RESEARCH

Prevalence and management of depressive symptoms in coronary heart disease patients and relationship with cardiovascular prognosis: a prospective cohort study

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Abstract

Aims Depressive symptoms are comorbid with coronary heart disease (CHD). There is a controversial debate about whether screening and intervention for depressive symptoms could improve cardiovascular prognosis. This study characterizes the prevalence, characteristics, cardiovascular prognosis and management need of depressive symptoms among CHD patients.

Methods CHD patients were recruited between November 18, 2020 and November 26, 2021. Depressive symptoms were evaluated with the Patient Health Questionnaire (PHQ-9). During the 12-month follow-up, cardiovascular disease (CVD) was the endpoint. Time-to-event data were estimated by Kaplan-Meier curves and Cox models.

Results Of 582 patients (25% women), 21.0% had mild depressive symptoms, and 7.5% had moderate-to-severe depressive symptoms during hospitalization. Mild and moderate-to-severe depressive symptoms were risk factor-adjusted predictors of the primary composite endpoints (adjusted HR = 2.20; 95%CI 1.19–4.03, and adjusted HR = 2.70; 95%CI 1.23–5.59, respectively). Platelet count and low-density lipoprotein were higher in mild depressive symptoms compared to no depressive symptoms.

Conclusion Depressive symptoms are prevalent in CHD patients. Mild and moderate-to-severe depressive symptoms are associated with higher risk of further CVD in CHD patients. Platelet function and behavioral mechanisms may contribute to this association.

Trial registration This research was registered at https://www.chictr.org.cn. Full data of first registration is 11/09/2020. The registration number is ChiCTR2000038139.

Keywords Depressive symptom, Coronary heart disease, Cardiovascular disease, Prognosis, Risk factor

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Introduction

Approximately 30 years earlier, depression was demonstrated as an independent risk factor for mortality following myocardial infarction (MI) [1]. Diagnosis of depression as a disease is based on either the Diagnostic And Statistical Manual Of Mental Disorders (DSM) or International Classification of Diseases (ICD) diagnostic systems [2, 3]. Compared with depression, depressive symptoms are more common (12% vs. 45.2%) [4], and may be a more modifiable prognostic factor for coronary heart disease (CHD), as papers of the American Heart Association (AHA) and the European Society of Cardiology have reported [5]. Diagnosis of depressive symptoms as an early manifestation of depression can be assessed by clinical scales or questionnaires [4, 6]. In recent years, there has been considerable interest in the impact of depressive symptoms on prognosis among CHD patients [4, 7–10]. A growing number of studies suggest CHD patients with depressive symptoms are associated with an increased risk of further cardiovascular disease (CVD) [4, 5, 8, 9, 11]. However, it is still uncertain whether screening and intervention for depressive symptoms can improve cardiovascular prognosis among CHD patients [5]. Two landmark studies provided valuable evidence that there is no significant difference in the composite endpoint of CVD, including cardiac mortality, between the treatment and control groups [12, 13]. Furthermore, another evidence suggests psychotherapy could be effective for depression in patients with CHD, but with less evidence of cardiac benefit [14]. The same conclusion has been reported [15]. The efficacy of antidepressant medication and psychotherapy in alleviating depressive symptoms in patients with CHD has been shown to be small to moderate [16]. Nevertheless, a secondary analysis concluded an encouraging conclusion that the participants, who received two home visits, had a significantly lower rate of cardiac mortality compared to the control group [17].

Over the past few decades, a growing body of evidence has suggested that mental health may be causally linked to biological processes and behaviors that lead to CVD [7]. Several biological and behavioral mechanisms may contribute to the adverse prognosis, such as autonomic nervous system activation, systemic inflammation, activation of the hypothalamic-pituitary-adrenal (HPA) axis, platelet dysfunction, endothelial dysfunction and common genetic vulnerability, as well as, physical inactivity, medication nonadherence, social isolation, and unhealthy diet [10, 16]. But no single factor has been shown to account for more than a fraction of the risk. Effective identification of 'high-risk' depressive symptoms subtypes, and an improved understanding of the bio-behavioral pathways linking depressive symptoms to increased risk of CVD are needed [16].

The aims of the this study were: (1) to investigate the prevalence and prognosis of mild and moderate-to-severe depressive symptoms in CHD patients after cardiac-related hospitalization; (2) to identify re-hospitalization rates for CVD among these patients, and (3) to explore the connection between depressive symptoms and CHD. Mild and moderate-to-severe depressive symptoms refers to a self-reported psychological status using a standard depression screening tool recommended by the AHA.

Methods

Study design

The current study was a prospective, single-central, cohort study that was performed in a comprehensive Class 3 A hospital, the First Affiliated Hospital of Shantou University Medical College. Patients with chest pain were consecutively screened during a hospital stay at the hospital. The project was approved by the ethics committees of the First Affiliated Hospital of Shantou University Medical College and registered at https://www.chictr.org.cn. The registration number is ChiCTR2000038139.

