Comorbidity of Depression and Anxiety Leads to A Poor Prognosis Following Angina Pectoris Patients: A Prospective Study

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Research Article

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Abstract

Background: Depression and anxiety are two common psychiatric problems in patients with cardiovascular disease (CVD) and are associated with poor cardiac prognosis. The comorbidity of depression and anxiety is considered to be a more severe psychological status than non-comorbid psychiatric disorders. However, little is known about the relationship between depression or anxiety and noncardiac readmission. We conducted a prospective study on the prognostic impact of depression, anxiety, and comorbidity in angina pectoris (AP) patients.

Method: In this prospective study, 443 patients with AP were included in the analysis. Follow-up assessments were performed 1 year, and 2 years after patient discharges. Clinical outcomes of interest included readmission, major cardiovascular event (MACE), and composite events. Depression and anxiety symptom scores derived from the patient health questionnaire-9 (PHQ-9) and generalised anxiety disorder-7 (GAD-7) questionnaire were used to assess mood symptoms. Participants with symptom scores of ≥ 10 on both questionnaires formed the comorbidity group. Using multivariable Cox proportional hazards models to evaluate the impact of psychiatric symptoms on clinical outcomes.

Results: Among all the AP patients, 271 (61.2%) had non-depression symptoms and 172 (38.9%) were determined to have depression symptoms. As for anxiety symptoms, 316 (71.3%), and 127 (28.7%) patients had non-anxiety, and anxiety respectively. After controlling covariates, we found that patients who endured clinical depression (hazard ratio [HR] = 2.12, 95% confidence interval [CI] 1.04–4.31, p=0.038) and anxiety ([HR] 2. 65, 95% [CI] 1.12–6.30, p=0.027) had a high risk of noncardiac readmission. Compared to participants with no psychiatric symptoms, those with comorbidities of depression and anxiety presented a greater risk of MACEs ([HR] 2.38, 95% [CI] 1.11–5.10, p=0.025) and noncardiac readmission ([HR] 2.91, 95% [CI] 1.03–8.18, p=0.043) while the single-symptom group did not show any significances on all the events.

Conclusion: Depression and anxiety had predictive value for noncardiac readmission among patients with AP. Furthermore, prognoses were found to be worse for patients with comorbidities of depression and anxiety than those with single psychiatric symptoms. Additional attention needs to be focused on the initial identification and long-term monitoring of psychiatric comorbidity.

Background

Depression and anxiety have been linked to increased risk of coronary heart disease (CHD) and poor prognoses among patients with established cardiovascular disease[1 – 7]. Although the traditional risk factors for the development and prognosis of CHD are well known, psychosocial factors, especially depression and anxiety, are increasingly recognised[8]. A majority of studies have shown that depression is associated with a twofold to threefold increase in mortality or the risk of nonfatal cardiac events among patients with diagnosed CHD[9 – 11]. Anxiety is also an important predictor of recurring CV events among patients diagnosed with myocardial infarction or unstable AP[12 – 14]. With recurring CV events, the incidence of readmission also rises, which increases the cost of medical care and morbidity rates and affects the quality of life of patients[15]. Although the authors of many related studies paid attention to CVD, such as myocardial infarction or heart failure, and mainly focused on mortality or cardiac-related prognosis[16], there is a paucity of depression and anxiety research concentrated on the population of AP and noncardiac recurrent events.

Depression and anxiety often cooccur. Some studies have shown that there is a high degree of comorbidity between depression and anxiety[17 – 19], and this comorbidity may increase the risk of all-cause mortality, which leads to reductions in functional status compared to those of patients with only one of these disorders. It has also been suggested that patients with both depression and anxiety are at an increased risk of CVD[20]. However, few researchers have studied the population with both depression and anxiety and the association of this comorbidity with noncardiac readmission and MACEs.

