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ARTYKUŁ ORYGINALNY / *ORIGINAL ARTICLE*

Association between anxiety and depression in patients with acute coronary syndromes due to financial crisis

Kostandinos Lampropoulos, Charalampos Kavvouras, Aikaterini Megalou, Pinelopi Tsikouri, Chrysanthi Kafkala, Dimitra Derka, Maria Bonou, John Barbetseas

Evagelismos General Hospital, Athens, Greece

Abstract

Background: The effect of anxiety and depression on patients with acute coronary syndromes (ACS) warrants investigation, especially during periods of economic crisis.

Aim: To investigate the relation between anxiety and depression in patients presenting with ACS due to financial crisis and to investigate whether these two entities could predict long-term cardiovascular mortality.

Methods and results: Anxiety and depression symptoms were assessed in 350 patients (210 men) presenting with ACS, with 70 (20%) patients showing elevated scores (Hellenic Heart Failure Protocol). Over a mean follow-up of 48 months there were 36 (10%) cardiovascular deaths. Cox proportional hazards models adjusted for other prognostic factors (including age, sex, marital status, creatinine levels, left ventricular ejection fraction, heart failure, atrial fibrillation, previous hospitalisation, and baseline medications) showed that elevated anxiety and depression scores significantly predicted cardiovascular mortality (primary outcome) and all-cause mortality.

Conclusions: Elevated anxiety and depression symptoms are related to cardiovascular mortality due probably to financial crisis, even after adjustment for other prognostic indicators in patients with ACS, who received optimised medical treatment.

Key words: anxiety, depression, acute coronary syndromes

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INTRODUCTION

The World Health Organisation ranks major depression as one of the most burdensome diseases in the world [1]. Authors of previous studies have shown that depression in patients with acute coronary syndrome (ACS) increases the risk of hospitalisation and mortality [2]. There may be some pathophysiological pathways and/or behaviour by which depression affects cardiovascular outcomes in patients with ischaemic heart disease.

Patients with prior ACS frequently report symptoms of anxiety and depression during the preceding months [3]. Both anxiety and depression are negative emotions that occur in response to perceived threats. Depressive symptoms can be defined as symptoms of anhedonia, accompanied by negative physical symptoms related to activity, appetite, and sleep, negative cognitive symptoms related to the ability to concentrate, and pessimism about the future. Depressive symptoms may exist with or without the presence of clinical depression. It is also well known that neurohormonal stress is highly associated with the symptoms of depression and anxiety and further regulates the blood pressure, the heart rate, and the circulating catecholamine levels, which in turn may promote a major cardiovascular event [4]. Beside that, depression is highly associated with poor adherence to cardiac rehabilitation, which may lead to a less optimal recovery and worsened prognosis. In addition, depression is an independent risk factor for future events [5]. Anxiety in patients with a recent ACS and its association with prognosis has been studied less than depression [6].

The purpose of our study was to investigate the association of self-reported symptoms of anxiety and depression with the risk of ACS, taking into account a large number of estab-

Address for correspondence:
Charalampos Kavvouras, MD, PhD, Evagelismos General Hospital, Marasli 8, Athina 106 76, Athens, Greece, e-mail: kavourasch@yahoo.gr

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lished cardiovascular risk factors. An unusual feature of the relationship between depression and coronary heart disease appears to be a difference between those patients who are depressed before the occurrence of an ACS and those who will develop depressive symptoms after the ACS. There is strong evidence that indicates an association of mortality and recurrent cardiac events in patients with new-onset depression, after having ACS.

METHODS

Between April 2011 and January 2013, among 400 patients who presented with ACS (STEMI, NSTEMI, unstable angina), 200 patients reported symptoms of anxiety and depression prior to the acute coronary event. Inclusion criteria were: known coronary heart disease, history of atrial fibrillation (AF), left ventricular ejection fraction (LVEF) < 50%, and history of symptomatic congestive heart failure (HF). Patients were excluded if they had cognitive difficulties or were expected to live less than one year, had LVEF < 20%, serious chronic obstructive pulmonary disease, renal failure requiring haemodialysis, or were scheduled for a coronary artery bypass surgery.

The treatment of ACS included: coronary angiography, dual antiplatelet therapy, anticoagulants, maximum tolerable dose of beta-blockers and angiotensin-converting enzyme inhibitors, or angiotensin-receptor antagonists, and spironolactone if needed.

