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Clinically significant ventricular arrhythmias and progression of depression and anxiety following an acute coronary syndrome

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ABSTRACT

Background: Depression and anxiety are common and associated with worse clinical outcomes in patients who experience an acute coronary syndrome (ACS). We investigated the association between major ventricular arrhythmias (VAs) with the progression of depression and anxiety among hospital survivors of an ACS.
Methods: Patients were interviewed in hospital and by telephone up to 12 months after hospital discharge. The primary outcome was the presence of moderate/severe symptoms of depression and anxiety defined as a Patient Health Questionnaire (PHQ)-9 score ≥ 10 and a Generalized Anxiety Disorder (GAD)-7 score ≥ 10 at baseline and 1 month and PHQ-2 ≥ 3 and GAD-2 ≥ 3 at 3, 6, and 12 months. We used marginal models to examine the association between major VAs and the symptoms of depression or anxiety over time.
Results: The average age of the study population (n = 2074) was 61.1 years, 33.5% were women, and 78.3% were white. VAs developed in 105 patients (5.1%). Symptoms of depression and anxiety were present in 22.2% and 23.5% of patients at baseline, respectively, and declined to 14.1% and 12.6%, respectively, at 1-month post-discharge. VAs were not significantly associated with the progression of symptoms of depression (adjusted relative risk [aRR] = 1.29, 95% confidence interval [CI] = 0.94–1.77) and anxiety (aRR = 1.22, 95% CI = 0.86–1.72), or with change in average scores of PHQ-2 and GAD-2 over time, both before and after risk adjustment.
Conclusion: The prevalence of symptoms of depression and anxiety was high after an ACS but declined thereafter and may not be associated with the occurrence of major in-hospital VAs.

1. Introduction

Among patients with an acute coronary syndrome (ACS), the co-existence of anxiety and depression is prevalent, with upwards of one quarter to one half of patients reporting symptoms of either condition [1–3]. These psychosocial disorders are highly interrelated, with co-existence in up to 80% of patients [4,5], and may be long-lasting in patients after an ACS [6,7]. Both depression and anxiety are associated with higher all-cause death rates, recurrent coronary events, and impaired quality of life [2,8–13]. However, these conditions are often undiagnosed and/or under-treated in patients hospitalized for an ACS, and have been called for greater recognition and attention by the American Heart Association [14].

The development of clinically significant ventricular arrhythmias, including ventricular tachycardia (VT), ventricular fibrillation (VF), or cardiac arrest after an ACS may lead to additional stress and fear in patients, which may worsen the symptoms of depression or anxiety. However, the impact of these life-threatening cardiac arrhythmias on the long-term progression of depression and anxiety among patients surviving an ACS has not been studied.

Using data from a large and sociodemographically diverse population of patients discharged from the hospital after an ACS, we describe the 12-month progression of symptoms of depression and anxiety, and the impact of the in-hospital occurrence of clinically significant ventricular arrhythmias, on the progression of symptoms of depression and anxiety over a one-year follow-up period.

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2. Methods

2.1. Study design and population

We used data from the Transitions, Risks, and Action in Coronary Events – Center for Outcomes Research and Education (TRACE-CORE) study for this investigation [15]. In brief, TRACE-CORE is a multicenter prospective cohort study which included adult men and women hospitalized with an ACS at three tertiary care and community medical centers in Worcester, MA, two hospitals in Atlanta, GA, and one hospital in Macon, GA, between April 2011 and May 2013. Each validated episode of an ACS was categorized as either an ST-segment elevation acute myocardial infarction (STEMI), a Non ST-segment elevation myocardial infarction (NSTEMI), or as unstable angina (UA) [15]. IRB approval was obtained from all participating sites and study subjects provided written informed consent.

Trained study staff collected a wide range of patient sociodemographic, lifestyle, and psychosocial characteristics at baseline (in-person hospital interview) and at 1, 3, 6, and 12 months after discharge (via phone interview). We also collected information about patient's clinical presentation, laboratory test results, and their receipt of cardiac medications and coronary reperfusion therapy from hospital electronic medical records [15].

2.2. Measurement of symptoms of anxiety and depression

The symptoms of anxiety and depression were assessed by the validated 7-item Generalized Anxiety Disorder (GAD)-7 questionnaire, with a range of scores from 0 to 21 [16], and 9-item Patient Health Questionnaire (PHQ)-9 [17], score range [0–29], at baseline and the first month post discharge, and by shorter versions, GAD-2 (score range [0–6]) [18] and PHQ-2 (score range [0–6]) [19], at 3, 6, and 12 months post discharge to reduce the burden on study participants. Both the GAD and PHQ assess symptoms of anxiety and depression during the prior 2 weeks. These questionnaires were administered in person during the first 2–3 days of the patient's index hospitalization (baseline interview) and by telephone interview at 1, 3, 6, and 12 months after hospital discharge. Due to its clinical significance, we chose the primary study outcome as the presence of moderate/severe symptoms of depression or anxiety. These were defined as scores of PHQ-9 $\geq$ 10 or PHQ-2 $\geq$ 3 for moderate/severe depression and GAD-7 $\geq$ 10 or GAD-2 $\geq$ 3 for moderate/severe anxiety. These cutoffs have been previously validated in general patient populations and in those with coronary heart disease with sensitivities of > 90% and specificities of > 80% [18–21]. We also generated the PHQ-2 and GAD-2 from the first two questions of the PHQ-9 and GAD-7, respectively, at baseline and 1 month and used scores of PHQ-2 and GAD-2 as our secondary study outcomes at all post hospital discharge time points.