We conducted a prospective cohort study to measure the prognostic impact of depression and anxiety on 443 AP patients. Our purpose was to examine the relationships between depression, anxiety, comorbidity, and noncardiac readmission in AP patients. We also analysed whether minor and major depression or anxiety symptoms, as assessed on a self-reported scale, can be used to predict the occurrence of CV events and readmission during a 29 months follow-up period after hospitalisation for AP.

Material And Methods

Study Design and Sample

This is a prospective study in which we investigated the association between depression, anxiety, comorbidity, and the occurrence of hospital readmission and recurrent CV events during a 29-month follow-up period among AP patients. Patients were admitted to Guangdong Provincial People's Hospital from October 2017 to January 2018 for a cross-sectional study and were followed up with every six months to observe their prognosis after discharges. Professional cardiologists in the hospital persistently incorporated 705 patients with suspected CHD into the study. All patients underwent examinations and therapies considered to be the most appropriate by the attending cardiologist. A total of 705 copies of the questionnaire were issued, and all the completed copies were retrieved. A well-trained psycho-cardiologist explained the psychiatric scale to each patient one day before the coronary angiography and assisted those with impaired vision or poor reading ability to understand the contents of the scale. The study was approved by the Medical Ethics Committee of Guangdong Provincial People's Hospital. Written informed consent was obtained from all participants. Details about our recruitment strategy and excluded patients have been described in our previous article[21]. A total of 443 individuals with AP (according to the Braunwald standard) and diagnosed CHD were included for analysis.

Follow-up
Follow-up assessments were performed by telephone at 1 year, and over 2 years after discharges. The average follow-up time was 26.33 ± 0.93 months. Endpoint events included all-causes mortality, readmission, nonfatal stroke, MACE, and readmission included cardiac and noncardiac readmissions. Moreover, the composite endpoint covered all the above events, as well as revascularisation and the recurrence of nonfatal myocardial infarction. MACE included death, nonfatal stroke, cardiac readmission, revascularisation, and recurrence of nonfatal myocardial infarction. Due to the insufficient samples of death, nonfatal stroke, revascularisation, and recurrence of nonfatal myocardial infarction, we did not analyse these clinical events.

### Depression And Anxiety Measures

Patient health questionnaire-9 (PHQ-9) and generalised anxiety disorder-7 (GAD-7) scales were used to assess depression and anxiety, respectively. We thoroughly elaborated on the utility of these scales in our previous article[21]. In our main analysis, a score of 5 or more was used as the depression symptom threshold because even mild depression symptoms, as classified by PHQ-9, are associated with relatively worse prognoses among cardiac patients[22]. We also used a cut-off score of 10 or more for the detection of clinical depression, and this diagnostic criteria has been shown to have 89% sensitivity and 89% specificity[23]. According to the wide use of the cut-off value of 5, we compared the differences between patients with GAD-7 scores of < 5 and ≥ 5. Moreover, a GAD-7 score of ≥ 10 indicated that the patient has clinical anxiety, in which the sensitivity and specificity for generalised anxiety disorder attained 89% and 82%, respectively[24, 25]. The Chinese version of PHQ-9 and GAD-7 has been validated in Chinese cardiac patients.[26, 27]

### Statistical Analysis

We compared the characteristics of patients with different depression and anxiety symptoms. The normality test was performed on continuous variables. Clinical characteristics were compared between patients with questionnaire scores of < 5, 5–9, and ≥ 10 with student's t-tests and Wilcoxon rank-sum tests for continuous variables and Chi-square or Fisher's exact test for categorical variables.

The survival analysis of depression and anxiety and baseline data was calculated using the Kaplan–Meier survival curve and the Log-Rank test. For statistically- or clinically-significant variables, the Cox proportional hazard regression model was used to adjust risk factors, including age, gender, education level, and severity of coronary artery stenosis. The specific classifications of covariates are illustrated in our previous article[21]. The interaction among all the covariates was considered. The HRs and 95% CIs of the endpoint events of the enrolled patients were calculated based on nonpsychiatric, mild psychiatric, and moderate to severe psychiatric symptom groups. A P value of < 0.05 indicates that the difference is statistically significant.