Psychiatric assessment

Anxiety and depression measurement. All the participants who reported symptoms of anxiety and depression were interviewed. Initially we used the SF-36 to evaluate the quality of life. The SF-36 is a short-form health survey with 36 questions, which has been used widely for patients with cardiovascular disease. It includes one multi-item scale that assesses eight health concepts: physical function (PF), role physical (RP), bodily pain (BP), general health (GH), vitality (VT), social function (SF), role-emotional (RE), and mental health (MH).

We evaluate anxiety symptoms using a Greek version of the State-Trait Anxiety Inventory (STAI). The STAI comprises two separate self-report scales, each containing 20 questions, one of which asks how the patients 'currently feel' (state anxiety) and one how they 'generally feel' (trait anxiety). The total score on both subscales ranges from 20 to 80, with higher scores indicating greater levels of anxiety. Scores of more than 40 on either subscale were used to indicate significant symptoms of anxiety [7, 8]. There is evidence that the reliability and the validity of the Greek translation of the STAI questionnaire is generally similar to those reported in the international literature [9].

Finally, we used a Greek version of the Zung self-rating depression scale (ZDRS), which uses 20 questions to evaluate emotional and psychological symptoms [10]. We further assessed antidepressant therapy (tricyclic antidepressants, monoamine oxidase inhibitors, selective serotonin reuptake inhibitors, or other antidepressants [amoxapine, trazodone, venlafaxine, maprotiline, mirtazapine, nefazodone, bupropion]) at index hospitalisation (angiography), at subsequent hospitalisation(s). Beside the Zung questionnaire, we used patient interviews to collect information on age, sex, race/ethnicity, marital status, and education level. Chart reviews were used to collect information on smoking status, ejection fraction, and medications. Height and weight were measured during the baseline visit.

Outcome measurement. The mean follow-up period for all the patients was 48 ± 12 months (range 24–60 months for survivors). Clinical variables and data on hospitalisation and cardiac events were assessed at follow-up visits at 6 weeks and 18 weeks. Thereafter, patients were seen every 12 months through four years. As in the overall study, the primary outcome for the present analyses was cardiovascular death and all-cause mortality.

Data analysis

We used Cox proportional hazard models to examine the associations of symptoms of depression and anxiety with subsequent risk for ACS and hazard ratios with 95% confidence intervals. Analyses were performed with SPSS 20.0 for Windows (SPSS Inc., Chicago, Ill.). Statistical tests were two-tailed, with $p < 0.05$ considered significant.

After proportionality assumptions were verified, Cox proportional hazards regression analyses were used to assess the prognostic importance of elevated depression symptoms both before and after covariate adjustment for the primary outcome (cardiovascular mortality) and for the two secondary outcomes (all-cause mortality)

RESULTS

Of the 200 patients interviewed, 125 (62%) were hospitalised with their first episode of ACS (STEMI, NSTEMI) and 20 (10%) with their first episode of unstable angina. Participants were 60 ± 11 years of age (range 39–84 years), and 43.7% were women. Overall, 100 (50%) patients had ZDRS scores of 45–59, 60 patients had scores of 60–69, and 40 patients had scores above 70.

The median follow-up was 48 months (700–1300 days). During these days the following events occurred among 200 patients who completed the study: four cardiovascular deaths, five new ACS requiring revascularisation, and two stroke.

Background characteristics of patients with and without elevated anxiety and depression symptoms appear in Table 1.

The mean ZDRS score before ACS was 45.21 ± 9.44, while this score showed a sharp increase to 59.68 ± 9.43, 48 months after the ACS ($p = 0.001$). Similarly, mean STAI-state and STAI-trait scores before ACS were 42.15 ± 8.39 and 40.12 ± 5.92, respectively, showing a steady increase to 46.54 ± 9.03 and 44.74 ± 11.03, respectively, 48 months

Table 1. Baseline characteristics, acute phase management, and medical treatments at discharge, grouped according to the depression status over a 48-month follow-up after acute coronary syndrome

General characteristics	Patients without depression	Patients with depression
Male sex	6.4%	16%
Age [years]	52 ± 18	60 ± 11
Education [%]	60%	40%
Married	69%	52%
Divorced	20%	29%
Diabetes mellitus	52%	56%
Hypertension	62%	72%
Left ventricular ejection fraction	50%	50%
Hospitalisation within 6 months prior to randomisation	45%	65%
Atrial fibrillation	12%	19%
Beta-blockers	95%	92%
Nitrates	88%	79%
DAPT	100%	98%
ACE/ARB	100%	95%
Lipid-lowering drugs	95%	85%

ACE/ARB — angiotensin converting enzyme/angiotensin-receptor blockers; DAPT — dual antiplatelet therapy

after the ACS ($p = 0.003$). On the other hand, mean SF-36 total score before ACS was 55.17 ± 10.09 instead of 48.05 ± 12.1, 48 months after the ACS, showing a sharp decrease ($p = 0.003$).