Eligible patients were required to have documented CHD (diagnosis in the medical chart) based on the coronary angiography results. CHD was defined according to accepted standards, i.e., the presence of at least one coronary artery with ≥50% lumen stenosis by quantitative coronary angiography (QCA) (equivalent to approximately ≥70% stenosis by regular visual estimate) [18]. The patients were divided into three groups: those without depressive symptoms, with mild depressive symptoms and moderate-to-severe depressive symptoms, and according to the PHQ-9 score. Depression disorder is a highly prevalent risk factor for CVD and mortality, independently of somatic comorbidity [4]. If the patients have a significant suicidal tendency, a professional evaluation or intervention by a psychiatrist or neurologist was needed [19]. As in studies of depression as a risk factor for incident CVD, the potential for residual confounding is a concern in patients with CHD [16]. Besides, the unpublished part of this cohort study involved the analysis of heart rate variability, which required the acquisition of a 5-minute resting electrocardiogram. Therefore, the patients with suicidal tendency, history of depression disorder or other psychiatric illness, or installed pacemaker were excluded in this study.

Inclusion criteria

(1) Age, 18–85 years old.
(2) CHD patients, the presence of at least one ≥50% stenosis with coronary angiography.

Exclusion criteria

(1) History of cognitive impairment disease, such as Alzheimer's disease and dementia.
(2) Suicidal tendency, based on the 9th item of PHQ-9 score ≥ 1.
(3) History of psychiatric illness, including depression disorder according to the Diagnostic and Statistical Manual of Mental Disorders, fifth edition (DSM-V).
(4) Terminal illness, the end-stage of illness, such as uremia.
(5) Insufficient language proficiency, such as illiteracy.
(6) With installed pacemakers.

Assessment and treatment needs of depressive symptoms

The severity of depressive symptoms was assessed using the PHQ-9 self-rating scale, which is a brief, validated depression screening tool with scores ranging from 0 to 27, and 9 items in total [6]. As it is recommended that future screening for depressive symptoms should ideally consider estimating probabilities of depressive symptoms across the full spectrum of PHQ-9 screening scores (rather than dichotomizing scores at a cut-off). The greater the number and severity of symptoms (as opposed to particular symptoms), the greater the probability of functional impairment they are likely to confer. A PHQ-9 ‹5 indicates no depressive symptoms. A PHQ-9 ≥ 5 indicates manifestation of depressive symptom, where a PHQ-9 5–9 indicates mild depressive symptoms, and a PHQ-9 ≥ 10 indicates moderate-to-severe depressive symptoms. The presence of a depressive symptom was defined using the PHQ-9 combined with a diagnosis of not having depression. PHQ-9 scoring was completed within 24 h after admission.

Participants fulfilling diagnostic criteria for a current episode of depressive symptoms were informed that they were suffering from depressive symptom, instructed to discuss their symptoms with their primary care provider, and provided with a list of local resources available for further evaluation and treatment and recommended referral to a psychiatrist or neurologist.

Somatic morbidity

A modified age-adjusted Charlson Comorbidity Index (aCCI) [20] was computed (exclusion of cardiac diagnoses, dementia and terminal illness). We collected and calculated the total scores of disease histories with different weighted scores (1–3 points) of comorbidity [20], including congestive heart failure (HF), peripheral vascular disease, cerebrovascular disease, chronic pulmonary disease (COPD), ulcer, mild liver disease, diabetes, hemiplegia, moderate and severe renal disease (GFR 30–59 ml/min), diabetes with end organ damage, any tumor, leukemia, lymphoma, moderate and severe liver disease, metastatic solid tumor, and acquired immune deficiency syndrome (AIDS).

Follow-up and endpoints

During the follow-up, all enrolled patients were contacted by telephone at 1, 3, and 12 months after their discharge from hospital. The primary endpoint at follow-up was a composite outcome of cardiac death, hospitalization for HF and hospitalization for MI, and we also evaluated cardiac death, hospitalization for HF and hospitalization for MI separately. The secondary endpoint was a composite event of angina and nonfatal stroke. The time of follow-up was defined as the interval between enrollment and the date of death or the date of observed endpoints. Additional information of the endpoints was obtained from the hospital admission records and family members.

Statistical analyses

The prevalence of depressive symptoms during the hospitalization and the prognosis of CVD are reported descriptively. All statistical tests were conducted using SPSS statistical software version 25.0 (IBM Corp). Continuous data conforming to a normal distribution was represented by $\bar{\chi} \pm SD$, otherwise they were expressed as the M (P_{25}-P_{75}), and categorical variables were expressed as frequency (n) or percentage (%). A t-test or Mann-Whitney U test was performed for comparisons between two groups. ANOVA, Kruskal-Wallis and chi-square tests were used for comparison of multiple groups, and differences with a $p < 0.05$ were considered significant.

Univariate and multivariate Cox proportional hazards regression models were applied to analyze the associations between depressive symptoms and CVD following adjustment for selected variables, such as age, sex, left ventricular ejection fraction (LVEF) and aCCI. The Kaplan-Meier method was used to evaluate the distribution of composite outcomes between with and without depressive symptoms.