### Results

#### Prevalence and Correlates of Depression and Anxiety

A total of 443 patients were enrolled in the study and assessed using PHQ-9 and GAD-7 scales. The baseline characteristics of the participants are shown in Table 1. The average participant was 63.9 years old (± 9.8 years), and there were 337 (76.1%) males and 106 females (23.9%). Among all the AP patients, there were 271 (61.2%) with no depression symptoms (PHQ-9 scores of < 5) and 172 (38.9%) with depression symptom (PHQ-9 scores of ≥ 5), of which 49 (11.1%) had clinical depression (PHQ-9 scores of ≥ 10). As for anxiety symptoms, 103 (23.3%), 13 (2.9%), and 11 (2.5%) patients had mild, moderate, and severe anxiety symptoms. The correlates of depression and anxiety were shown in our previous article[21].
Table 1
Baseline characteristic of depression, anxiety and comorbidity in AP patients.

| Variates                      | Total | Non-depressed (score < 5) | Depressed (N = 172) | Non-anxious (score < 5) | Anxious (N = 127) | Clinical Comorbidity |
|-------------------------------|-------|---------------------------|---------------------|-------------------------|-------------------|----------------------|
|                               |       | N = 271                   | mild dep. (5 ≤ score < 10) | mod-severe dep. (score ≥ 10) | N = 316           | mild anx. (5 ≤ score < 10) | mod-severe anx. (score ≥ 10) | (N = 19) |
| Age, mean ± SD, y             |       | 63.9 ± 9.8                | 63.0 ± 9.5          | 65.5 ± 10.0             | 64.9 ± 10.8       | 64.2 ± 9.9           | 64.4 ± 8.9             | 62.5 ± 12.7 | 64 ± 9.8 |
| Male, No. (%)                 |       | 337 (76.1)                | 223 (82.3)          | 79 (64.2)               | 35 (71.4)         | 256 (81.0)          | 63 (61.2)              | 18 (75.0) | 14 (73.7) |
| Married, No. (%)              |       | 412 (93.0)                | 258 (95.2)          | 112 (91.1)              | 42 (85.7)         | 294 (93.0)          | 96 (93.2)              | 22 (91.7) | 17 (89.5) |
| Divorced or Widowed, No. (%)  |       | 31 (1.6)                  | 13 (4.8)            | 11 (8.9)                | 7 (14.3)          | 22 (7.0)            | 7 (6.8)                | 2 (8.3) | 2 (10.5) |
| Severity of coronary stenosis, No. (%) | | 93 (21.0) | 51 (18.8) | 33 (26.8) | 9 (18.4) | 56 (17.7) | 32 (31.1) | 5 (20.8) | 4 (21.1) |
| 2                             | 82 (18.5) | 54 (19.9) | 19 (15.4) | 9 (18.4) | 64 (20.3) | 11 (10.7) | 7 (29.2) | 5 (26.3) |
| 3                             | 268 (60.5) | 166 (61.3) | 71 (57.7) | 31 (63.3) | 196 (62.0) | 60 (58.3) | 12 (50.0) | 10 (52.6) |

*: Clinical comorbidity was combined with clinical depression and clinical anxiety (both score ≥ 10).

Abbreviation: dep.: depression; mod-severe dep.: moderate or severe depression; anx.: anxious; mod-severe anx.: moderate or severe anxious.

Follow-up Events

All 443 patients received follow-up calls for readmissions, MACEs, and composite endpoints. The censored data contained loss to follow-up and endpoint events that had not occurred at the end of the study. There were 88 MACEs and 129 composite endpoints during the 29-month follow-up period. In this study, there were 74 cardiac readmissions and 46 noncardiac readmissions (Figure 1). The incidence of follow-up events in different groups is shown in Table 2.