Based on our study, approximately one of two patients hospitalised for ACS had at least mild-to-moderate symptoms of depression ZDRS score from 45 to 90.

Participants with elevated depression symptoms ZDRS score > 45 were significantly more likely to be males, to be divorced, to have lower levels of education (9.8 vs. 13.5, $p < 0.001$), and to earn less than 6000 euros per year, than those with lower levels of depression. They were more likely to have been hospitalised for previous ACS or decompensated HF in the 12 months before randomisation, and to have paroxysmal AF events. There were no differences in hypertension, diabetes mellitus, body mass index (BMI), creatinine level, LVEF, or concomitant medical therapies at baseline.

The mean ZDRS score for the entire sample was 51 ± 8.7, and 20% of the sample (n = 200) had clinically significant depressive symptoms. Eighty-four of the patients with depressive symptoms were taking antidepressants. Patients with depressive symptoms had higher total comorbidity score (3.5 vs. 2.9, $p < 0.001$) compared to patients who had no depressive symptoms. Besides that, higher proportions of patients with depressive symptoms were minorities (25% vs. 39%, $p < 0.001$). Participants with depression had a history of myocardial infarction (74% vs. 33%, $p = 0.001$) or HF (22% vs. 11%, $p < 0.004$).

Patients with anxiety were more likely to be younger (50 vs. 64, $p < 0.002$), had a higher average BMI (34 vs. 31, $p = 0.003$), and higher total comorbidity score (3.9 vs. 2.4, $p < 0.001$) compared to patients who were not anxious. Among patients who were anxious, there were higher proportions of women (48% vs. 18%, $p < 0.001$).

Covariate adjustment made little difference in the hazard ratios for the links between anxiety, depression and cardiovascular mortality or between depression and either of the secondary outcomes (all-cause mortality). After adjustment for other baseline factors, elevated depression symptoms predicted a 42.7% increase in the hazard ratio for cardiovascular death. Table 2 shows the multivariable model for time to cardiovascular death.

DISCUSSION

The main findings in our study are that (a) depression and anxiety and quality of life as they were assumed from ZDRS, STAI-trait, and SF-36 questionnaires, at baseline and 48 months after the ACS, differ statistically significantly, (b) anxiety and depression as it was depicted in STAI-trait questionnaire and Zung self-rating depression scale respectively were independent predictors of a major advance cardiac event (MACE) after ACS, and (c) quality of life, depression, and anxiety symptoms in patients 48 months after the acute coronary event were more pronounced.

Several studies have tried to investigate the relationship between psychological variables and ischaemic heart

Table 2. Multivariable model for hazard ratio for cardiovascular death

Baseline characteristic	HR (95% CI)	P
At least mild to moderate depression not depressed	1.57 (1.20–2.07)	0.001
Age (per SD increase)	1.15 (0.98–1.34)	0.09
Married	0.76 (0.58–0.99)	0.04
Creatinine level (per SD increase in mol/L)	1.36 (1.22–1.52)	0.001
Ischaemic cause of CHF	1.77 (1.29–2.43)	0.001
Left ventricular ejection fraction	0.91 (0.80–1.04)	0.16
Previous hospitalisation for AF	0.79 (0.60–1.04)	0.10
NYHA class > II	1.08 (0.81–1.45)	0.59
Beta-blockers at baseline	0.74 (0.54–0.99)	0.05
Nitrates at baseline	1.18 (0.85–1.64)	0.31
ACE inhibitors at baseline	0.83 (0.59–1.16)	0.28
Oral anticoagulants at baseline	0.62 (0.43–0.91)	0.01
Lipid-lowering drugs at baseline	0.89 (0.66–1.19)	0.42

ACE — angiotensin converting enzyme; CHF — congestive heart failure; CI — confidence interval; HR — hazard ratio; NYHA — New York Heart Association

disease [11]. Patients diagnosed with ACS have more psychological distress than healthy individuals. It also seems that patients with symptoms of ischaemic heart disease have diminished quality of life and correlate with psychological distress in the form of depression and anxiety [12]. It is well known that anger and tension are well recognised as risk factors for acute coronary events especially in males [13]. Another study [14] revealed that postoperative anxiety was associated with an increased likelihood of death after coronary artery bypass grafting. Lange et al. [15] concluded that depression is a major risk factor for recurrence of AF after electrical cardioversion in patients with persistent AF. Similarly, in our study both anxiety and depression were independent predictors of cardiovascular death. In the Finmonica MI Register Study held in Finland, low-income status was associated with excess mortality rate after an ACS [16, 17]. Similar findings have been reported in Canada and Taiwan [18, 19]. It seems that low income may affect health status because such patients are prone to unhealthy behaviour patterns, including smoking and alcohol consumption.