Results

Study cohort and population characteristics

A total of 1265 inpatients were screened between November 18, 2020 and November 26, 2021, of whom 653 were excluded because the diagnosis of CHD was unclear (Fig. 1). A further 30 participants who had Alzheimer's disease, suicidal tendency, an installed pacemaker, or who were illiterate were excluded. Eventually, 582 CHD patients were included in this study. Study participants were divided into one of the following three groups based on PHQ-9 scores evaluated upon hospitalization: no depressive symptoms (PHQ-9 ‹5), mild depressive
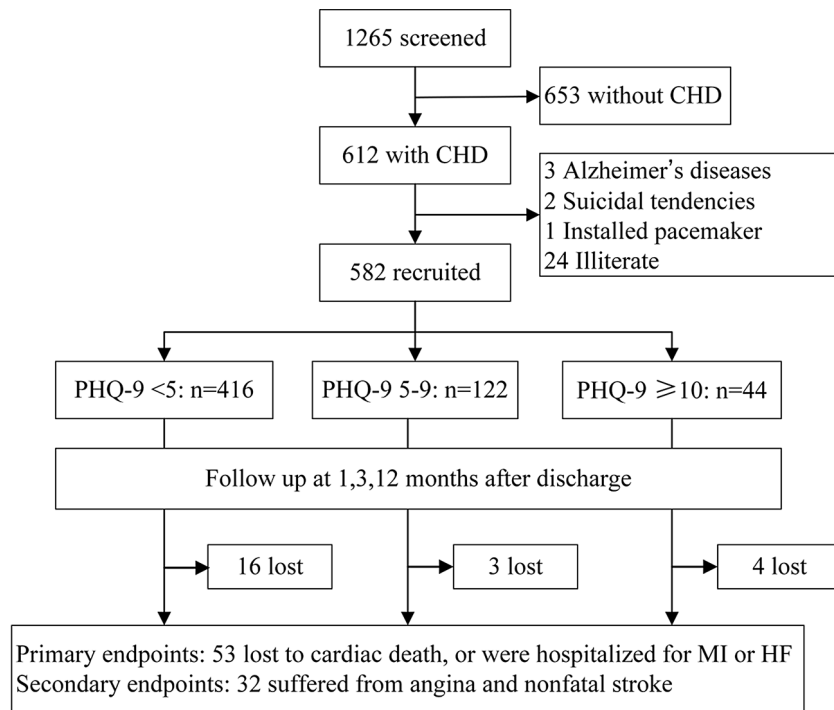
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Fig. 1 Flow diagram of this study

symptoms (PHQ-9 5–9) or moderate-to-severe depressive symptoms (PHQ-9≥10). Cronbach alpha scores for PHQ-9 is 0.78.

The characteristics of the study population are displayed in Table 1. The mean age of participants in the CHD cohort was 63.0±10.4 years. 148 (25.4%) were women and 333 (57.2%) were smokers or former smokers. The characteristics of the participants in the no depressive symptom cohort were similar to those of mild and moderate-to-severe depressive symptom cohorts (Table 1). The mild depressive symptom cohort had higher platelet count (234.8±70.8 vs. 217.8±59.6, 10^9/L; $p<0.001$) and low-density lipoprotein (3.2±1.1 vs. 2.9±0.9, mmol/L, < 0.001) compared with the no depressive symptom cohort. There were also no statistically significant differences in sociodemographic characteristics and clinical variables.

Outcomes and availability among different depressive symptoms groups

Among all 582 patients, 122 (21.0%) were with mild depressive symptoms, 44 (7.5%) were with moderate-to-severe depressive symptoms, and 416 (71.5%) had no signs of depressive symptoms during hospitalization (Fig. 2). The median duration of follow-up in censored patients was 477 days (IQR 376–563) (the time was for primary outcomes). During follow-up, 14.6% ($n=85$) of patients were re-hospitalized, of whom 9.1% ($n=53$) showed primary composite outcomes, and 5.5% ($n=32$)

suffered from secondary composite outcomes (Supplementary Table 1). Additionally, the CVD readmission rates of CHD patients with depressive symptoms were significantly higher in comparison to the general CHD population (p ˂ 0.05) (Supplementary Table 1). In particular, among patients with depressive symptoms, the rate of re-hospitalization for all CVD in this study was 25.3%, whereas the rates of re-hospitalization for MI and angina pectoris were 11.4% and 9.6%, respectively (Supplementary Table 1). 23 (4.0%) patients were lost to follow-up, in which 3 died of non-cardiac deaths. Compared to groups with no depressive symptoms, Kaplan-Meier survival analysis demonstrated that CHD patients with mild and moderate-to-severe depressive symptoms had a significantly higher risk of endpoints of hospitalization for MI, HF and/or cardiac death ($p<0.05$) (Fig. 3.A, B), and MI hospitalization (Fig. 3.C), as well as secondary composite endpoints (Supplementary Fig. 1). However, there is no significant difference in the single endpoint of hospitalization for HF (Fig. 3.D). Cardiac death was not analyzed separately in this comparison because none of the cardiac deaths occurred in the moderate-to-severe depressive symptom group.