Table 2
The incidence of follow-up events in depression, anxiety and comorbidity groups.

| Event | No. (%) | Non-depressed (score < 5) | Depressed (N = 172) | Non-anxious (score < 5) | Anxious (N = 127) | Clinical Comorbidity* N = 19 |
|-------|---------|---------------------------|---------------------|-------------------------|-------------------|--------------------------|
|       |         | N = 271                   | mild dep. (5 ≤ score < 10) | mod-severe dep. (score ≥ 10) | N = 316 | mild anx. (5 ≤ score < 10) | mod-severe anx. (score ≥ 10) | |
| Cardiac | 74      | 44 (59.5)                 | 21 (28.4)           | 9 (12.2)                | 54 (73.0)   | 15 (20.3)            | 5 (6.8) | 4 (21.0) |
| noncardiac | 46      | 19 (41.3)                 | 17 (37.0)           | 10 (21.7)               | 32 (70.0)   | 8 (17.4)            | 6 (13.0) | 5 (10.9) |
| Mace   | 88      | 49 (18.1)                 | 25 (20.3)           | 14 (28.6)               | 61 (69.3)   | 18 (20.5)           | 9 (10.2) | 8 (9.1)  |
| Composite | 129     | 69 (25.5)                 | 39 (31.7)           | 21 (42.9)               | 91 (70.5)   | 24 (18.6)           | 14 (10.9) | 12 (9.3) |

*: Clinical comorbidity was combined with clinical depression and clinical anxiety (both score ≥ 10).

Abbreviation: dep.: depression; mod-severe dep.: moderate or severe depression; anx.: anxious; mod-severe anx.: moderate or severe anxious.

Unadjusted HRs were estimated from a Cox proportional regression model for patients with nonpsychiatric, mild psychiatric, and moderate to severe psychiatric symptoms. Between the nondepressed and depressed group (see Additional file 1: Table S1), a significant difference of depression symptoms...
Discussion

Severity of coronary artery stenosis, comorbidity was found to be an even stronger predictor of MACE ([HR] 2.38) and composite endpoint ([HR] 2.52). We performed Kaplan–Meier (KM) curves of endpoint events among the three groups (Fig. 2). After controlling for age, gender, marriage, and severity of coronary artery stenosis, comorbidity was found to be a strong predictor of MACE ([HR] 2.71, 95% [CI] 1.15–6.40, p = 0.023) and the composite endpoint event ([HR] 2.15, 95% [CI] 1.23–3.74, p = 0.007) while MACE was found to be borderline significant in this group ([HR] 1.98, 95% [CI] 0.99–3.94, p = 0.053).

### Table 3

| Event       | Clinical dep. vs not clinical dep. | Clinical anx. vs not clinical anx. |
|-------------|-----------------------------------|------------------------------------|
|             | Unadjusted                       | 95% CI                             | P       | Adjusted                       | 95% CI                             | P       | Unadjusted                       | 95% CI                             | P       | Adjusted                       | 95% CI                             | P       |
| Noncardiac  | 2.32                             | 1.15–4.68                          | 0.018* | 2.12                             | 1.04–4.31                          | 0.038* | 2.714                             | 1.15–6.40                          | 0.023* | 2.65                             | 1.12–6.30                          | 0.027* |
| Cardiac     | 1.09                             | 0.54–2.19                          | 0.810  | 1.22                             | 0.61–2.46                          | 0.569  | 1.259                             | 0.51–3.12                          | 0.619  | 1.26                             | 0.51–3.13                          | 0.621  |
| Mace        | 1.52                             | 0.86–2.70                          | 0.569  | 1.62                             | 0.91–2.88                          | 0.099  | 1.978                             | 0.99–3.94                          | 0.053  | 2.02                             | 1.01–4.05                          | 0.046* |
| Composite   | 1.59                             | 0.997–2.54                         | 0.052  | 1.60                             | 1.001–2.57                         | 0.049* | 2.146                             | 1.23–3.74                          | 0.007* | 2.20                             | 1.26–3.84                          | 0.006* |

