, whereas pain severity, dyspnea, depression, gender, age, revascularization treatment type, employment, education level, marital status, and income level did not. Those who felt

Table 2. Associations between psychological and clinical characteristics and posttraumatic stress symptoms.

Variables	Total population	PTS symptoms present ($n=24$)	PTS symptoms absent ($n=66$)	OR (95% CI)
	n (%)	*n* (%)	*n* (%)	
Feeling fear of dying	39 (43.3)	16 (66.7)	23 (34.8)	3.74*; 1.39–10.05
Chest pain intensity (score > 4)	61 (67.8)	15 (62.5)	46 (69.7)	0.73; 0.27–1.93
Feeling of helplessness	24 (26.7)	12 (50.0)	12 (18.2)	4.50*; 1.63–12.43
Feeling dyspnea	38 (42.2)	12 (50.0)	26 (39.4)	1.54; 0.60–3.94
Inaugural chest pain (>1 year)	35 (38.9)	13 (54.2)	22 (33.3)	2.36; 0.91–6.13
Acceptance-focused coping	43 (47.8)	10 (41.7)	33 (50.0)	0.71; 0.28–1.84
Problem-focused coping	40 (44.4)	7 (29.2)	33 (50.0)	0.41; 0.15–1.12
Emotion-focused coping	44 (48.9)	13 (54.2)	31 (47.0)	1.33; 0.52–3.41
Avoidance-focused coping	45 (50.0)	18 (75.0)	27 (40.9)	4.33;* 1.52–12.34
Anxiety status				
No	62 (68.9)	10 (41.7)	52 (78.8)	
Probable	19 (21.1)	8 (33.3)	11 (16.7)	3.78; 1.22–11.76
Severe	9 (10)	6 (25.0)	3 (4.5)	10.4*; 2.22–48.62
Depression status				
No	66 (73.3)	17 (70.8)	49 (74.2)	
Probable	19 (21.1)	6 (25.0)	13 (19.7)	1.33; 0.44–4.05
Severe	5 (5.6)	1 (4.2)	4 (6.1)	0.72; 0.075–6.90

OR: odds ratio; CI: confidence interval.
*$p < 0.01$.

Table 3. Number of patients with or without fear of dying, as well as with or without PTS symptoms.

	PTS symptoms present	PTS symptoms absent	Total
Fear of dying present	16	23	39
Fear of dying absent	8	43	51
	24	66	

CI: confidence interval; PPV: positive predictive value; NPV: negative predictive value.
Sensitivity: 66.7%; 95% CI: 44.7–84.4.
Specificity: 65.2%; 95% CI: 52.4–76.5.
PPV: 41.0%; 95% CI: 25.6–57.9.
NPV: 84.3%; 95% CI: 71.4–93.0.

fear of dying had significantly more anxiety and avoidance-focused coping strategies (data not shown in the tables).

Previous studies reported a prevalence of PTSD between 9.4 percent and 27 percent after ACS (Bedi and Arora, 2007; Bluvstein et al., 2013; Edmondson et al., 2011; Ginzburg, 2006; Guler et al., 2009; Shemesh et al., 2006; Spindler and Pedersen, 2005; Von Kanel et al., 2011; Whitehead et al., 2006; Wikman et al., 2008). According to the DSM-IV definition, PTSD has to occur after a traumatic event or life-threatening illness (Gander and Von Kanel, 2006). Regarding this last point, assessing the fear of dying in patients hospitalized for an ACS, which is life-threatening disease, might

be relevant for the diagnosis of PTSD. Fear of dying, feeling of helplessness, and anxiety (Chung et al., 2007; Guler et al., 2009; Whitehead et al., 2006) are important factors in development of PTSD, whereas demographic factors are probably not (Edmondson et al., 2012; Whitehead et al., 2006). In the specific context of ACS, the fear of dying has been associated with marked inflammatory process: reduced cortisol secretion, increased plasma tumor necrosis factor alpha (TNFα), and reduced heart rate variability (Steptoe et al., 2011). In addition to the biological process of inflammation reported in patients with ACS and feeling fear of dying, other neurobiological mechanisms have been described, such as hyperactivity in the hypothalamic–pituitary–adrenal axis and adrenergic hypersensitivity in the development of PTSD (Yehuda, 2002). Moreover, some genetic traits implicated in the dopaminergic and serotonergic neurotransmission have also been observed in patients with PTSD (Stein et al., 2002). Those observations suggest that some subjects are more prone to develop PTSD, and the occurrence of a life-threatening acute event, such as ACS, might contribute to the development of definitive PTSD.

