Associations of mood symptoms with NYHA functional classes in angina pectoris patients: a cross-sectional study

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Abstract

Background: Depression and anxiety are prevalent and associated with a worse prognosis in coronary heart disease (CHD) patients. However, the influence of disease severity on mood symptoms is unknown. The specific associations of mood symptoms with NYHA classes remain unexplored.

Methods: In this cross-sectional study, 443 consecutive inpatients with angina pectoris (AP) confirmed by angiography were included into analysis. Somatic and cognitive symptom scores derived from Patient Health Questionnaire (PHQ-9) and Generalized Anxiety Disorder Scale (GAD-7) were used to assess mood symptoms. Predictors for depression and anxiety with strict and lax standards were compared. We hypothesized NYHA classification to be an indicator of disease severity through analyses with clinical features using ordinal logistic model. Applying both binary and ordinal logistic models, we evaluated the associations of mood symptoms with NYHA classes.

Results: Discrepancy of disease severity existed between the depressed and nondepressed. NYHA classification was proved to be an integrated index under influence of age, coronary stenosis, heart failure and diabetes. NYHA class I and II individuals with AP were at equivalent risk for depression (NYHA II vs I: binary model OR 1.32 (0.59,2.96), p = 0.50; ordinal model OR 1.17 (0.73,1.88), p = 0.52), however NYHA class III/IV patients shared a sharply higher risk (NYHA III/IV vs I: binary model OR 3.32 (1.28,8.61), p = .013; ordinal model OR 3.94 (2.11,7.36), p < .001). Analyses on somatic and cognitive depressive symptoms confirmed this finding and hinted a greater impact of education background on mood when patient’s condition is unstable. Anxiety seemed in the whole picture irrelevant with NYHA classes. Comparing with NYHA class I/II, AP patients in NYHA class III/IV tended to be less anxious. However, when CHD became unstable, the calmness may immediately be broken up. A great distinction of the ratio of anxiety and depression symptom scores between NYHA class III/IV stable and unstable AP patients (p = .018) was observed.

Conclusions: Mood symptoms in CHD patients are to a great extend derived from disease itself. Only for patients with relatively serious physical condition, unexpected discomforts caused by disease notably impact the emotions. Education background tends to influence the mood especially when disease is still unstable.

Keywords: Depression, Anxiety, Angina pectoris, New York heart association class
Background

Depression and anxiety, more prevalent in CHD patients than the general population, are associated with an increased risk of worse prognosis [1–4]. However, these associations in many studies weaken or vanish when adjusted for variables that can reflect physical conditions [5–7], indicating a close correlation between emotional symptoms and disease severity [8–10]. Few researchers have particularly studied the alteration pattern of mood symptoms along with deterioration of CHD. Reasons for this phenomenon lie: (1) no explicit criteria exists for disease severity grading; (2) it seems a common sense for seriously ill patients to be in a bad state of mind. It is obvious that disease severity influences the clinical outcomes. Knowing the specific association of mood symptoms with disease severity may help to reach a better understanding of the impact of mood on prognosis, see through some confusing findings about anxiety and depression and find out the most efficient therapies for patients.

Searching through the articles, there are hardly any researches adjusting with same variables to eliminate the influence of disease severity on outcomes. New York Heart Association (NYHA) classification [11], as a widely used clinical tool which emphasizes the subjective cardiac symptoms on daily activity, possesses good predictive value of cardiopulmonary function [12, 13], physical status [14], quality of life [15] and clinical outcomes for example stroke [16], hospitalization [15] and mortality [15, 17]. We hypothesize NYHA class to be a simple but integrated indicator of physical status and can be utilized to assess the associations of mood symptoms with physical condition.

To fully understand the differences of emotional state under different physical condition, and under the background that several recent studies report that somatic rather than cognitive depressive symptoms correlate with lower heart rate variability [18] and predict worse long-term outcomes in CHD patients [19–22], we split PHQ-9 into somatic and cognitive depressive symptoms based on confirmatory factor analysis and analyzed the correlation of depression, anxiety and their internal relations with NYHA classes in both stable angina pectoris (SAP) and unstable angina pectoris (UAP) patients. Through all these analyses, we hoped to reach a better understanding of mood symptoms in CHD patients and its change pattern along with worsening of physical condition. This may be of guiding significance for the timing of intervention and the selection of treatment.

Methods

Design

This is a cross-sectional study for investigating the discrepancies of mood symptoms of Chinese patients in different coronary condition and CHD subtypes and the determinants for depression and anxiety. 705 consecutive inpatients with primary diagnosis of CHD at admission in Guangdong Provincial People’s Hospital were surveyed between October 2017 and January 2018. Results of clinical tests and coronary angiography (CAG) as well as discharge diagnosis were acquired from medical records to ensure the correct patient categorization (Fig. 1). Chinese version of PHQ-9, GAD-7 and a self-designed short questionnaire about valuable information were applied. All participants were surveyed in comparatively stable condition and under supervision of one well-trained psycho-cardiologist, who was responsible for elucidating the PHQ-9 and GAD-7 questionnaires, assisting patients with failing eyesight or low literacy and conducting a concise review to guarantee data accuracy.