*:P < 0.05

Abbreviation: dep.: depression; anx.: anxious

The multivariable-adjusted analysis of depression and anxiety included four factors, age, gender, education, and severity of coronary artery stenosis. Compared to patients without depression symptoms, patients with depression symptoms (as indicated by PHQ-9 scores of ≥ 10) remained at higher risk for noncardiac readmission ([HR] 1.98, 95% [CI] 1.08–3.63, p = 0.03) (see Additional file 1: Table S1). Participants with clinical depression ([HR] 2.12, 95% [CI] 1.04–4.31, p = 0.038) and clinical anxiety ([HR] 2.65, 95% [CI] 1.12–6.30, p = 0.027) were found to be at greater risk of noncardiac readmission than others, even after adjustment. Moreover, clinical anxiety participants reported significantly more MACEs ([HR] 2.02, 95% [CI] 1.01–4.05, p = 0.046) than nonclinical anxiety participants after adjustment (Table 3). In addition to depression and clinical anxiety, old age was identified as a risk factor for noncardiac readmission events. No statistical significance was shown between depression or anxiety and cardiac readmission events.

Furthermore, we divided participants with psychiatric disorders into three groups: those with no mental disorders, those with only one mental disorder, and those with both depression and anxiety. The unadjusted analysis (Table 4) showed that comorbidity had great significance in increasing noncardiac readmission ([HR] 2.34, [CI] 1.39–10.1, p = 0.009), MACE ([HR] 2.27, [CI] 1.07–4.81, p = 0.033), and composite endpoint ([HR] 2.44, [CI] 1.31–4.52, p = 0.005). We performed Kaplan–Meier (KM) curves of endpoint events among the three groups (Fig. 2). After controlling for age, gender, marriage, and severity of coronary artery stenosis, comorbidity was found to be an even stronger predictor of MACE ([HR] 2.38) and composite endpoint ([HR] 2.52).

### Table 4

| Event       | Depression or anxiety vs no psychiatric symptom | Comorbidity vs no psychiatric symptom |
|-------------|-----------------------------------------------|--------------------------------------|
|             | Unadjusted HR | 95% CI | P       | Adjusted HR | 95% CI | P       | Unadjusted HR | 95% CI | P       | Adjusted HR | 95% CI | P       |
| Noncardiac  | 2.29           | 0.91–5.78 | 0.078 | 2.11       | 0.82–5.38 | 0.120 | 3.74       | 1.39–10.1 | 0.009* | 2.91       | 1.03–8.18 | 0.043* |
| Cardiac     | 0.97           | 0.41–2.28 | 0.940 | 1.24       | 0.52–2.97 | 0.623 | 1.25       | 0.45–3.50 | 0.670  | 1.32       | 0.47–3.7  | 0.604  |
| Mace        | 1.05           | 0.47–2.34 | 0.899 | 1.19       | 0.63–2.68 | 0.670 | 2.27       | 1.07–4.81 | 0.033* | 2.38       | 1.11–5.10 | 0.025* |
| Composite   | 1.16           | 0.61–2.21 | 0.643 | 1.22       | 0.64–2.34 | 0.549 | 2.44       | 1.31–4.52 | 0.005* | 2.52       | 1.35–4.69 | 0.004* |

*:P < 0.05

Abbreviation: dep.: depression; anx.: anxious

The results for clinical depression and clinical anxiety as predictors of follow-up events are shown in Table 3.
Following our previous cross-sectional analysis, in this study, we followed-up with the patients for 6 months, 1 year, and over 2 years, and several clinical outcomes were observed. We found that, whether or not multiple factors were adjusted, patients enduring AP with depression symptoms had a significantly high rate of noncardiac readmission and incidence of composite endpoint events while AP patients with anxiety symptoms did not. People with clinical depression and anxiety were found to be at an increased risk of noncardiac readmission and composite endpoint events. Meanwhile, clinical anxiety was found to be associated with MACES. What we discovered but many other researchers did not keep an eye on was the relationship between the comorbidity of depression and anxiety and prognosis in AP patients, and we elaborated on the fact that this comorbidity might be a predictor of increased risk of noncardiac readmission, MACES, and composite endpoints.