2.3. Clinically significant ventricular arrhythmias

In the present study, the occurrence of VT, VF, and cardiac arrest was based on physicians' progress notes. To reduce the possible misclassification of VT and VF due to the underreported occurrence of these arrhythmias in physicians' notes, the study research physicians also reviewed patients' ECG and telemetry strips in their hospital medical records. Ventricular tachycardia was defined as a cardiac arrhythmia of three or more consecutive complexes originating in the ventricles at a rate of > 100 beats per minute (cycle length < 600 milliseconds) [22]. Ventricular fibrillation was defined as a rapid, usually > 300 beats per minute (cycle length 200 millisecond or less), grossly irregular, ventricular rhythm with marked variability in QRS cycle length, morphology, and amplitude [22]. Cardiac arrest was defined as the sudden cessation of cardiac activity such that the victim became unresponsive without normal breathing or signs of circulation [23]. Patients were considered as having a life-threatening ventricular arrhythmia (VAs) if they developed either VT, VF, or cardiac arrest during their acute index hospital stay.

2.4. Other covariates

Comorbidity burden was calculated using the Charlson comorbidity index [24]. Severity of the acute coronary event was calculated by the GRACE-risk score which included data on age, heart rate, systolic blood pressure, Killip class, the presence of renal failure, ST-segment deviation, cardiac arrest, and serum levels of creatinine and troponin [25]. Information on additional important comorbidities, including hypertension, depression, and anxiety, which were not included in the Charlson index, was also collected. Cognitive function was measured using the Telephone Interview for Cognitive Status (TICS) [26]. Social support was measured by the 6-item Medical Outcomes Study Social Support Survey [27]. Pharmacotherapy for depression or anxiety included the receipt of serotonin reuptake inhibitors (SSRIs), serotonin–norepinephrine reuptake inhibitors (SNRIs) and oral benzodiazepines (including lorazepam, diazepam, clonazepam, alprazolam, clorazepate, oxazepam, chlordiazepoxide) as documented in medical records at the time of hospital discharge. Antiarrhythmic agents included disopyramide, flecainide, lidocaine, mexiletine, moricizine, phenytoin, procainamide, propafenone, quinidine, tocainide, amiodarone, bretylium, dofetilide, dronedarone, and sotalol. We also collected data on the hospital receipt of the following cardiac medications: aspirin, P2Y12 inhibitors (clopidogrel, prasugrel, ticagrelor, cangrelor), beta blockers, Angiotensin converting enzyme inhibitors/Angiotensin II receptor blockers (ACE-I/ARBs), and statins.

2.5. Statistical analysis

In the present study, we excluded 82 patients who died within 1 year after hospital discharge and 55 patients who had missing data on the symptoms of depression and anxiety at all examined post discharge time points. The final study sample consisted of 2074 patients with an independently confirmed ACS. Among the 2074 participants included in this prospective study, 327 (15.8%) dropped out after the baseline hospital interview. Of the 1747 patients who remained in the study, 886 (50.7%) had complete data at all follow-up time points (1, 3, 6, and 12 months post discharge) while 861 had data missing from at least one of the follow-up periods. In general, patients who had missing follow-up data were younger, were less likely to be white or married, and were less likely to have an advanced education or health insurance. They also were more likely to have reported worse symptoms of depression and anxiety at baseline. We imputed 30 datasets for each missing score of the PHQ-9, PHQ-2, GAD-7, and GAD-2 using multiple imputation by the chained equations method and predictive mean matching (PMM) models [28]. Information regarding differences in the baseline study characteristics and symptoms of depression or anxiety during follow up between patients who did and did not have further follow up data were used to predict the values of missing data in our multiple imputation models. The PMM assigned the score from a randomly chosen patient among 10 patients who had predictive scores that were most closely matched with the predictive score of a missing patient to that missing patient [29]. The PMM models have the advantage of generating imputed scores that have a similar distribution compared with observed scores, especially when the scores are discrete and bounded. All analyses were conducted in Stata 13.0.

We compared the distribution of various sociodemographic and clinical characteristics in patients who did and did not experience clinically significant VAs at the time of baseline study enrollment. We described changes over the 12-month follow up period in the prevalence of moderate/severe symptoms of depression and anxiety, and the mean scores of PHQ-2 and GAD-2 over time, overall, in patients

Table 1
Baseline characteristics of patients discharged from the hospital after an acute coronary syndrome according to the presence of clinically significant ventricular arrhythmia (VAs).