After adjustment for age, sex, LVEF and aCCI, mild depressive symptoms were associated with an increased risk of primary and secondary composite endpoints (adjusted HR=2.2; 95% CI 1.19–4.03, and adjusted HR=3.06; 95% CI 1.4–6.64 [per unit increase], respectively), moderate-to-severe depressive symptoms were

Table 1 Characteristics of all study participants (*N* = 582)

Variables	*n* = 582	PHQ-9 <5 *n* = 416(71.5%)	PHQ-9 5–9 *n* = 122(21.0%)	PHQ-9 ≥ 10 *n* = 44(7.5%)	*p*[a]
Age, year	63.0 ± 10.4	63.4 ± 10.4	61.9 ± 11.3	61.2 ± 9.0	0.18
Female, n (%)	148 (25.4%)	81 (19.5%)	35 (28.7%)	32 (27.3%)	0.07
BMI, kg/m^2	24.2 ± 3.4	24.1 ± 3.3	24.8 ± 3.6	24.6 ± 3.8	0.20
Smoker, n (%)	333 (57.2%)	250 (60.1%)	60 (49.2%)	23 (52.3%)	0.08
Alcohol consumption, n(%)	162(27.8%)	115(27.6%)	34(27.9%)	13 (29.5%)	0.07
Education					0.36
1–6 years, n (%)	273 (46.9%)	193 (46.4%)	64 (52.4%)	16 (36.4%)	
7–9 years, n (%)	165 (28.4%)	122 (29.3%)	30 (24.6%)	13 (29.5%)	
≥ 10 years, n (%)	144 (24.7%)	101 (24.3%)	28 (23.0%)	15 (34.1%)	
LVEF					0.88
Preserved LVEF (≥ 50%), n (%)	474 (81.4%)	336 (80.8%)	101 (82.8%)	37 (84.1%)	
Mid-range LVEF (40–49%), n (%)	79 (13.6%)	62 (14.9%)	14 (11.5%)	3 (6.8%)	
Reduced LVEF (ᶜ40%), n (%)	29 (5.0%)	18 (4.3%)	7 (5.7%)	4 (9.1%)	
aCCI score					0.47
0–2, n (%)	83 (14.3%)	56 (13.5%)	18 (14.8%)	9 (20.5%)	
3–5, n (%)	340 (58.4%)	256 (61.5%)	63 (51.6%)	21 (47.7%)	
≥ 6, n (%)	159 (27.3%)	104 (25.0%)	41 (33.6%)	14 (31.8%)	
Hb, 10^9/L	133.5 ± 18.0	134.6 ± 18.2	130.1 ± 18.6	130.8 ± 17.4	**0.03**
PLT, 10^9/L	223.1 ± 62.8	217.8 ± 59.6	234.8 ± 70.8	234.9 ± 51.9	**0.01**[b]
Lipid level					
TC, mmol/L	4.5 ± 1.5	4.4 ± 1.4	4.7 ± 1.7	4.8 ± 1.3	0.11
TG, mmol/L	1.8 ± 1.3	1.7 ± 1.3	1.9 ± 1.3	1.7 ± 1.2	0.32
LDL, mmol/L	2.9 ± 1	2.9 ± 0.9	3.2 ± 1.1	3.1 ± 0.9	**0.01**[b]
HDL, mmol/L	1.1 ± 0.4	1.1 ± 0.4	1.2 ± 0.4	1.1 ± 0.2	0.39

Values are presented as χ ± SD, median (IQR) or n (%); aCCI, age-adjusted Charlson Comorbidity Index; BMI, body mass index; Hb, hemoglobin; HDL, high-density lipoprotein; LDL, low-density lipoprotein; LVEF, left ventricular ejection fraction; PHQ-9, Patient Health Questionnaire; PLT, platelet count; TC, total cholesterol; TG, triglyceride;. [a] Values refer to overall comparisons. Significant p-values (p ᶜ 0.05) are highlighted in bold. Significant post hoc comparisons are indicated by superscripts; p was set at ᶜ 0.017 after Bonferroni correction. [b] PHQ-9 ᶜ5 vs. PHQ-9 5–9 (all p ᶜ 0.017)

also related to an increased risk of primary and secondary composite endpoints (adjusted HR = 2.7; 95% CI 1.23–5.95, and adjusted HR = 2.93; 95% CI 1.48–10.41 [per unit increase], respectively) (Table 2). Univariate and multivariate Cox regression analyses for primary and secondary composite outcomes are displayed in the supplementary materials (Supplementary Tables 2–5).