Patients selection

The current paper concerns a cross-sectional analysis of the baseline status of the angina pectoris inpatients. Inpatients with main discharge diagnosis of angina pectoris and a history of coronary artery bypass grafting or coronary stent implantation or with at least one narrow epicardial coronary artery (≥50%) confirmed by CAG during this hospitalization were included. Participants with severe valvular heart disease, or severe cardiomyopathy unlikely caused by coronary stenosis, or other complications that might interfere the mechanism that symptoms were primarily resulted from the narrowed coronary were excluded, leaving a sample of 443 subjects (187 SAP and 256 UAP according to Braunwald criteria [23]) into analysis (Fig. 1). The study was approved by the Medical Ethics Committee of Guangdong Provincial People’s Hospital. Written informed consent were obtained from all participants.

New York heart association classification

NYHA classification [11] is a widely used clinical tool that measures the cardiac functional capacity. The assessment of NYHA class was mainly based on the medical records at admission. However, for the missing data, two cardiologists separately estimated the NYHA class and discussed with a third doctor if inconsistence appeared. To unify the criteria, we defined that conditions triggering fatigue, palpitation, dyspnea, or anginal pain of NYHA class III patients were walking 20–100 m or climbing one flight of stairs at normal pace.

Patient health questionnaire – 9

The PHQ-9 is a valid screening tool for depression in accordance with DSM-IV criteria for major depressive disorder (MDD) [24, 25]. The 9 items which evaluate the depression symptoms are rated on a 0–3 Likert-type
A number of researches have proved that PHQ-9 has two-factor structure and can be divided into somatic and cognitive depression symptom subscales. To be accurate, we listed 5 representative models (one-factor model: Model 1 [28]; four two-factor models: Model 2a [29–31], Model 2b [18, 19, 21], Model 2c [32–34], Model 2d [30]) (see Additional file 1: Table S1), and implemented confirmatory factor analysis (CFA) with items as continuously-scaled and maximum likelihood estimation with a mean-adjustment analysis method for non-normality data using Mplus 7 software. Model 2c turned out to be the best model with fit indices indicating adequately fit [35]. Internal consistency coefficients (Cronbach’s α) were 0.76 for factor 1 (somatic) and 0.79 for factor 2 (cognitive). The error-free factors were correlated at 0.85. We accordingly calculated the sum scores of the two dimensions as factor scores (somatic and cognitive).

**Generalized anxiety disorder scale – 7**

GAD-7 is a 7-item self-report scale based on DSM-IV criteria [36]. Items of GAD-7 are also rated on a 0–3 Likert-type scale. It measures the severity of generalized anxiety disorders and also exhibits good convergent validity when compared with other commonly-used anxiety scales [37]. Total score ranges from 0 to 21 with a score of 0–4, 5–9, 10–14, 15–21 representing normal, mild, moderate and severe levels of anxiety, respectively. Analogously, GAD-7 score ≥ 10 indicates clinical anxiety, since the sensitivity and specificity for generalized anxiety disorder reached 89 and 82%, respectively. The minimal clinical important difference has not been established. Considering the widely use of the cutoff of 5 to distinguish patients from normal state, differences between patients with GAD-7 score < 5 and ≥ 5 have also been compared. The Chinese version of GAD-7 has been validated in Chinese cardiac patients [38]. Previous studies have shown the underlying structure of GAD-7 to be unidimension [37, 39].
Coronary artery stenosis severity, education background and creatinine clearance

Coronary artery stenosis severity was assessed according to the number of three main vessels with stenosis ≥50% as shown by angiography. However, a ≥30% lumen stenosis in left main coronary artery would be directly classified as the highest level of severity.

Due to the difference of education systems, the school year for participants in each stage may not be the same. The four levels of education background represented illiteracy or primary school, junior high school, senior high school and technical school or college or university level.

Creatinine clearance was estimated using the Cockcroft-Gault formula with the value of serum creatinine.

Statistical analysis

Statistical analysis mainly contained three parts: (1) We first compared patients’ characteristics according to different cutoffs for depression and anxiety to figure out the dominant predictors of mood disturbance; (2) Next, we evaluated whether NYHA classification could be an integrated index indicating patients’ status; (3) Finally, we explored the association between NYHA classes and depression or anxiety symptoms.

- Part 1 Clinical characteristics were compared between patients with questionnaire score < 10 and ≥10 as well as < .5 and ≥ .5 with Student’s t-test and Wilcoxon rank-sum test for continuous variables and Chi-square or Fisher’s Exact test or Cochran-Mantel-Haenszel test for categorical variables.

- Part 2 Since only 6 patients were categorized as NYHA IV, we incorporated NYHA III and NYHA IV and compared clinical characteristics between the 3 groups using one-way analysis of variance (ANOVA) or chi-square tests or Kruskal-Wallis test. We chose to model NYHA classes (I, II, III/IV) as ordinal outcomes using ordinal logistic regression, adjusting for all physical condition variables with a significant association in univariate analyses along with age, sex, body mass index and education background.