The development of PTSD after ACS is associated with major cardiovascular (CV) events and increased all-cause mortality (Edmondson et al., 2011; Gamper et al., 2004). Other psychological disorders, such as anxiety and/or depression (Ginzburg, 2006), are also common among patients who experienced ACS. In a meta-analysis of 20 studies and 249,846 subjects with a mean follow-up of 11.2 years, anxiety was an independent risk factor for incident CVD and cardiac mortality (Roest et al., 2010). Among women with coronary artery disease, anxiety correlated with cardiac symptom indicators (night-time angina, nitroglycerin use, shortness of breath, and angina frequency) and higher CVD-related healthcare costs during a 5-year follow-up period (Rutledge et al., 2013). Coping with the illness of ACS is a long-term and complicated dynamic process of dealing with varied emotions that remain understudied (Kristofferzon et al., 2005; Nilsson et al., 2013; Salminen-Tuomaala et al., 2012). Coping responses may be broadened into two components: (1) adaptive (problem-focused and acceptance-focused) and (2) maladaptive (emotion-focused and avoidance-focused) (Lowe et al., 2000). The maladaptive component has been previously associated with PTS symptoms in the context of ACS (Chung et al., 2008; Son et al., 2012).

Our study showed that fear of dying was associated with helplessness, anxiety, and development of PTS symptoms. In addition, we also observed that those patients had more difficulties in coping with an acute stressor event. Avoidance-focused coping was associated with the development of PTS symptoms 1 month after ACS, as well as with fear of dying and helplessness (data not shown in the tables). This last point is important, as assessing the fear of dying might be a pragmatic bedside approach to identify patients at higher risk of developing PTSD and propose an intervention focusing on their coping capacities. Recent ESC guidelines acknowledge the importance of psychosocial risk factors in the development of CVD and also their contribution in the worse clinical prognosis, but there is still limited evidence that routine screening for psychosocial risk factors might contribute to fewer cardiac events and translate into improved healthcare (Perk et al., 2012).

We found that NPV of fear of dying as a screening question for later PTS symptoms was high (Table 3), indicating that patients who had no fear of dying are probably not going to develop PTS symptoms. Since most patients indicate no fear of dying, asking about fear of dying is a relatively effective strategy.

Our study has some limitations. First, in this prospective observational study, we have a relatively small sample size, although we found statistically significant results. We did not evaluate some potential cofounder, such as traditional CV risk factors and the attendance to cardiac rehabilitation. We did not assess objective measures of ACS severity (number of treated vessels, heart failure, and size of MI); however, in previous studies, those factors were not significant

predictors of PTSD (Edmondson et al., 2012; Guler et al., 2009; Whitehead et al., 2006). We assessed PTS symptoms and did not confirm the diagnosis of PTSD with an external expert, such as psychiatrist. Therefore, we cannot exclude some possible misclassification of the outcome, but our observations were in concordance with previous studies. And finally, our findings cannot be generalized to other settings.

The association between feeling fear of dying and the development of PTSD is a clinically important factor. Assessing the fear of dying at hospital using a simple question might be a pragmatic approach to identify patients at high risk of developing PTSD. In the future, interventions axed on improving coping strategies should be examined in randomized controlled studies with adapted sample size. PTSD has been proven to influence the prognosis after ACS (Edmondson et al., 2011; Von Kanel et al., 2011) and the control of CV risk factors (Edmondson et al., 2012; Shemesh et al., 2006). Recognizing and preventing the development of PTSD should be integrated in the secondary prevention measures after ACS as other traditional CV risk factors. In this context, the impact of hospital-based psychological support intervention with a continuum in cardiac rehabilitation or outpatient setting should be investigated in patients with ACS.

Conclusion

In conclusion, PTS symptoms are highly prevalent among the ACS survivors. Psychological factors related to subjective ACS experience (fear of dying, feeling of helplessness), anxiety, and avoidance-focused coping with the extremely stressful life situations strategies influenced the development of PTS symptoms. Patients who did not present fear of dying tended not to develop PTS symptoms; therefore, detecting the fear of dying during hospitalization might be a simple approach to identify patients at risk of PTSD and propose a support to manage anxiety and coping strategies. Further studies are needed to assess the impact of interventions based on improving coping strategies in those patients.

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