Discussion

In this consecutive cohort of hospitalized CHD patients, depressive symptoms at the time of hospital treatment were prevalent and related to increased 12-month CVD risk. We primarily investigated the association between mild and depressive symptom levels and subsequent CVD prognosis among CHD patients. Our results demonstrated 12-month composite endpoints were about 2- and 3-fold higher in the groups with depressive symptoms (involving mild and moderate-to-severe depressive symptoms), compared with the no depressive symptom group, even after adjustment for age, sex, and risk factors.

Prevalence of depressive symptoms

At hospitalization, less than one third (29%) of patients had depressive symptoms, with mild depressive

symptoms accounting for the majority (74%). The rate is higher in comparison to the general population and at the lower end of prevalence reported for other CHD participants, which have ranged between 7 and 45% [4, 9]. Poor recognition of depressive symptoms by healthcare providers has previously been reported [4, 21, 22]. In contrast to most studies with CHD patients, we evaluated depressive symptoms by not only using PHQ-9 ≥ 10, but also by including PHQ-9 5–9 [9]. This low-level of depressive symptoms could actually be another performance of dysthymia. It is the more chronic form of depression and common among CHD patients [4], which is equally burdensome, and tends to progress into depression [4]. Our data are similar to a previous consecutive cohort study showing that there is a small proportion of female among CHD patients, which is more consistent with the epidemiology of CHD in the real world. We still adjusted for gender differences, although the difference between groups was not statistically significant (*p* = 0.77).

Re-hospitalization rates for CVD

We expand on previous literature in readmission rate among CHD patients. Interestingly, patients with the comorbidity of CHD and depressive symptoms were 1–2
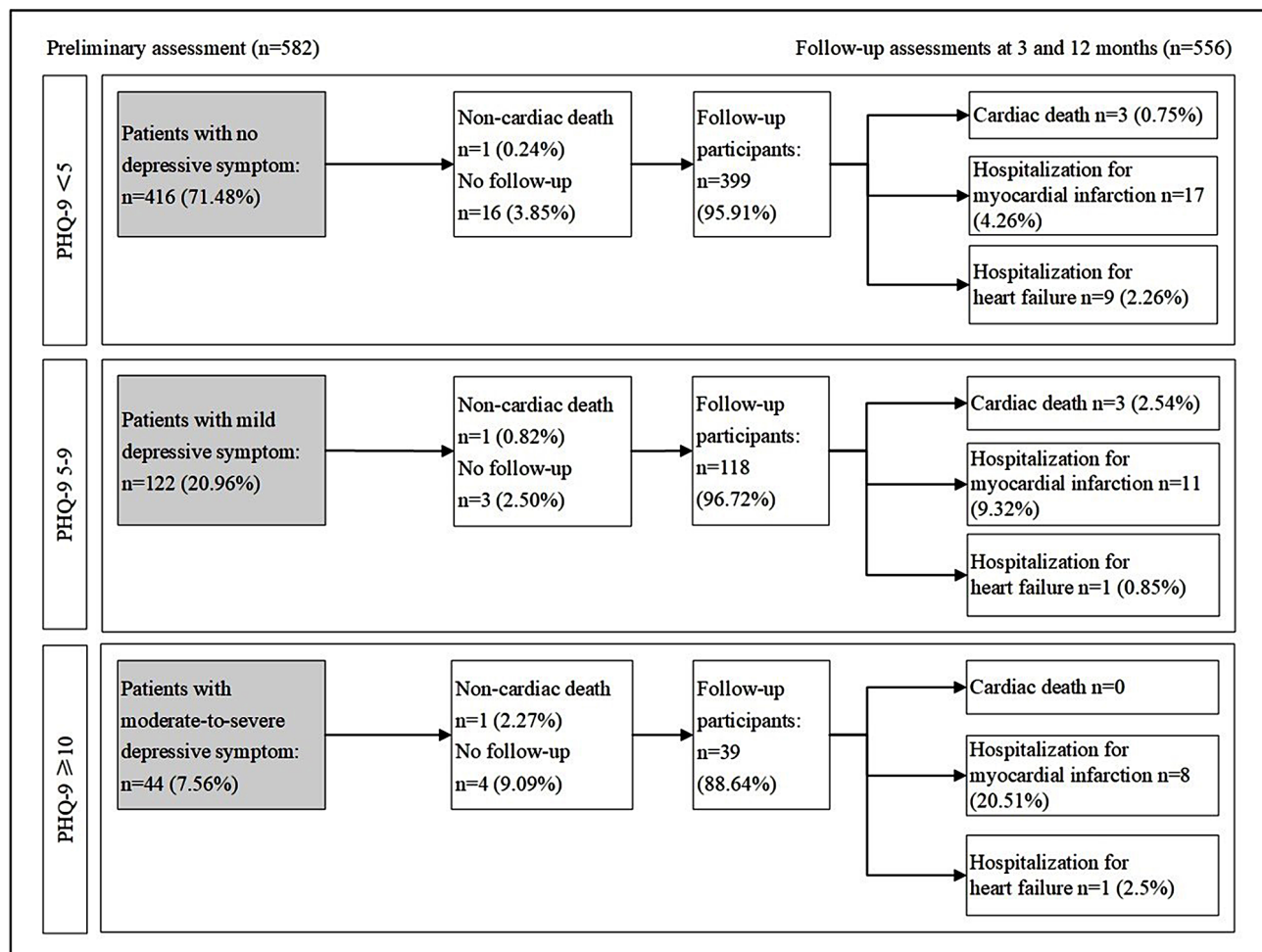
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Fig. 2 Primary outcomes and availability among different groups