	VAs present (n = 105)	VAs absent (n = 1969)	*p-Value*
Age (mean, years)	58.8	61.2	< **0.001**
Women (%)	23.8	34.0	**0.031**
Race/ethnicity (%)			0.64
White	81.8	78.1	
Black	15.7	15.7	
Other	5.8	6.3	
Marital status (%)			0.29
Married/lived as married	60.0	58.8	
Separate/divorced/widowed	24.8	30.2	
Single/never married	15.2	11.1	
Educational attainment (%)			0.68
College graduate or higher	26.7	25.2	
Some technical school or college	26.7	29.0	
High school graduate	33.3	29.2	
Less than high school	13.3	16.6	
Insurance coverage (%)			0.54
Medicare plus private insurance	15.2	18.7	
Private insurance only	50.5	49.6	
Medicare only	13.3	13.2	
Medicaid	8.6	10.4	
Uninsured	12.4	8.1	
Unemployed/retired (%)	54.3	58.1	0.44
Social support (mean)	20.6	20.1	0.29
Disease impact scale (mean)	34.6	32.6	0.50
Cognitive function (mean)	32.2	31.7	0.21
Previously diagnosed (%)			
Anxiety	4.8	8.7	0.16
Depression	7.6	12.5	0.14
Hypertension	68.6	75.4	0.12
Charlson Comorbidity Index (mean)	2.7	3.3	**0.013**
Physiologic findings at admission (mean)			
Systolic blood pressure (mmHg)	135.5	142.4	**0.008**
Diastolic blood pressure (mmHg)	80.0	80.6	0.75
Heart rate (beat/min)	83.0	77.3	**0.002**
GRACE risk score	94.4	94.3	0.98
In hospital complications (%)			
Acute kidney injury	8.6	4.9	0.10
Heart failure/cardiogenic shock	8.6	2.1	< **0.001**
Atrial fibrillation/flutter	18.1	6.4	< **0.001**
ACS Type (%)	0.0	0.0	**0.003**
Unstable angina	18.1	32.1	
STEMI	27.6	17.5	
NSTEMI	54.3	50.4	
Reperfusion treatment received (%)			**0.004**
Medical treatment	8.6	20.6	
PCI	72.4	67.5	
CABG	19.0	11.8	
Medications at hospital discharge (%)			
Antiarrhythmic agents	34.3	9.4	< **0.001**
Aspirin	97.1	96.5	0.74
P2Y12 inhibitors	89.5	84.9	0.20
ACE-I/ARBs	64.8	61.8	0.54
Beta-blockers	97.1	89.3	**0.017**
Statins	88.6	86.8	0.61
SSRI/SNRIs	15.2	16.2	0.79
Benzodiazepines	41.0	29.1	**0.010**
Length of hospital stay (days)	6.0	4.9	0.70
30-day hospital readmission (%)	12.4	11.8	0.85

NSTEMI: non-ST-segment elevation myocardial infarction, STEMI: ST-segment elevation myocardial infarction, PCI: percutaneous coronary intervention, CABG: coronary artery bypass graft surgery, ACE-I/ARBs: Angiotensin converting enzyme inhibitor/Angiotensin receptor blockers, SSRI: selective serotonin reuptake inhibitors, SNRI: serotonin and norepinephrine reuptake inhibitors.
Benzodiazepines included lorazepam, diazepam, clonazepam, alprazolam, clorazepate, oxazepam, chlordiazepoxide.
The bold values indicate the statistical significance at $p < 0.05$.

with and without VAs, and in those without a history of depression or anxiety. We used generalized estimating equations (GEE) with a Poisson distribution, a log link, robust variance estimation, and exchangeable correlation structure to estimate the relationship between the VAs examined and progression of symptoms of depression and anxiety over the 12-month follow-up period [30,31]. The Charlson comorbidity index, GRACE-risk scores, and study sites were a priori included in all regression models. Other variables were tested in an iterative fashion and variables which materially changed the estimates by > 10% were retained in the final models. We also conducted an analysis in which patients with a history of depression or anxiety were excluded since the impact of VAs on the progression of depression or anxiety over time may differ among these patients.

3. Results

3.1. Baseline characteristics

The study population (n = 2074) was, on average, 61.1 years old, 33.5% were women, 78.3% were white, and 15.5% were black. A history of depression and anxiety were present in 255 patients (12.3%) and 177 patients (8.5%), respectively. Ventricular arrhythmias developed in 105 patients (5.1%); 21 patients experienced a cardiac arrest, 16 patients had VF, and 68 patients developed VT at any time during their acute hospitalization.

Compared with patients who did not develop VAs, patients who developed VAs were approximately 2 years younger on average, had a lower comorbidity burden as measured by the Charlson comorbidity index, were more likely to have developed heart failure, cardiogenic shock, or atrial fibrillation/flutter during hospitalization, were less likely to have been hospitalized for unstable angina, and were more likely to have undergone a PCI or coronary artery bypass graft surgery (CABG). These patients were more likely to have been treated with antiarrhythmic agents, beta-blockers, or benzodiazepines during their acute hospitalization than patients who did not develop VAs (Table 1).

3.2. Progression of symptoms of depression and anxiety over time

Depression and anxiety frequently coexisted, with 59.2% to 68.4% of patients who reported moderate/severe symptoms of depression also reported moderate/severe symptoms of anxiety at any given time point. Overall, moderate/severe symptoms of depression and anxiety were present in 22.2% and 23.5% of patients at baseline, respectively (Fig. 1, top panel). The prevalence of depression and anxiety rapidly declined to 14.1% and 12.6% at 1 month and remained relatively stable thereafter until the end of the 12-month follow-up period. Although the frequencies of moderate/severe symptoms of depression in patients with a history of depression (44.5%) and anxiety in patients with a history of anxiety (51.7%) were higher than among those without a history of depression (19.0%) or anxiety (20.9%), each of these patient groups experienced a rapid decrease in their symptoms of these conditions during the first month post discharge as did the overall patient population (Fig. 1, middle and bottom panels).

