Comparing the effects of depression, anxiety, and comorbidity on quality-of-life, adverse outcomes, and medical expenditure in Chinese patients with acute coronary syndrome

Kun Xia[1], Le-Feng Wang[1], Xin-Chun Yang[1], Hong-Yan Jiang[2], Li-Jing Zhang[3], Dao-Kuo Yao[4], Da-Yi Hu[5], Rong-Jing Ding[5]

[1]Heart Center, Chaoyang Hospital, Capital Medical University, Beijing 100020, China;
[2]Heart Center, Beijing First Hospital of Integrative Chinese & Western Medicine, Beijing 100021, China;
[3]Heart Center, Dongzhimen Hospital, Beijing University of Chinese Medicine, Beijing 100700, China;
[4]Heart Center, Friendship Hospital, Capital Medical University, Beijing 100050, China;
[5]Heart Center, Peking University People's Hospital, Beijing 100044, China.

Abstract

Background: Depression and anxiety have been correlated with elevated risks for quality-of-life (QOL), adverse outcomes, and medical expenditure in patients with acute coronary syndrome (ACS). However, the relevant data are lacking for Chinese ACS populations, especially regarding different effects of major depression, anxiety, and comorbidity. The objective of this study was to evaluate the dynamic changes of depression and/or anxiety over 12 months and examine the effects of depression, anxiety, and comorbidity on QOL, adverse outcomes, and medical expenditure in Chinese patients with ACS.

Methods: For this prospective longitudinal study, a total of 647 patients with ACS were recruited from North China between January 2013 and June 2015. Among them, 531 patients (82.1%) completed 12-month follow-ups. Logistic regression model was utilized for analyzing the association of baseline major depression, anxiety, and comorbidity with 12-month all-cause mortality, cardiovascular events, QOL, and health expenditure.

Results: During a follow-up period of 12 months, 7.3% experienced non-fatal myocardial infarction (MI) and 35.8% cardiac re-hospitalization. Baseline comorbidity, rather than major depression/anxiety, strongly predicted poor 12-month QOL as measured by short-form health survey-12 (odds ratio [OR]: 1.77, 95% confidence interval [CI]: 1.22–2.52, $P = 0.003$). Regarding 12-month non-fatal MI and cardiac re-hospitalization, baseline anxiety (OR: 2.83, 95% CI: 1.33–5.89, $P < 0.01$; OR: 4.47, 95% CI: 1.50–13.00, $P < 0.01$), major depression (OR: 2.58, 95% CI: 1.02–6.15, $P < 0.05$; OR: 5.22, 95% CI: 1.42–17.57, $P < 0.03$), and comorbidity (OR: 6.33, 95% CI: 2.96–13.79, $P < 0.0001$, OR: 14.08, 95% CI: 4.99–41.66, $P < 0.0001$) were all independent predictors, and comorbidity had the highest predictive value. Number of re-hospitalization stay, admission frequency within 12 months and medical expenditure within 2 months were the highest in patients with ACS with comorbidity.

Conclusions: Major depression and anxiety may predict 12-month non-fatal MI and cardiac re-hospitalization. However, comorbidity has the highest predictive value with greater medical expenditure and worse QOL in Chinese patients with ACS. And depression with comorbid anxiety may be a new target of mood status in patients with ACS.

Keywords: Acute coronary syndrome; Major depression; Anxiety; Comorbidity; Adverse outcome

Introduction

Despite rapid developments of sophisticated interventions and preventive strategies, cardiovascular disease (CVD) has been the leading cause of mortality and accounts for a quarter of medical expenditure in China, resulting in substantial direct medical burdens and indirect costs of productivity losses.[1] Primary and secondary preventive strategies in China have focused largely upon hypertension, hyperlipidemia, diabetes mellitus, and smoking. And numerous domestic epidemiological studies in China supported these measures.

As demonstrated by prospective studies, systematic reviews, and meta-analyses, there existed a robust association between depression and higher morbidity and mortality after acute coronary syndrome (ACS). And American Heart Association has identified depression as one major risk factor for poor prognosis among patients

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Correspondence to: Dr. Rong-Jing Ding, Peking University People's Hospital, Room 405, Medical Building, Beijing 100044, China
E-Mail: drj2003@vip.163.com

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with ACS.[2] Although there was a rich source of systematic reviews and meta-analyses, no data of Chinese populations were available. Few small-scale studies reported the relationship between depression and adverse outcomes in Chinese patients with ACS. Their sample sizes were small and follow-ups (<1 year) too short. Considering cultural variations between western and eastern countries, reaffirming such a relationship between depression and adverse outcomes in Chinese populations is needed.