times more likely to be readmitted to hospital for CVD than the general CHD. The readmission rate for further CVD was 14.6%, which is consistent with the readmission rate reported before in China [23]. On the one hand, rates of re-hospitalization for MI were 6.2%. Our results are similar to prior reports, and in the mid-range of re-hospitalization rates for MI reported in other CHD populations, which range between 2.5% and 7.1% [24, 25]. As a Chinese cohort study showed that the recurrent MI rate was 2.5–4.1% during the 1 year follow-up [24]. Additionally, a multicenter cohort study suggested that 1-year recurrent MI rate is 5.1–7.1% among Americans in 2004 [25]. Our re-hospitalization rate for angina pectoris is lower compared to the results of another cohort study that reported the readmission rate is 8.5% after a median follow-up of 64 months [26]. On the other hand, rate of re-hospitalization for acute coronary syndrome (ACS) was 11.2%, which is comparable to those observed in other countries [27]. A recent study from Ethiopia reported that 12.35% of patients experienced recurrent ACS among 469 patients diagnosed with primary ACS

[27]. The higher readmission rates further strengthen the notion that depressive symptoms as risk factors for adverse cardiovascular events could significantly increase the adverse prognosis among CHD patients [28].

Cardiovascular prognosis
Mild depressive symptoms should be given adequate attention among CHD patients. Our data confirms previous findings that depressive symptoms are risk factors for worse prognosis in CHD patients, independently of somatic comorbidity [4]. This applies to both mild and severe-to-severe depressive symptoms, which is noteworthy that few studies on the comorbidity of CHD and depressive symptoms have assessed mild depressive symptoms and its relationship with CVD prognosis [4, 5, 9, 29]. One cohort study showed that the 10-year atherosclerotic cardiovascular disease risk is positively associated with depressive symptoms in the general population [30]. These results suggest that mild depressive symptoms may be an important risk factor for the prognosis of CHD patients. Moreover, our data indicate that CHD patients
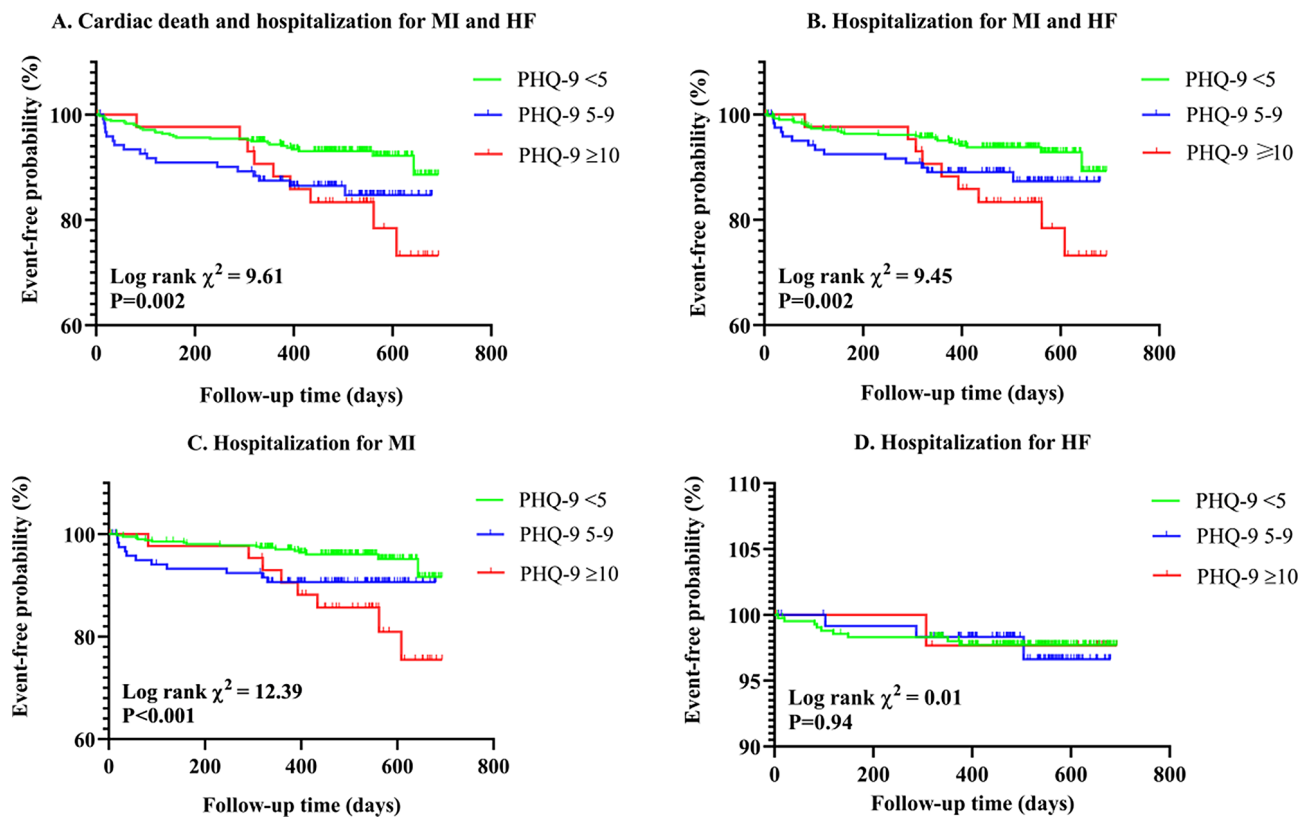
Fig. 3 Kaplan-Meier curves for the primary endpoints stratified by PHQ-9 ᐸ5, PHQ-9 5–9 and PHQ-9 ≥ 10 in CHD patients (*N* = 582). Compared with the control group of PHQ-9 ᐸ5, composite endpoints (**A** and **B**) and hospitalization for MI (**C**) were significantly higher in the PHQ-9 5–9 and PHQ-9 ≥ 10 groups. Hospitalization for HF (**D**) showed no significant difference between the three groups. HF, heart failure; MI, myocardial infarction; PHQ-9, Patient Health Questionnaire