- Part 3 We conducted ordinal logistic regression analyses taking into account all depression and anxiety severities as ordinal outcomes (0, 1, 2, 3) and compared the results with binary logistic regression models, which treated questionnaire scores as dichotomous outcome variables with the cutoff point of 10. Analogous analyses were also made with somatic and cognitive depressive symptom scores through converting them to dichotomous variables depending on whether the upper quartile was reached. All models were adjusted for age, sex, body mass index (BMI) and education background. The correlation between PHQ-9 and GAD-7 scores was assessed using Pearson’s correlation coefficients. Their internal relation of AP, SAP and UAP patients in different NYHA classes were analyzed with linear regression model and plotted with R software (version 3.5.1). Ratio of anxiety and depression symptom score between SAP and UAP groups was compared using Student’s t-test.

Except for data of Nt-ProBNP and LVEF, model independent variates were missing for at least 1 study variate in 14 patients (3.2%), with no study variate having > 1.8% missing data. Mean or median imputation depending on distribution pattern were applied using SAS STDIZE procedure. All tests for significance were two-tailed at the threshold of 0.05 and were performed with SAS 9.4 software.

Results

Predictors of elevated depression and anxiety symptoms

Of the 443 consecutive angina pectoris inpatients screened, 123 (27.8%), 34 (7.7%) and 15 (3.4%) inpatients were categorized as with mild, moderate and moderately severe to severe depression symptom, 103 (23.3%), 13 (2.9%), 11 (2.5%) with mild, moderate and severe anxiety symptom. Patients’ characteristics were presented in Table 1 and Additional file 2: Table S2.

Compared with individual who had no or mild depression symptom, those with clinical depression (PHQ-9 score ≥10) were more likely to be less educated (p = .041), with higher NYHA classes (p = .017) and a history of antidepressant treatment (p < .001). A slight trend toward significance was observed for a prescription of loop diuretics (p = .062) or aldosterone receptor antagonist (p = .083). However, when comparing those not depressed with depressed patients, features that marked worse physical status became quite outstanding (see Table 1). Besides, the depressed participants tended to be older (p = .019), female (p < .001), without marriage partner (p = .023) and less educated (p < .001). The average scores of somatic depressive depression symptoms in each depression severity groups were 1.39 (SD 1.18), 4.37 (SD 1.44), 8.90 (SD 2.81), taking up 78.1, 68.9 and 63.3% of the total score, respectively.

Unlike depression, no difference except for an antidepressant treatment history (p = .10) was observed between the patients with or without clinical anxiety. Interestingly in comparison of the anxious and non-anxious, we noticed that anxious subjects tended to be female (p < .001), less educated (p = .001), with less severe coronary artery stenosis (p = .050) and a history of antidepressant treatment (p < .001) (see Additional file 2: Table S2).

NYHA classes and clinical characteristics

In univariate analyses (Table 2), we discovered that significant differences existed among groups in age (p
Table 1 Characteristics of patients stratified by depression severity