The prevalence of moderate/severe symptoms of depression and anxiety were slightly, but nonsignificantly, higher in patients with VAs compared with patients who did not develop VAs at baseline and during the first 3 months after hospital discharge; the frequencies of these conditions were relatively similar at 6 and 12 months post discharge (Fig. 2).

3.3. Association between VAs and progression of symptoms of depression and anxiety

Since differences in the frequency of moderate/severe symptoms of depression and anxiety were most notably observed in the first 3 months after hospital discharge, we compared the risk of reporting symptoms of depression and anxiety during the first 3 months after hospital discharge between patients who did and did not develop VAs during their acute hospitalization. After adjusting for study site, comorbidity burden, severity of the ACS episode, and the use of antiarrhythmic agents, the risk of developing symptoms of moderate/severe depression (adjusted Relative risk [aRR] = 1.29, 95% confidence interval [CI] = 0.94–1.77) and anxiety (aRR = 1.22, 95% CI = 0.86–1.72) during the first 3 months after hospital discharge was not associated with the in-hospital occurrence of VAs (Table 2). Similar findings were found for moderate/severe symptoms of depression (aRR = 1.41, 95% CI = 0.99–2.02) and anxiety (aRR = 1.34, 95% CI = 0.91–1.98) in our secondary sensitivity analysis when patients with a history of depression or anxiety were excluded.

When we examined changing trends in the symptoms of depression and anxiety in terms of absolute scores of the PHQ-2 and GAD-2, the average scores of depression and anxiety were similar between patients who did and did not develop VAs at all time points examined (Fig. 3). In regression models, both before and after adjusting for several potentially confounding factors, the presence of VAs was not associated with higher scores of symptoms of depression or anxiety during the first 3 months after hospital discharge (Table 3).

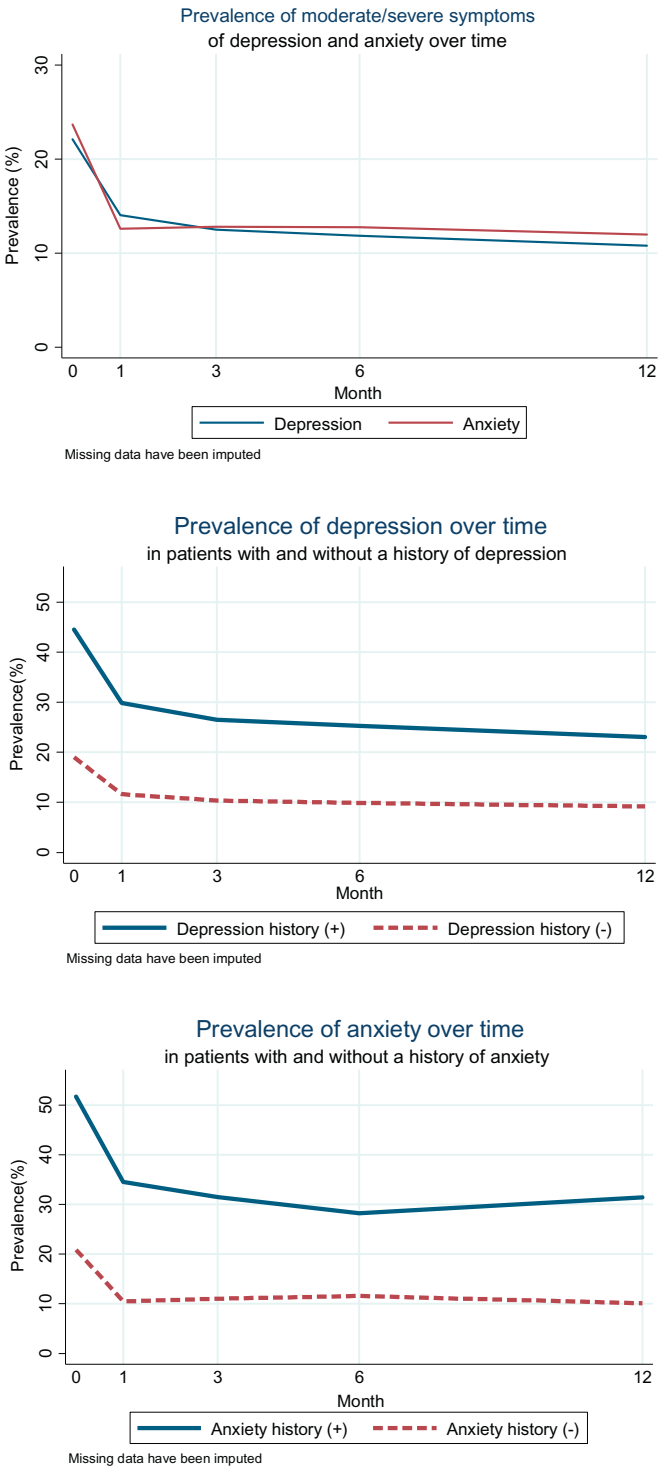
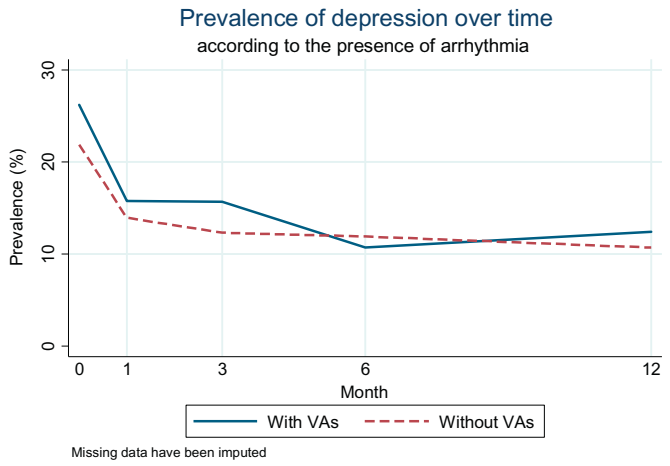