with depressive symptoms have no significant differences in age, sex, and risk factors such as electrolytes, hepatic function, renal function, total cholesterol and comorbidities compared to patients with no depressive symptoms, which is different from CHD patients comorbid with depression, who are more likely to be female, younger and have more comorbidities compared to patients without depressive symptoms [4]. Based on this characteristic of mild depressive symptoms, it is feasible that it is not easy to recognize mild depressive symptoms in the general population [22], and unapparent clinical manifestation may also be responsible for poor prognosis of CVD, which is known from other studies [4, 5].

Our results show CHD patients with mild and moderate-to-severe depressive symptoms are at higher risk of CVD. Similar findings have previously been reported [5, 31, 32]. There is no statistical difference in the prognosis of hospitalization for HF when we analyzed it independently in this study, which is similar to the findings from the Reasons for Geographic And Racial Differences in Stroke (REGARDS) Study that depressive symptoms are not associated with incident hospitalization for HF (ejection fraction ᐸ 50%) among CHD patients [33]. While our population is too small to test whether people with

depressive symptoms have an increased risk of cardiac death, previous studies have shown that depressive symptoms are associated with an elevated risk of mortality [32, 34]. Several groups have investigated possible effects of depressive symptoms on clinical CVD [4, 5, 9, 30, 31]. One recent study, which analyzed pooled data of 563, 255 participants data in 22 prospective cohorts, showed that depressive symptoms are significantly associated with incident CVD, including scores lower than the threshold of clinical depression [5]. In a cohort of 401, 219 participants with a 8.1-year median follow-up from the UK Biobank, mild depressive symptoms significantly increased the risk of CVD, after adjustment for risk factors. Evidence from a broad range of studies suggests that not only depression, but also depressive symptoms, even though mild, should be given attention.

The impact of depressive symptoms on secondary prognosis are similar to previous studies. One meta-analysis provided strong evidence that both depressive symptoms and clinical depressive disorders are associated with a significantly increased risk of ischemic stroke (HR=1.45; 95% CI 1.29–1.63, p ᐸ 0.001) [19]. In the REGARDS cohort study, depressive symptoms were associated with a trend toward significance for stroke

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Table 2 Multivariate Cox regression analysis for the primary and secondary composite endpoints

Variables	Primary composite endpoints [a]		Secondary composite endpoints [b]	
	adjusted HR (95%CI)	p	adjusted HR (95%CI)	p
PHQ-9 score				
PHQ-9 <5[*]				
PHQ-9 5–9	2.2 (1.19–4.03)	**0.01**	3.06 (1.40–6.64)	**0.01**
PHQ-9 ≥ 10	2.7 (1.23–5.95)	**0.01**	2.93 (1.48–10.41)	**0.01**
LVEF				
Preserved LVEF (≥ 50%)[*]				
Mid-range LVEF (40–49%)	2.23 (1.31–4.94)	**0.02**		
Reduced LVEF (<40%)	2.64 (1.17–5.94)	**0.02**		
aCCI score				
0–2[*]				
3–5	1.55 (0.55–4.72)	0.43		
≥6	2.67 (0.97–8.87)	0.09		

*Reference category. Significant p-values (p < 0.05) are highlighted in bold. [a] Primary composite endpoints include cardiac death, hospitalization for MI, hospitalization for HF. [b] Secondary composite endpoints include angina and nonfatal stroke. aCCI, age-adjusted Charlson comorbidity Index; CI, confidence interval; HF, heart failure; HR, hazard ratio; LVEF, left ventricular ejection fraction; MI, myocardial infarction; PHQ-9, Patient Health Questionnaire

(HR 1.26, 95% CI 0.99–1.60) among participants without baseline CVD [35]. Furthermore, in our analysis, we found that the correlation of mild and moderate-to-severe depressive symptoms with composite events of angina and nonfatal stroke is also significant, whereas that between nonfatal stroke independently was not, by reason of only 2 nonfatal stroke were observed during the follow-up. A cross-sectional study also suggest depressive symptoms and angina had a significant correlation (OR = 2.72; 95%CI 1.96–3.79) [11].