To our knowledge, this is the first study with an examination of the relationship between depression, anxiety, comorbidity, and noncardiac readmission among AP patients. Current studies underscore the complex relationship between depressive or anxiety symptoms and prognosis in patients with CVD. However, most related studies were focused on populations with myocardial infarction or heart failure, and few medical researchers pay attention to AP. Besides, the endpoint events of many previous studies were normally related to death or reoccurrence of cardiovascular admission instead of noncardiac readmission.

**Association of Depression and Prognosis**

In our study, patients with clinical depression symptoms were found to have a 3.41-times higher risk of death and 2.32-times higher risk of noncardiac readmission than those who did not suffer from clinical depression. Pederson et al.[28] showed that depression might be an unrecognised and possibly changeable independent risk factor for unexpected readmission or premature death. Depression is difficult to detect in an acute care environment and is often undertreated. Patients with moderate to severe depression symptoms at discharge with no history of depression may face a twofold increase in the risk of short-term hospital readmission or death. Mitchell et al.[29] reported that the risk of hospital readmission or emergency department treatment within 30 days after discharge among patients with PHQ-9 scores of \( \geq 5 \) was increased by 73%. Cancino et al.[30] reported a 49% increase in readmission within 30 days of discharge for patients with mild depression and a 96% increase for patients with moderate to severe depression. Moraska et al.[31] found that high clinical depression scores on the PHQ-9 were associated with increased risk of hospitalisation (adjusted HR: 1.79, 95% CI: 1.30–2.47). In a small study of 144 patients, Kartha et al.[32] found that patients who were diagnosed with severe depression using a standardised scoring algorithm based on PHQ-9 were three times more likely than others to be rehospitalised within 90 days of discharge. We used PHQ-9 scores of \( < 5, 5–9, \) and \( \geq 10 \) as the thresholds for non-depression, mild depression, and moderate to severe depression. We also found that both mild and moderate to severe depression symptoms were associated with noncardiac readmission and composite events.

Previous literature has shown that CHD combined with depression symptoms will lead to an increase in mortality and rehospitalisation, thereby aggravating the severity of the disease, medical expenses, and waste of resources. A cumulative number of studies[33] have shown that comorbidity of mental and physical illnesses would increase the severity of the disease, frequencies of readmissions, and medical expenses. Even the presence of isolated psychiatric symptoms might bring the risk of medical comorbidities[34]. People with psychiatric symptoms, but no psychiatric diagnosis, were prone to more lifelong diseases, healthy problems, and length of hospital stay than those without psychiatric diagnosis or symptoms. Our study has shown that both mild depression and moderate to severe depression could be risk factors for hospital readmission.

**Association of Anxiety and Prognosis**

Previous literature has shown that anxiety is a significant risk factor for recurrent CV events or mortality[3, 13, 35-37]. Although we did not analyse death, revascularisation, or nonfatal myocardial infarction independently due to a lack of valid samples, we summed up cardiac readmission, nonfatal stroke, and all the above as MACES. Tully et al.[38] found that in patients with confirmed CHD, anxiety was a prognostic risk of subsequent MACES, such as myocardial infarction, left ventricular failure, and stroke. Another study showed that generalised anxiety disorder increased the MACE risk of acute coronary syndrome outpatients by nearly two times within two years[39]. Similar to previous researchers, we identified an association between clinical anxiety and poor CVD prognoses. Although there are few studies in which the authors analysed the relationship between anxiety and noncardiac readmission, we found a positive correlation between clinical anxiety and noncardiac readmission. We did not observe this association in the anxiety symptom group (GAD-7 scale > 5), possibly because the anxiety symptom is transient and usually triggered by a perceived threat, and once the threat diminishes, the anxiety will diminish too. It has been proven that anxiety is prone to poor quality of life of patients with CHD, especially after an acute coronary syndrome event, and that anxious patients have more disabilities and somatic symptoms than others[40-42].