| Variables                  | Total   | Non-depressed | depressed mild dep. | mod-severe dep. | p value | p value |
|---------------------------|---------|---------------|---------------------|-----------------|---------|---------|
|                           | N = 443 | N = 271       | N = 123             | N = 49          |         |         |
|                           |         | 61.2% (score < 5) | 27.8%              | 11.1% (score ≥ 10) |         |         |
| Demographics              |         |               |                     |                 |         |         |
| Age, mean ± SD, y         | 63.9 ± 9.8 | 63.0 ± 9.5    | 65.5 ± 10.0         | 64.9 ± 10.8     | 0.47    | .019    |
| Male, No. (%)             | 337(76.1) | 223(82.3)     | 79(64.2)            | 35(71.4)        | 0.42    | <.001   |
| Body mass index, mean ± SD, kg/m² | 24.5 ± 3.1 | 24.6 ± 2.7    | 24.4 ± 3.5          | 24.2 ± 3.7      | 0.51    | 0.41    |
| Clinical characteristics  |         |               |                     |                 |         |         |
| NYHA class I-IV, No. (%)  | .017    |               | <.001               |                 |         |         |
| Class I                   | 115(26.0) | 79(29.2)      | 27(22.0)            | 9(18.4)         |         |         |
| Class II                  | 261(58.9) | 169(62.4)     | 66(53.7)            | 26(53.1)        |         |         |
| Class III-IV              | 67(15.1)  | 23(8.5)       | 30(24.4)            | 14(28.6)        |         |         |
| Ejection Fraction, mean ± SD, % | 59.3 ± 11.0 | 60.3 ± 9.9 N = 238 | 56.4 ± 12.3 N = 112 | 60.8 ± 12.0 N = 43 | 0.33    | .024    |
| NT-ProBNP, median (interquartile), pg/mL | 123(50–382) | 106(48–309) | 180(72–721) N = 231 | 124(47–341) N = 39 | 0.98    | <.013   |
| Creatinine Clearance, mean ± SD, ml/min | 65.5 ± 21.7 | 68.4 ± 20.1 | 61.1 ± 22.4 | 60.7 ± 26.3 | 0.17    | <.001   |
| Type of angina pectoris, No. (%) |         |               |                     |                 | 0.92    | 0.94    |
| Unstable angina pectoris  | 256(57.8) | 157(57.9)    | 71(57.7)            | 28(57.1)        |         |         |
| Stable angina pectoris    | 187(42.2) | 114(42.1)    | 52(42.3)            | 21(42.9)        |         |         |
| Severity of coronary stenosis, No. (%) |         |               |                     |                 | 0.62    | 0.34    |
| 1                         | 93(21.0)  | 51(18.8)     | 33(26.8)            | 9(18.4)         |         |         |
| 2                         | 82(18.5)  | 54(19.9)     | 19(15.4)            | 9(18.4)         |         |         |
| 3                         | 268(60.5) | 166(61.3)    | 71(57.7)            | 31(63.3)        |         |         |
| Social factors            |         |               |                     |                 | .041    | <.001   |
| Education, No. (%)        |         |               |                     |                 |         |         |
| less than 6 years         | 115(26.0) | 50(18.5)     | 44(35.8)            | 21(42.9)        |         |         |
| 7–9 years                 | 126(28.4) | 85(31.4)     | 31(25.2)            | 10(20.4)        |         |         |
| 10–12 years               | 97(21.9)  | 63(23.2)     | 25(20.3)            | 9(18.4)         |         |         |
| more than 12 years        | 105(23.7) | 73(26.9)     | 23(18.7)            | 9(18.4)         |         |         |
| Marriage, No. (%)         | .068    |               | .023                |                 |         |         |
| Married                   | 412(93.0) | 258(95.2)    | 112(91.1)           | 42(85.7)        |         |         |
| Divorced or Widowed or Single | 31(7.0)  | 13(4.8)      | 11(8.9)             | 7(14.3)         |         |         |
| Medical history, No. (%)  |         |               |                     |                 |         |         |
| Hypertension              | 276(62.3) | 162(59.8)    | 78(63.4)            | 34(69.4)        | 0.25    | 0.26    |
| Diabetes mellitus         | 154(34.8) | 83(30.6)     | 52(42.3)            | 19(38.8)        | 0.53    | .022    |
| Prior PCI                 | 167(37.7) | 102(37.6)    | 43(35.0)            | 22(44.9)        | 0.27    | 0.97    |
| History of antidepressant treatment | 17(3.8) | 4(1.5) | 6(4.9) | 7(14.3) | <.001 | .001 |
| Medication use, No. (%)   |         |               |                     |                 |         |         |
| ACEI or ARB               | 317(71.6) | 190(70.1)    | 93(75.6)            | 34(69.4)        | 0.72    | 0.40    |
| β blocke r               | 384(86.7) | 230(84.9)    | 109(88.6)           | 45(91.8)        | 0.26    | 0.16    |
| Mono antiplatelet therapy | 63(14.2)  | 38(14.0)     | 19(15.4)            | 6(12.2)         | 0.67    | 0.88    |
| Dual antiplatelet therapy | 370(83.5) | 228(84.1)    | 100(81.3)           | 42(85.7)        | 0.66    | 0.66    |
| Statin                    | 430(97.1) | 266(98.2)    | 120(97.6)           | 47(95.9)        | 0.36    | 0.46    |
| Aldosterone receptor antagonist | 42(9.5)  | 16(5.9)      | 18(14.6)            | 8(16.3)         | 0.83    | .001    |
Associations of NYHA classes with depression and anxiety

The Pearson’s correlation coefficients of PHQ-9 and GAD-7 scores was 0.72 ($p < .001$). As shown in Fig. 2, a non-differential interrelation of depression and anxiety in different NYHA classes in AP (Fig. 2A) and UPA patients (Fig. 2B) was observed. For SAP, subjects in NYHA class III/IV seemed to be less anxious than those in NYHA class I and II under the same level of depression (Fig. 2B). The ratio of anxiety and depression symptom scores differed significantly between SAP and UAP patients in NYHA class III/IV with at least mild depression symptoms ($p = .018$), but no difference between groups exiting in separate analyses neither for anxiety nor depression.

Comparing the results of the binary and ordinal logistic models (see Table 3), a great consistency was observed in analyses for depression and anxiety in SAP patients, but not in UAP counterparts. For SAP patients, NYHA classes was significantly associated with levels of depression (binary model: $p = .010$; ordinal model: $p < .001$). This close correlation was also verified in UAP patients though only with ordinal model (binary model: $p = .046$; ordinal model: $p = .005$). Detailed analyses demonstrated that NYHA class I and II subjects in all AP types were statistically at equivalent risk for depression (for AP: NYHA II vs I binary model OR 1.32 (0.59,2.96), $p = 0.50$; ordinal model 1.17 (0.73,1.88), $p = 0.52$), although NYHA II subjects with UAP seemed more likely to be depressed in comparison with those SAP counterparts through the results of both models and analyses of somatic and cognitive depressive symptoms. One possible reason for this phenomenon is that SAP patients in NYHA class II may more frequently have the psychological expectancy of angina when doing excessive activities, but NYHA class I patients may not. NYHA III/IV patients, by contrast, shared a sharply higher risk (for AP: NYHA III/IV vs I binary model OR 3.32 (1.28,8.61), $p = .013$; ordinal model 3.94 (2.11,7.36), $p < .001$). NYHA class was found to be not associated with levels of anxiety regardless of the AP types. Additionally, education background was demonstrated to correlate with the risk for depression and anxiety only in UAP inpatients.

Similar trend was also revealed in binary logistic analyses for somatic and cognitive depressive symptoms as shown in Table 4. The only difference beyond their synchronous changes was that cognitive depressive symptoms in UAP and AP patients were affected by gender (for UAP patients: OR 2.11 (1.08,4.11), $p = .029$; for AP patients: OR 1.82 (1.10,3.01), $p = .020$), but somatic symptoms were not.