Possible mechanisms and treatment needs for depressive symptoms

Our results are an indication that mild depressive symptom already has a series of biological and behavioral changes. Available evidence shows that patients who have CHD and depressive symptoms, have elevated levels of markers of platelet activity, especially β-thromboglobulin and platelet factor 4 [16], However, a result from the Heart and Soul Study did not support a role for platelet activation in the association between depressive symptoms and CVD among patients with stable CHD [36]. The precise mechanisms of comorbidity between depressive symptoms and CHD remains elusive [36–38], and more researches are needed to elucidate this relationship. It has been proven that behavioral mechanisms strongly contribute to the association that depressive symptoms are associated with increased morbidity and mortality

in individuals with CHD [9], the same as our findings have proven that individuals with mild depressive symptom have higher low-density lipoprotein. It suggests that cognitive-behavioral treatment could be potential treatments.

Nevertheless, there are many uncharted areas worth exploring. Because options for managing depressive symptoms include everything from low-dose psychological and social support measures such as educational programs, lifestyle advice, and activating positive behavior to more intensive treatments like psychotherapy, medications, and various other psychiatric interventions [19]. The choice of treatment relies on the individual's preferences and needs, the severity and history of their symptoms, potential side effects, and how effectively the treatment works for them [4, 19]. There is no doubt that, based on our findings and the results of previous studies, depressive symptoms are independent risk factors for poor prognosis of CVD in patients with CHD. Whether improving depressive symptoms can improve the cardiovascular outcomes of patients with CHD, and how to intervene in depressive symptoms, including intervention times, intervention methods, and intervention frequency, are questions that remain to be answered [16, 39].

Strengths and limitations

There are several strengths in our study. In this prospective cohort study, participants were enrolled from chest pain patients who were consecutively recruited from a cardiac center, which makes the study population close to a real-life healthcare setting for CHD patients. Furthermore, characteristics during hospitalization showed almost no significant differences between patients with no depressive, mild depressive and moderate-to-severe depressive symptoms, which makes the data comparable and results credible. In addition to these findings on the prognosis of adverse CVD, our study also has important implications for future mechanistic studies and potential interventions for CHD and depressive symptoms. Finally, although we used a short self-report procedure to measure depressive symptoms at a single point in time, its ease of use and positive correlation with outcomes suggest potential for wider application in clinical and research settings. As mentioned in the preceding text, the evaluation was a self-reported questionnaire, and the exact prevalence of depressive symptoms may be underestimated. As a single-center study, our study population was small.

Conclusion

Depressive symptoms are prevalent in CHD patients. Mild and moderate-to-severe depressive symptoms are associated with higher risks of further CVD in CHD patients. Platelet function and behavioral mechanisms

may contribute to these risks. As depressive symptoms are preliminary manifestations of depression, assessment and intervention of depressive symptoms in the primary prevention in CHD patients are needed.

Abbreviations

ACS	Acute coronary syndrome
aCCI	age-adjusted Charlson Comorbidity Index
AHA	American Heart Association
AIDS	Acquired immune deficiency syndrome
CVD	Cardiovascular disease
COPD	Chronic pulmonary disease
CI	Confidence interval
CHD	Coronary heart disease
DSM-V	Diagnostic and Statistical Manual of Mental Disorders, fifth edition
HF	Heart failure
HR	Hazard ratio
HPA	Hypothalamic-pituitary-adrenal
ICD	International Classification of Diseases
LVEF	Left ventricular ejection fraction
MI	Myocardial infarction
PHQ-9	Patient Health Questionnaire
QCA	Quantitative coronary angiography

Supplementary Information

The online version contains supplementary material available at https://doi.org/10.1186/s12888-024-06117-z.

Supplementary Material 1

Data availability
The datasets generated and/or analyzed during the current study are not publicly available due the research is ongoing and the results have not been published, but are available from the corresponding author on reasonable request.

Declarations

Ethics approval and consent to participate
The study was approved by the Ethics Committee of the First Affiliated Hospital of Shantou University Medical College (approval number: No.2020-014), and was performed in accordance with the Declaration of Helsinki. All participants gave written informed consent.

Consent for publication
This manuscript contains only anonymised data. Participants gave consent for the publication of this data.

Competing interests
The authors declare no competing interests.

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