Fig. 1. Prevalence of moderate/severe symptoms of depression and anxiety overall and by the presence of a history of these conditions among patients discharged from the hospital after an acute coronary syndrome.



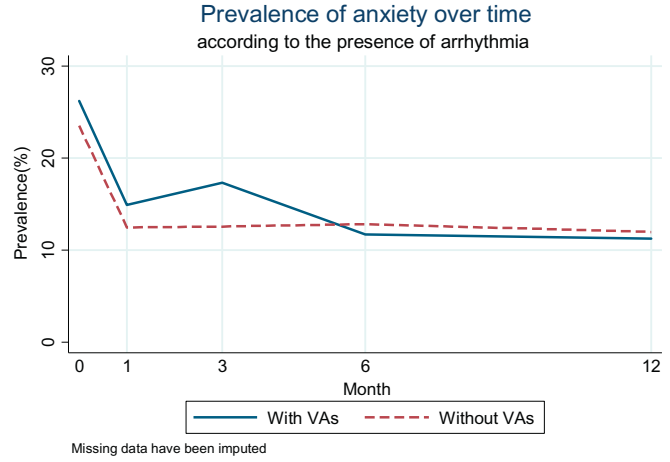
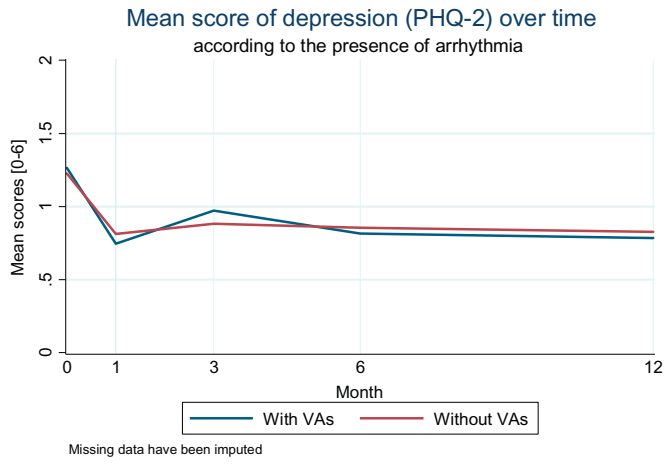


Fig. 2. Prevalence of moderate/severe symptoms of depression and anxiety among patients discharged from the hospitalafter an acute coronary syndrome with and without in-hospital clinically significant ventricular arrhythmias (VAs).



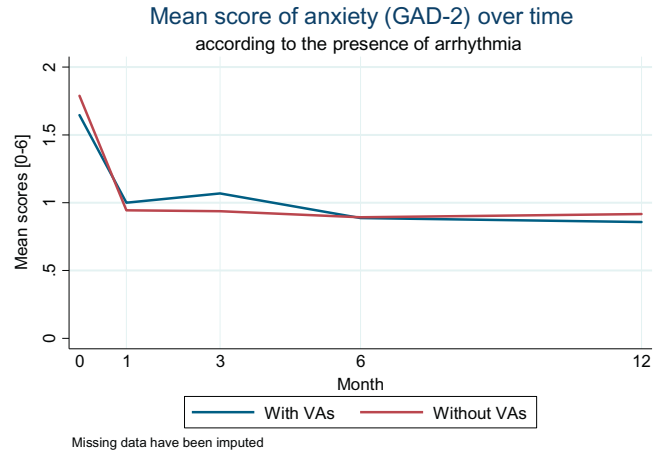


Fig. 3. Change in mean scores of symptoms of depression (PHQ 2) and anxiety (GAD 2) over time andaccording to the presence of clinically significant ventricular arrhythmias (VAs) in patients discharged from the hospital following an acute coronary syndrome.

Table 2
Association (Relative risk, 95%Confidence interval) between occurrence of in-hospital clinically significant ventricular arrhythmias (VAs) and progression of moderate/severe symptoms of depression and anxiety in the first 3 months following hospital discharge in patients with an acute coronary syndrome.