**Association of Comorbidity and Prognosis**

The authors of many related studies analysed depression or anxiety as single risk indicators, but we studied them as a comorbid symptom. We discovered that most clinical anxiety patients also have depression symptoms. Denollet and Strik et al.[35, 43] reported that a mixed emotional state consisting of anxiety and depression symptoms, not just depression, was the most common manifestation of patients with myocardial infarction[43]. The author, thus, concluded that anxiety was a common factor of depression after myocardial infarction. A similar symptom overlap was found by Frasure-Smith[39]. Some authors[44, 45] found that this connection was produced by the same dysfunctional biology or that depression and anxiety might be derived from parallel genetic dispositions. Furthermore, Scott et al. showed that comorbid depressive-anxiety disorder increased the risk of a series of physical symptoms occurring at the same time[46]. In a follow-up study of women with suspected myocardial ischemia, depression or anxiety could be used to predict CVD events and death more accurately than the independent symptoms[47]. Phillip et al.[48] demonstrated that even after adjustment, the strongest association between CVD and death from all causes appeared in major depressive disorder and generalised anxiety disorder comorbidities.
Similar to previous researchers, we identified a greater risk of MACEs, noncardiac readmission, and composite events among participants with depression and anxiety.

Limitations

First, due to the small sample size and prognostic events, some statistical analyses in this study may suffer from overfitting. Second, patients with clinical depression or anxiety were categorised into one group because there were only five patients who had anxiety rather than depression, but this did not affect the analysis of comorbidity and prognosis. Although we did not carry out professional psychiatric interviews to confirm the diagnosis of psychiatric symptoms, we used an easy-to-deploy screening tool that has been fully validated. Moreover, our research was conducted in only one hospital specialised in cardiac care, which ensured the consistency of examination tools, methods, and follow-up times and procedures but limited the generalizability of the findings.

Conclusion

AP patients with depression symptoms tend to have a higher incidence of noncardiac readmission and composite events than others. Clinical anxiety patients were found to be at increased risk of MACEs. Besides, depression and anxiety seemed to appear simultaneously, and this combination may lead to a worse prognosis than one disorder alone. How clinicians understand this overlap of symptoms will help them determine diagnoses, treatment options, and possible referrals for additional testing and services. In the future, researchers should use effective and reliable measurement methods to further examine the relationship between depression, anxiety, and CHD while paying close attention to the overlapping symptoms.

Abbreviations

CVD: cardiovascular disease; AP: angina pectoris; MACE: major cardiovascular event; PHQ: patient health questionnaire; GAD: generalised anxiety disorder; HR: hazard ratio; CI: confidence interval; CHD: coronary disease; CV: cardiovascular; KM: Kaplan–Meier

Declarations

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None.

Authors’ contributions

BB surveyed the prognostic information. HY collected the baseline data. HW, FL, YL, and AL entered data into the database. BB, HM, and LG did the statistical analyses. BB and HY wrote the first draft. QG, LG, and HM revised the paper. QG, LG were senior physicians principally responsible for the study. All authors read and approved the final manuscript.

Ethics approval and consent to participate

Ethical approval was given by the medical ethics committee of Guangdong General Hospital with the following reference number: No.GDREC2017203H. All participants gave written informed consent.

Consent for publication

Not applicable.

Availability of data and materials

The datasets obtained and/or analysed during the current study are available from the corresponding author on reasonable request.

Competing interests

The authors declare that they have no competing interests.

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This study was a prospective cohort study, following STROBE Statement. All methods were carried out in accordance with relevant guidelines and regulations.

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