**Discussion**

In a sample of 443 AP inpatients, we compared patients’ characteristics according to different cutoffs for depression and anxiety and inferred that depression symptoms...
### Table 2: Characteristics of patients stratified by New York Heart Association functional class

| Variables                                           | Total (N = 443) | NYHA class I (N = 115) | NYHA class II (N = 261) | NYHA class III-IV (N = 67) | p value |
|-----------------------------------------------------|------------------|------------------------|-------------------------|---------------------------|---------|
| Characteristics of patients                         |                  |                        |                         |                           |         |
| Age, mean ± SD, y                                    | 63.9 ± 9.8       | 61.3 ± 9.3             | 64.0 ± 9.8              | 68.2 ± 9.5                | <.001   |
| Male, sex, No. (%)                                   | 337 (76.1)       | 85 (73.9)              | 199 (76.2)              | 53 (78.1)                 | 0.73    |
| Body mass index, mean ± SD, kg/m²                    | 24.5 ± 3.1       | 25.3 ± 2.0             | 24.5 ± 2.6              | 24.6 ± 3.6                | 0.94    |
| Ejection Fraction, mean ± SD, %                      | 59.3 ± 11.0      | 61.0 ± 8.2             | 60.8 ± 12.3             | 50.1 ± 16.1               | <.001   |
| NT-proBNP, median (interquartile), pg/mL             | 123 (50–382)     | 88 (37–234)            | 118 (50–309)            | 73 (133–3892)             | <.001   |
| Creatinine Clearance, mean ± SD, ml/min              | 65.5 ± 21.7      | 69.5 ± 18.2            | 67.0 ± 22.2             | 53.0 ± 21.0               | <.001   |
| Type of angina pectoris, No. (%)                     |                  |                        |                         |                           | 0.24    |
| Unstable angina pectoris                             | 256 (57.8)       | 65 (56.5)              | 158 (60.5)              | 33 (49.3)                 |         |
| Stable angina pectoris                               | 187 (42.2)       | 50 (43.5)              | 103 (39.5)              | 34 (50.7)                 |         |
| Severity of coronary artery stenosis, No. (%)        |                  |                        |                         |                           | <.001   |
| 1                                                    | 93 (21.0)        | 40 (34.8)              | 46 (17.6)               | 7 (10.4)                  |         |
| 2                                                    | 82 (18.5)        | 19 (16.5)              | 54 (20.7)               | 9 (13.4)                  |         |
| 3                                                    | 268 (60.5)       | 56 (48.7)              | 161 (61.7)              | 51 (76.1)                 |         |
| Mood symptoms                                        |                  |                        |                         |                           | <.001   |
| Depression severity, No. (%)                         |                  |                        |                         |                           |         |
| Non-depressed                                       | 271 (61.2)       | 79 (68.7)              | 169 (64.8)              | 23 (34.3)                 |         |
| Mild depression symptom                              | 123 (27.8)       | 27 (23.5)              | 66 (25.3)               | 30 (44.8)                 |         |
| Moderate or severe depression symptom                | 49 (11.1)        | 9 (7.8)                | 26 (10.0)               | 14 (20.9)                 |         |
| Somatic depressive symptom score, mean (SD)         | 3.05 (2.87)      | 2.81 (2.64)            | 2.79 (2.76)             | 4.48 (3.28)               | <.001   |
| Cognitive depressive symptom score, mean (SD)        | 1.36 (1.98)      | 1.21 (1.94)            | 1.20 (1.76)             | 2.24 (2.58)               | <.001   |
| Anxiety severity, No. (%)                            |                  |                        |                         |                           | 0.99    |
| Non-anxious                                         | 316 (71.3)       | 80 (69.6)              | 186 (71.3)              | 50 (74.6)                 |         |
| Mild anxiety symptom                                 | 103 (23.3)       | 30 (26.1)              | 62 (23.8)               | 11 (16.4)                 |         |
| Moderate or severe anxiety symptom                   | 24 (5.4)         | 5 (4.3)                | 13 (5.0)                | 6 (9.0)                   |         |
| Social economic factors                              |                  |                        |                         |                           | 0.83    |
| Education, No. (%)                                   |                  |                        |                         |                           |         |
| less than 6 years                                    | 115 (26.0)       | 26 (22.6)              | 69 (26.4)               | 20 (29.9)                 |         |
| 7–9 years                                           | 126 (28.4)       | 33 (28.7)              | 75 (28.7)               | 18 (26.9)                 |         |
| 10–12 years                                         | 97 (21.9)        | 29 (25.2)              | 52 (19.9)               | 16 (23.9)                 |         |
| more than 12 years                                   | 105 (23.7)       | 27 (23.5)              | 65 (24.9)               | 13 (19.4)                 |         |
| Marriage, No. (%)                                    |                  |                        |                         |                           | 0.57    |
| Married                                             | 412 (93.0)       | 109 (94.8)             | 240 (92.0)              | 63 (94.0)                 |         |
| Divorced or Widowed or Single                        | 31 (7.0)         | 6 (5.2)                | 21 (8.0)                | 4 (6.0)                   |         |
| Medical history, No. (%)                             |                  |                        |                         |                           |         |
| Hypertension                                        | 276 (62.3)       | 56 (48.7)              | 173 (44.8)              | 45 (67.2)                 | .003    |
| Diabetes mellitus                                    | 154 (34.8)       | 28 (24.3)              | 90 (34.5)               | 36 (53.7)                 | <.001   |
| Prior PCI                                            | 167 (37.7)       | 42 (36.5)              | 93 (35.6)               | 34 (50.7)                 | .069    |
| History of antidepressant treatment                 | 17 (3.8)         | 4 (3.5)                | 9 (3.4)                 | 4 (6.0)                   | 0.61    |
| Medication use, No. (%)                              |                  |                        |                         |                           |         |
| ACEI or ARB                                          | 317 (71.6)       | 76 (66.1)              | 192 (73.6)              | 49 (73.1)                 | 0.32    |
| β blocker                                           | 384 (86.7)       | 95 (82.6)              | 232 (88.9)              | 57 (85.1)                 | 0.23    |
| Aldosterone receptor antagonist                      | 42 (9.5)         | 2 (1.7)                | 14 (5.4)                | 26 (38.8)                 | <.001   |
| Loop diuretic                                       | 47 (10.6)        | 2 (1.7)                | 16 (6.1)                | 29 (43.3)                 | <.001   |
| Anticoagulant                                        | 20 (4.5)         | 3 (2.6)                | 12 (4.6)                | 5 (7.5)                   | 0.31    |
| Antidepressant                                       | 9 (2.0)          | 1 (0.9)                | 6 (2.3)                 | 2 (3.0)                   | 0.55    |