	Depression		Anxiety	
	Unadjusted	Adjusted[a]	Unadjusted	Adjusted[a]
All patients				
VAs	1.18 (0.86–1.63)	1.29 (0.94–1.77)	1.17 (0.84–1.64)	1.22 (0.86–1.72)
Time (month)	**0.83 (0.79–0.87)**	**0.83 (0.79–0.86)**	**0.82 (0.78–0.86)**	**0.96 (0.95–0.97)**
Patients without a history of depression or anxiety				
VAs	1.30 (0.90–1.88)	1.41 (0.99–2.02)	1.22 (0.84–1.79)	1.34 (0.91–1.98)
Time (month)	**0.82 (0.77–0.87)**	**0.82 (0.77–0.87)**	**0.81 (0.76–0.86)**	**0.81 (0.76–0.86)**

Estimates are from generalized estimating equation marginal models with exchangeable correlation matrix.
The bold values indicate the statistical significance at $p < 0.05$.
[a] Additionally adjusted for the Charlson comorbidity index, GRACE risk score, study site, and the use of antiarrhythmic agents.

4. Discussion

Comorbid depression and anxiety are common and have been previously shown to contribute to worse clinical outcomes in patients admitted to the hospital for an ACS. We found that the prevalence of moderate/severe symptoms of depression and anxiety quickly declined during the first month after hospital discharge for an ACS and remained relatively stable thereafter. The occurrence of VAs appeared to have a small, relatively negligible, effect on the symptoms of moderate/severe depression and anxiety over the short-term, but failed to show any significant association with the progression of symptoms of depression and anxiety over our 12-month follow-up period.

4.1. Progression of symptoms of depression and anxiety

A number of prior studies have described the natural progression of symptoms of depression or anxiety in patients with coronary artery disease, but they were either based on a very small and non-diverse sample of patients [6,32,33], were potentially biased due to complete-case analysis [32,34], included non-ACS patients [35], or had limited reassessment of these psychosocial symptoms over a prolonged follow up period [32,34]. Several studies have suggested that the symptoms of depression and anxiety resolve relatively quickly after the acute coronary event [33,36]. For example, a study of 226 women admitted to 4 hospitals for acute myocardial infarction (AMI) or CABG surgery in Melbourne, Australia found that > 80% of patients experienced a

Table 3
Differences in mean score (95% Confidence Interval) of depression (PHQ-2) and anxiety (GAD-7) symptoms during the first 3 months following hospital discharge between patients with and without in-hospital clinically significant ventricular arrhythmias (VAs) after an acute coronary syndrome.

	Depression		Anxiety	
	Unadjusted	Adjusted	Unadjusted	Adjusted
VAs	0.04 (−0.23; 0.30)	0.14 (−0.11; 0.39)[a]	0.02 (−0.30; 0.34)	0.04 (−0.26; 0.34)[b]
Time (month)	**−0.10 (−0.13; −0.08)**	**−0.10 (−0.13; −0.08)**[a]	**−0.25 (−0.28; −0.23)**	**−0.25 (−0.28; −0.23)**[b]

Estimates are from generalized estimating equation marginal models with exchangeable correlation matrix.
The bold values indicate the statistical significance at $p < 0.05$.
[a] Additionally adjusted for the Charlson comorbidity index, GRACE risk score, study sites, and history of depression.
[b] Additionally adjusted for Charlson comorbidity index, GRACE risk score, study sites, age, sex, history of depression, and the use of benzodiazepines.

decrease in their symptoms of depression and anxiety at 2 and 4 months post discharge, which remained at these levels throughout the 12 month follow up period [35]. On the other hand, several studies suggest a more chronic course of symptoms of anxiety or depression following an acute coronary event [6,37]. In a study of 287 patients discharged after an AMI from 4 hospitals in the Netherlands between 2003 and 2005, patient's symptoms of depression were essentially similar throughout the baseline, 2, and 12 month post discharge assessments [6].

In the present study, we found that overall, the prevalence of moderate/severe symptoms of depression and anxiety rapidly declined by > 50% in relative terms, from approximately 25% to 12%, during the first month after hospital discharge for an ACS. The proximal stress and fear resulting from an acute coronary event may contribute to the high prevalence of moderate/severe symptoms of depression and anxiety several days thereafter, which is what we observed in the present study. On the other hand, the perceived susceptibility and stress associated with the acute coronary event may be less prominent at the first month post discharge or later, which resulted in a lower prevalence of self-reported moderate/severe symptoms of depression and anxiety that we observed. Other factors, including the hospital setting, and in-person interview during the patient's acute hospitalization, might have also triggered worse self-reported symptoms compared with the first month and later time points, when the patients were interviewed via telephone at home. Regardless of the underlying reasons or contributory causes, our findings suggest that a single screening for symptoms of depression and anxiety during the acute hospital stay may overestimate the burden of these comorbidities in patients who have experienced an ACS. Since the prevalence of moderate/severe symptoms of depression and anxiety were stable after 1 month, screening for the symptoms of depression or anxiety in the outpatient setting may be more appropriate than an in-hospital assessment after an acute coronary event.