Despite the fact that it remains unclear how the acute psychological disturbances lead to an acute coronary event, some possible mechanisms have been proposed. Psychological stress may lead to exaggerated cardiovascular responses as well as to enhanced platelet aggregation, coronary vasoconstriction, myocardial ischaemia, arrhythmias, and plaque rupture — all components of the pathogenic processes contributing to cardiac morbidity and mortality maintenance of arrhythmias, which may have a role for MACE [20–22]. Atherosclerosis may facilitate depressive symptoms even before ischaemia, creating a spurious association between depression and atherosclerosis. One possible pathway is the depressogenic action of the increased inflammatory activity [23, 24].

There are data suggesting that people with both depression and anxiety have higher levels of inflammatory markers (TNF-A, intereukin-6, and C-reactive protein) [25, 26]. Bjerkeset et al. [27], in a large sample from a normal population, found that the association of C-reactive protein and depression was influenced by confounding factors such as chronic illness, smoking, and BMI > 30, because the odds ratio was reduced from 1.28 to 1.08 by controlling these factors.

Limitations of the study

This study is a prospective, non-randomised study that evaluated and compared the role of anxiety and depression before and after an acute coronary event. The results are derived from a small sample size, and therefore larger trials are needed in order to confirm our study's results. Furthermore, there are several limitations caused by estimating quality of life improvement.

CONCLUSIONS

In conclusion, anxiety and depression in a period of financial crisis seems to be an independent predictor of poor outcome of patients after an ACS.

Conflict of interest: *none declared*

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Wpływ lęku i depresji spowodowanych kryzysem finansowym na rokowanie u chorych z ostrymi zespołami wieńcowymi

Kostandinos Lampropoulos, Charalampos Kavvouras, Aikaterini Megalou, Pinelopi Tsikouri, Chrysanthi Kafkala, Dimitra Derka, Maria Bonou, John Barbetseas

Evagelismos General Hospital, Athens, Grecja

Streszczenie

Wstęp: Wpływ lęku i depresji na chorych z ostrymi zespołami wieńcowymi (ACS) stanowi zagadnienie warte przeanalizowania, zwłaszcza w okresach kryzysów ekonomicznych.

Cel: Badanie przeprowadzono w celu oceny oddziaływania lęku i depresji z powodu kryzysu finansowego u chorych z ACS oraz zbadanie, czy te dwa zaburzenia mogą być przydatne w prognozowaniu odległej śmiertelności sercowo-naczyniowej.

Metody i wyniki: Objawy lęku i depresji oceniano u 350 chorych (210 mężczyzn), u których rozpoznano ACS. U 70 (20%) pacjentów stwierdzono podwyższone wskaźniki tych zaburzeń (*Hellenic Heart Failure Protocol*). Po okresie średnio 48-miesięcznej obserwacji odnotowano 36 (10%) zgonów z przyczyn sercowo-naczyniowych. Analiza z zastosowaniem modelu proporcjonalnego hazardu Coxa, skorygowanego względem czynników prognostycznych (w tym wieku, płci, stanu cywilnego, stężenia kreatyniny, frakcji wyrzutowej lewej komory, niewydolności serca, migotania przedsionków, wcześniejszej hospitalizacji i podstawowego leczenia farmakologicznego), wykazała, że podwyższone wskaźniki lęku i depresji miały istotne znaczenie w prognozowaniu ryzyka zgonu sercowo-naczyniowego (główny punkt końcowy) i zgonu z jakiejkolwiek przyczyny.

Wnioski: Nasilone objawy lęku i depresji z powodu kryzysu finansowego u chorych z ACS, którym zapewniono optymalną opiekę medyczną, korelują ze śmiertelnością sercowo-naczyniową nawet po skorygowaniu względem innych czynników prognostycznych.

Słowa kluczowe: lęk, depresja, ostre zespoły wieńcowe

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Adres do korespondencji:
Charalampos Kavvouras, MD, PhD, Evagelismos General Hospital, Marasli 8, Athina 106 76, Athens, Greece, e-mail: kavourasch@yahoo.gr
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