Abbreviation: PCI: percutaneous transluminal coronary intervention; ACEI: angiotensin converting enzyme inhibitor; ARB: angiotensin receptor blocker
Fig. 2 (See legend on next page.)
were aggravated along with the worsening of physical condition. Univariate analyses of NYHA classes with clinical characteristics further confirmed such inference. Next, though multivariate analysis we proved that NYHA classification could be an integrated index reflecting patients’ physical status. Finally, we explored the association between NYHA classes and depression or anxiety symptoms and concluded that only for patients with relatively serious physical condition, unexpected discomforts caused by disease notably impacted the emotions.

There has been a debate whether depression disorder in general population is the same thing as in the cardiac patients since long time ago. Our previous analyses of inpatients without or with coronary stenosis $< 50\%$ from the same cross-sectional study sample found the prevalence of clinical depression to be almost twice as high as the one in present study. With the findings mentioned above, it is reasonable to believe that “these two depression disorders” are not the same and may exist at the same time. Analysis of the ratio of somatic and cognitive symptom scores hinted a greater fluctuation of cognitive symptoms with the increase in depression severity. As a result, when cutoff point reached a certain value, the screening for depression becomes more dependent on cognitive symptoms. That is the reason why there is a difference in the results between using the cutoff point of 10 and 5, and why ordinal logistic model is more sensitive to physical condition than binary logistic model.

The rough correlation of mood state and NYHA class has been reported in univariate analyses of considerable previous studies [40–43]. However, in consideration of collinearity with other clinical features such as Pro-BNP, EF, creatinine and so on, few studies have treated NYHA classes as an integrated index reflecting disease severity and explored the associations with mood symptoms in multivariate regression models. Our finding was consistent with the expectation that angina pectoris patients in NYHA class III/IV compared to NYHA class I and II were at greater risk for depression.

In accord with the finding from Assari S. [44], our univariate analyses revealed that for AP patients, less coronary stenosis was associated with elevated anxiety symptoms. It seems that anxiety is more likely to be a stress response. Perhaps our body though constantly adjustment might have learned to “keep calm” in case of sympathetic activation or myocardial ischemia induced by mental stress [45] when with severe CHD. However, when it comes a stress exceeding the threshold physically or mentally, for example the loss of stability of CHD, the calmness may immediately be broken up.

Additionally, quite consistent with our common sense, it was discovered that education background engendered greater effect on mood symptoms in UAP patients. This might attribute to the differences in perception and anticipatory anxiety influenced by knowledge and the social support obtained from social status. In other words, this may indicate that patients in acute phase of CHD for example UAP or even AMI (acute myocardial infarction) can get more benefit from health education, or antidepressant therapy and psychological counseling. Several recent researches have indeed confirmed this hypothesis [46, 47].

To our knowledge, it is the first time that in one study the associations between NYHA classes and depression/anxiety in both SAP and UAP patients are explored, meanwhile linkage with somatic and cognitive depressive symptoms is assessed. Our findings reveal that depression symptoms in CHD patients are actually to a large extend derived from the disease itself and exacerbate along with the deterioration of physical status especially when CHD is unstable. Discomfort, as the reason leading to the increment of somatic symptom score, probably at the same time arouses cognitive symptoms. Anxiety symptoms, though generally positively correlate with depression symptoms, may exhibit an inverse relation along with the worsening of physical condition. However, no significant association between NYHA classes and anxiety in the separate analysis was discovered. These findings can at least partly be supported by the phenomenon that left ventricular assist device can help heart failure patients reduce anxiety and depression [48] and antidepressant is hardly to be efficient to improve prognosis in CHD patients [49, 50].