Several studies that have analyzed their findings using latent group analysis have suggested that patients with coronary artery disease may consist of several groups of patients with distinct trajectories of depression and/or anxiety over time [7,35,38,39]. These studies, despite being based on relatively small samples of patients, suggest that serial measurement of symptoms of depression and anxiety may be necessary to identify high risk groups of patients with worsening psychosocial trajectories that need further intervention. However, when, where, and how to screen for potentially serious signs of sustained depression and anxiety following an acute coronary event that may warrant further intervention versus simple monitoring deserves further study.

As expected, patients who had a history of depression or anxiety had greater frequencies of symptoms of moderate/severe depression or anxiety compared with patients who did not have these comorbid conditions. However, despite baseline differences, the progression of symptoms of depression and anxiety over the subsequent several months was similar among the two groups of patients. These findings suggest that any acute stress or fear that patients might have after the ACS may only exert an acute impact on the symptoms of depression and anxiety, but are not likely to change the chronic course of these symptoms in patients with a history of depression or anxiety. It is also important to note that the progression of depression and anxiety was relatively similar during the one-year follow-up period. This was perhaps due to the fact that close to two-thirds of patients who had moderate/severe symptoms of depression or anxiety also reported symptoms of the other condition. These findings also demonstrate the close clinical association between these two conditions, which may share long-term trajectories of progression, and further emphasizes the need to screen for both conditions simultaneously.

4.2. Association between VAs and progression of symptoms of depression and anxiety

The association between depression and anxiety and VAs has been previously studied. For example, several small studies have suggested that the presence of depression or anxiety in the setting of an ACS may be associated with a higher risk of developing VAs [40,41]. However, to the best of our knowledge, the present study is the first to examine the occurrence of serious VAs as a risk factor for the progression of symptoms of depression and anxiety among patients discharged from the hospital following an ACS. Although patients with VAs had a modestly higher prevalence of moderate/severe symptoms of depression or anxiety during the first 3 months after hospital discharge compared with patients who did not have VAs, these differences were not statistically significant. In both unadjusted and adjusted analyses, the development of VAs was not associated with a greater risk of having symptoms of depression or anxiety at 3 months after hospital discharge. These results were also confirmed in our secondary analysis, when the symptoms of both depression and anxiety were treated as numerical scores. Thus, in contrast to our initial expectations, experiencing a serious VA after an ACS might not increase the risk of developing moderate/severe symptoms of depression or anxiety over time. It is, however, possible that our study did not have sufficient power to detect differences in the symptoms of depression and anxiety caused by VAs since only 5.1% of our study population developed these clinically significant cardiac arrhythmias. Thus, larger or more efficient studies, which utilize matching participant selection or oversampling of patients who develop VAs after an ACS, are necessary to confirm our findings.

4.3. Study strengths and limitations

This study is the first to examine the psychological impact of VAs in patients who were hospitalized with an ACS and trends in the symptoms of moderate/severe depression and anxiety over time. It also included a large, geographically and sociodemographically diverse patient population, which enhances the generalizability of our findings. We were also able to adjust our principal study findings for the potentially confounding influence of several important demographic and clinical factors. On the other hand, there were several limitations of the present study that need be kept in mind in interpreting our results. While patients were likely to be aware of their having experienced a cardiac arrest, VT, or sustained VT, we did not measure whether patients were aware of having experienced a non-sustained VT. However, given its prognostic significance and possibility of deterioration into more hemodynamically unstable arrhythmias, physicians involved in the care of these patients were likely to have discussed this finding with patients. Other relevant information, such as echocardiography results, were not available for the majority of patients in the present study,

perhaps partially due to recent trends in early discharge after being hospitalized for an ACS [42], and were not able to be analyzed. In addition, although we have addressed missing data by appropriate statistical methods, it is recommended that readers interpret our findings with appropriate caution given the considerable amount of missing data. Future studies should consider an assessment of the perceived psychological impact of VAs on affected patients as well as echocardiographic measurements, including the evaluation of patient's left ventricular ejection fraction, in their data collection efforts.

5. Conclusions

In this study of a large and diverse population discharged from the hospital after an ACS, we found the prevalence of self-reported moderate/severe symptoms of depression and anxiety to be high at the time of the in-hospital index interview, but quickly declined during the first month after hospital discharge and remained stable thereafter. The occurrence of VAs was not associated with an elevated risk of moderate/severe symptoms of depression or anxiety after hospital discharge. Future studies should focus on the appropriate time to screen for symptoms of depression and anxiety in the setting of an ACS, and examine the progression of symptoms of depression or anxiety over an extended period in a larger group of patients with VAs for purposes of identifying high risk groups for these psychological disturbances in whom intervention efforts could be directed.