Our findings should be considered in light of several potential limitations. First, due to small sample size, NYHA class IV group of patients could not be investigated separately. Therefore, the present study may be unable to represent the seriously ill classification of NYHA IV. Besides, a small sample size might lead to an inaccurate outcome, especially for the analysis on clinical anxious patients and some variables could therefore not been adjusted. However, it should be noted that most of our findings were obtained based on the same outcomes with two criteria, which makes the conclusion more persuasive. Second, this is a single centered study. The advantage is that we could minimize the measuring error by fixing the tester. The disadvantage is that
| NYHA classes | Gender | Age | Education | Odds Ratio (95% CI) | p value | Odds Ratio (95% CI) | p value | Odds Ratio (95% CI) | p value | Odds Ratio (95% CI) | p value | Odds Ratio (95% CI) | p value | Odds Ratio (95% CI) | p value |
|--------------|--------|-----|-----------|---------------------|---------|---------------------|---------|---------------------|---------|---------------------|---------|---------------------|---------|---------------------|---------|
| Stable angina pectoris | depression as dichotomous variable | 0.98 (0.28,3.47) | 0.09 | 5.01 (1.30,19.3) | <0.01 | 1.48 (0.47,4.67) | 0.51 | 0.98 (0.93,1.04) | 0.56 | 0.51 (0.12,2.15) | 0.36 | 1.25 (0.31,5.07) | 0.75 | 0.93 (0.23,3.83) | 0.92 |
| as ordinal variable | 0.84 (0.41,1.71) | 0.63 | 4.36 (1.77,10.7) | 0.01 | 2.27 (1.11,4.66) | 0.03 | 1.00 (0.97,1.04) | 0.97 | 0.62 (0.26,1.49) | 0.29 | 1.30 (0.52,3.24) | 0.58 | 0.98 (0.40,2.38) | 0.97 |
| Unstable angina pectoris | depression as dichotomous variable | 1.52 (0.52,4.47) | 0.44 | 2.49 (0.60,10.4) | 0.21 | 0.87 (0.33,2.27) | 0.78 | 0.99 (0.94,1.04) | 0.60 | 0.30 (0.10,0.88) | 0.29 | 0.19 (0.05,0.75) | 0.17 | 0.27 (0.08,0.93) | 0.38 |
| as ordinal variable | 1.61 (0.84,3.10) | 0.15 | 4.39 (1.77,10.9) | 0.01 | 1.48 (0.80,2.74) | 0.21 | 0.99 (0.97,1.02) | 0.68 | 0.32 (0.16,0.64) | 0.01 | 0.26 (0.12,0.56) | <0.01 | 0.25 (0.11,0.55) | <0.01 |
| Angina pectoris | depression as dichotomous variable | 1.32 (0.59,2.96) | 0.50 | 3.32 (1.28,8.61) | 0.13 | 1.06 (0.52,2.19) | 0.87 | 0.99 (0.95,1.02) | 0.45 | 0.38 (0.16,0.87) | 0.23 | 0.43 (0.18,1.06) | 0.05 | 0.43 (0.18,1.04) | 0.06 |
| as ordinal variable | 1.17 (0.73,1.88) | 0.52 | 3.94 (2.11,7.36) | <0.01 | 1.73 (1.09,2.75) | 0.19 | 1.00 (0.98,1.02) | 0.83 | 0.43 (0.25,0.72) | 0.02 | 0.50 (0.28,0.88) | 0.16 | 0.44 (0.25,0.79) | 0.05 |
| Stable angina pectoris | anxiety as dichotomous variable | 2.59 (0.29,22.9) | 0.39 | 3.59 (0.30,34.8) | 0.32 | 0.59 | 1.21 (0.23,6.41) | 0.82 | 0.98 (0.90,1.06) | 0.05 | # |
| as ordinal variable | 1.13 (0.52,2.44) | 0.76 | 0.80 (0.28,2.33) | 0.69 | 0.77 | 1.71 (0.82,3.59) | 0.16 | 1.00 (0.96,1.04) | >0.99 | # |
| Unstable angina pectoris | anxiety as dichotomous variable | 0.85 (0.24,3.01) | 0.80 | 2.27 (0.47,10.9) | 0.31 | 0.36 | 1.08 (0.29,3.97) | 0.91 | 0.98 (0.93,1.04) | 0.55 | 0.82 (0.22,3.07) | 0.76 | 0.39 (0.07,2.22) | 0.29 | 0.62 (0.13,2.89) | 0.54 |
| as ordinal variable | 0.98 (0.51,1.88) | 0.94 | 1.37 (0.51,3.66) | 0.53 | 0.74 | 2.27 (1.19,4.33) | 0.13 | 0.96 (0.93,1.00) | 0.14 | 0.50 (0.25,1.02) | 0.08 | 0.45 (0.20,0.99) | 0.04 | 0.17 (0.06,0.46) | <0.01 |
| Angina pectoris | anxiety as dichotomous variable | 1.21 (0.41,3.53) | 0.73 | 2.39 (0.66,8.73) | 0.19 | 0.35 | 0.93 (0.33,2.63) | 0.88 | 0.97 (0.93,1.02) | 0.28 | 0.37 (0.12,1.20) | 0.10 | 0.38 (0.11,1.35) | 0.13 | 0.46 (0.14,1.53) | 0.21 |
| as ordinal variable | 0.99 (0.60,1.92) | 0.97 | 0.96 (0.47,1.95) | 0.91 | 0.99 | 1.93 (1.18,3.16) | 0.08 | 0.98 (0.95,1.00) | 0.50 | 0.50 (0.29,0.88) | 0.17 | 0.56 (0.30,1.03) | 0.06 | 0.36 (0.19,0.69) | 0.02 |

**Abbreviation:** NYHA class New York Heart Association functional class, BMI body mass index

# due to the limitation of small sample size, binary and ordinal logistic regression models were only adjusted for age, sex, and BMI for patients with stable angina pectoris
Table 4 Associations of somatic and cognitive depressive symptoms with NYHA classes using binary logistic regression model

| NYHA classes          | Gender | Age per 1 year increase | Education |          |          |
|----------------------|--------|-------------------------|-----------|----------|----------|
|                      | NYHA class II vs I | NYHA class III/IV vs I | overall female vs male | 7-9 years vs less than 6 | 10-12 years vs less than 6 | more than 12 vs less than 6
|                      | Odds Ratio (95% CI) | p value | Odds Ratio (95% CI) | p value | Odds Ratio (95% CI) | p value | Odds Ratio (95% CI) | p value | Odds Ratio (95% CI) | p value |
| Stable angina pectoris |        |                        |           |          |          |          |          |          |          |          |
| Somatic depressive symptoms | 0.61 (0.28,1.33) | 0.22 | 3.41 (1.29,9.00) | .013 | <.001 | 1.77 (0.79,3.93) | 0.16 | 0.81 (0.31,2.11) | 0.67 | 1.80 (0.65,4.95) | 0.25 |
| Cognitive depressive symptoms | 0.89 (0.40,1.97) | 0.78 | 4.56 (1.69,12.3) | .003 | <.001 | 1.64 (0.74,3.67) | 0.23 | 0.46 (0.17,1.24) | 0.12 | 0.79 (0.28,2.19) | 0.64 |
| Unstable angina pectoris |        |                        |           |          |          |          |          |          |          |          |          |
| Somatic depressive symptoms | 1.41 (0.72,2.76) | 0.32 | 2.80 (1.08,7.31) | 0.85 | 0.11 | 1.63 (0.85,3.11) | 0.14 | 0.44 (0.22,0.90) | 0.24 | 0.30 (0.13,0.69) | 0.04 |
| Cognitive depressive symptoms | 1.23 (0.62,2.43) | 0.55 | 2.77 (1.04,7.38) | 0.042 | 0.11 | 2.11 (1.08,4.11) | 0.029 | 0.70 (0.34,1.43) | 0.32 | 0.33 (0.14,0.78) | 0.12 |
| Angina pectoris |        |                        |           |          |          |          |          |          |          |          |          |
| Somatic depressive symptoms | 1.01 (0.61,1.66) | 0.98 | 2.86 (1.47,5.56) | .002 | .001 | 1.60 (0.98,2.61) | 0.60 | 0.55 (0.32,0.96) | 0.35 | 0.60 (0.33,1.10) | 0.06 |
| Cognitive depressive symptoms | 1.07 (0.64,1.78) | 0.80 | 3.28 (1.67,6.44) | <.001 | <.001 | 1.82 (1.10,3.01) | 0.20 | 0.98 (0.96,1.01) | 0.14 | 0.61 (0.35,1.08) | 0.09 |

*Abbreviation: NYHA class New York Heart Association functional class, BMI body mass index*
Conclusions
In summary, our study demonstrated a high synchronized alteration of somatic and cognitive depressive symptoms along with the progress of disease severity. However, more intense mood symptoms are prone to be aroused when patients are in bad functional status. Education background has greater impact on mood when patient’s condition is unstable. These findings may trigger deeper rethink of the associations of mood symptoms with CHD and with the prognosis, lead to a better understanding of the mechanism of mood disorder in CHD patients and help to make the intervention more timely and efficient.

Additional files

Additional file 1: Table S1. Comparison of fit statistics for the five previously hypothesized factor models of PHQ-9. (DOCX 16 kb)
Additional file 2: Table S2. Characteristics of patients stratified by anxiety severity. (DOCX 22 kb)
Additional file 3: Table S3. Association between NYHA classes and clinical features using multivariate ordinal logistic regression model. (DOCX 17 kb)

Abbreviations
ACBP: angiotensin converting enzyme inhibitor; AMI: acute myocardial infarction; ANOVA: one-way analysis of variance; AP: angina pectoris; ARB: angiotensin receptor blocker; BMI: body mass index; CAG: coronary angiography; CFA: confirmatory factor analysis; CHD: coronary heart disease; GAD: Generalized Anxiety Disorder Scale; LVEF: left ventricular ejection fraction; NYHA class: New York Heart Association functional class; PCI: percutaneous transluminal coronary intervention; PHQ: Patient Health Questionnaire; SAP: stable angina pectoris; UAP: unstable angina pectoris

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Authors’ contributions
YH alone surveyed all patients. LYT, MH collected and entered data into database. LYT, LGH did statistical analyses. YH, GL, GQS wrote the paper. GQS, GL 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.

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The authors declare that they have no competing interests.

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