Disclosures

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Appendix A. Characteristics of patients discharged from the hospital after an acute coronary syndrome according to missing longitudinal data on symptoms of anxiety or depression (TRACE-CORE)

	Complete longitudinal data	Missing longitudinal data	*p-Value*
	n = 886	*n* = 1188	
Age (years)	63 [55–71]	59 [52–68]	< **0.001**
Age group (%)			< **0.001**
< 55	23.9	34.3	
55–64	29.1	33.7	
65–75	31.7	20.8	
≥75	15.2	11.2	
Women (%)	33.1	33.9	0.684
Race/ethnicity (%)			< **0.001**
White	83.0	72.7	
Black	9.8	19.5	
Other	6.4	5.6	
Marital status (%)			< **0.001**
Married/lived as married	64.6	54.6	
Separate/divorced/widowed	26.0	32.7	
Single/never married	9.4	12.7	
Educational attainment (%)			< **0.001**
College graduate or higher	31.5	20.6	
Some technical school or college	31.3	27.1	
High school graduates	29.0	29.6	
Less than high school	8.2	22.6	
Insurance coverage (%)			< **0.001**
Medicare plus private insurance	24.4	14.1	
Private insurance only	50.1	49.2	
Medicare only	12.9	13.5	
Medicaid	8.6	11.5	
Uninsured	4.1	11.5	
Unemployed/retired (%)	59.1	57.0	0.33
Previously diagnosed (%)			
Anxiety	7.7	9.2	0.23
Chronic kidney disease	9.4	10.4	0.46
Congestive heart failure	10.4	14.7	**0.004**
Coronary artery disease	26.3	26.0	0.88
Depression	12.0	12.5	0.69
Diabetes	35.4	38.6	0.14
Hypertension	74.8	\	0.83
Physiologic findings at admission			

Systolic blood pressure (mmHg)	142 [125–157]	140 [125–157]	0.32
Diastolic blood pressure (mmHg)	79 [69–90]	80 [70–91]	**0.045**
Heart rate (beat/min)	73 [64–86]	76 [66–88]	**0.002**
Laboratory findings at admission			
Creatinine (mg/dl)	0.97 [0.8–1.13]	0.97 [0.81–1.19]	0.28
Glucose (mg/dl)	126 [105–168]	126 [105–171]	0.84
GRACE risk score	95.2 [76.9–112.0]	90.2 [72.1–111.5]	**0.004**
Potassium (mmol/l)	4.1 [3.8–4.3]	4.0 [3.7–4.4]	**0.022**
White blood cell count (109 cell/L)	8.5 [6.7–10.8]	8.5 [6.8–10.9]	0.57
In hospital complications (%)			
Acute kidney injury	2.8	6.8	< **0.001**
Heart failure/cardiogenic shock	2.1	1.4	0.22
Atrial fibrillation/flutter	8.4	6.1	**0.044**
ACS Type (%)			0.08
Unstable angina	32.2	30.1	
STEMI	15.7	19.8	
NSTEMI	51.5	49.8	
Reperfusion treatment received (%)			**0.028**
Medical treatment	17.5	21.9	
PCI	70.8	65.6	
CABG	11.7	12.5	
Medications at hospital discharge (%)			
Antiarrhythmic agents	10.8	10.5	0.82
Aspirin	96.3	96.8	0.52
P2Y12 inhibitors	86.3	84.3	0.19
ACE-I/ARBs	60.7	62.9	0.32
Beta-blockers	90.2	89.3	0.52
Statins	87.0	86.9	0.92
SSRI/SNRI/atypical antidepressants	14.0	17.8	**0.021**
Benzodiazepines	27.7	31.1	0.09
Length of hospital stay (days)	2 [1–4]	3 [2–5]	< **0.001**
Depression symptoms (absolute scores)			
Baseline	4 [1–7]	5 [2 − 10]	< **0.001**
1 month	2 [1–5]	3 [1–7]	**0.021**
3 months	0 [0–1]	0 [0–2]	< **0.001**
6 months	0 [0–1]	0 [0–2]	< **0.001**
12 months	0 [0–1]	0 [0–2]	< **0.001**
Anxiety symptoms (absolute scores)			
Baseline	3 [1–7]	5 [2–10]	< **0.001**
1 month	0 [1–5]	2 [0–6]	**0.019**
3 months	0 [0–1]	0 [0–2]	< **0.001**
6 months	0 [0–1]	0 [0–2]	< **0.001**
12 months	0 [0–1]	0 [0–2]	**0.003**
Moderate/severe depression symptoms (%)			
Baseline	17.0	25.8	< **0.001**
1 month	9.5	15.5	**0.001**
3 months	8.9	14.0	**0.004**
6 months	7.9	15.1	< **0.001**
12 months	6.4	15.9	< **0.001**
Moderate/severe anxiety symptoms (%)			
Baseline	18.1	27.7	< **0.001**
1 month	8.7	14.3	**0.001**
3 months	9.5	13.9	**0.012**
6 months	8.8	16.9	< **0.001**
12 months	8.9	14.0	**0.005**

Note: continuous variables were reported in median [interquartile range]; sum may not add up to 100% due to missing data.

NSTEMI: non-ST-segment elevation myocardial infarction, STEMI: ST-segment elevation myocardial infarction, PCI: percutaneous coronary intervention, CABG: coronary artery bypass graft surgery, ACE-I/ARBs: Angiotensin converting enzyme inhibitor/Angiotensin receptor blockers, SSRI: selective serotonin reuptake inhibitors, SNRI: serotonin and norepinephrine reuptake inhibitors.

Atypical antidepressants included bupropion, mirtazapine, nefazodone. Benzodiazepines included lorazepam, diazepam, clonazepam, alprazolam, clorazepate, oxazepam, chlordiazepoxide.

The bold values indicate the statistical significance at $p < 0.05$.

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