Anxiety disorders are highly prevalent in both Chinese and Western patients with ACS.[3,4] Some studies examined the relationship between anxiety and adverse outcomes in Western patients with ACS. One meta-analysis pooled 44 articles from western countries with a total of 30,527 patients with ACS. After adjusting for covariates, insignificant relationship existed between anxiety and mortality.[5] In light of these diverging results, continuously exploring the effect of anxiety on outcomes of Chinese patients with ACS is also necessary.

Mounting evidence has indicated that depression and anxiety were correlated[6-8] but individually predicted mortality and cardiac events among patients with ACS.[5,9-11] None of existing studies explored the effect of comorbid depression/anxiety on outcomes in patients with ACS. A previous study revealed that comorbidity rather than depression alone accounted for lower heart rate variability.[12] Another cross-sectional study confirmed that comorbidity had the strongest relationship with hypertension in a cohort of 4180 males.[13] In a veteran population of 4256 healthy subjects, anxiety and major depression could predict all-cause mortality during 15-year follow-ups. And comorbidity had the greatest risk of subsequent mortality.[14] Besides depression, comorbidity might be a new risk factor and it should be further examined in Chinese patients with ACS.[15,16]

Besides the relationship between psychological factors and prognosis on morbidity and mortality after ACS, the effect of depression on angina and re-hospitalization has been strongly established. Meta-analysis indicated that effective mental health interventions could reduce hospital readmission rates and lower financial burdens.[17] However, up until now, no existing data have elucidated the effect of depression/anxiety on medical expenditure in Chinese patients with ACS.

The objective of this study was to evaluate the dynamic changes of depression and/or anxiety over 12 months and examine the effects of depression, anxiety, and comorbidity on quality-of-life (QOL), adverse outcomes, and medical expenditure in Chinese patients with ACS.

Methods

Ethical approval

The study protocol was approved by the Peking University Research Ethics Service and all subjects provided informed consent.

Patients and procedures

This prospective longitudinal study was intended to determine the effects of depression, anxiety, and comorbidity on QOL, adverse outcomes, and medical expenditure among a cohort of Chinese inpatients with ACS. Patients admitted into the Coronary Care Unit with a primary diagnosis of ACS and aged 18 years or above were recruited and evaluated within 7 days of symptom onset at five participating hospitals between January 2013 and June 2015. All subjects were expected to complete 3/6/9/12-month follow-ups. ACS was comprised of ST-segment elevation myocardial infarction (STEMI), non-STEMI, and unstable angina according to the definitions of clinical practice guidelines.[18] STEMI and non-STEMI were diagnosed according to the universal definitions of acute myocardial infarction. And unstable angina was determined through the presence of its classic symptoms together with a culprit lesion on coronary angiography. Exclusion criteria included comorbid conditions potentially influencing either symptom onset or questionnaire responses such as cognitive dysfunction, taking previous or current antidepressants for psychological problems, comorbid lethal diseases, and active substance abusing or dependence. Anticipated life expectancy under 1 year or those unwilling to participate were also excluded.

A dynamic database was maintained for collecting the data of clinical profiles, demographics, health behaviors, social psychological status, all-cause mortality, cardiovascular events, and medical expenditure.

Social psychological status was evaluated by depression (measured by patient health questionnaire [PHQ-9]),[15] anxiety (measured by generalized anxiety disorder [GAD-7][19,20]), QOL (measured by short-form health survey [SF-12]).[21] Follow-up assessments of mood, QOL, and health behaviors were conducted at 1, 3, 6, and 12 months post-discharge. And major adverse events (all-cause mortality, cardiac mortality, cardiac re-hospitalization, non-fatal myocardial infarction [MI]), and medical expenditure were collected from clinical records and patient self-reports.

A standard threshold score of 10 or higher on PHQ-9/GAD-7 was employed to define major depression/anxiety.[15,19,20] And a threshold score of 50 or higher on SF-12, SF-mental component summary (MCS) and SF-physical component summary (PCS) were used for defining good QOL. Smoking was assessed as current, ever and never smoker. Active physical activity was defined as over 30 min daily and 5 days weekly during the previous 4 weeks. Medical expenditure was defined as cardiac re-hospitalization and/or number of hospitalization within 1 year, number of admission within 1 year, number of non-scheduled outpatient or emergency clinic and/or medical cost within the last 2 months. Cardiovascular history, clinical status at admission, biochemical results (troponin I, cholesterol, triglycerides, and glucose), and anthropometric measurements, including systolic blood pressure, diastolic blood pressure, height, and weight, were obtained from clinical records and left ventricular function (LVEF) from echocardiogram.

Statistical analyses

All data were analyzed by JMP software (Version 9, SAS Institute Inc., Minneapolis, MN, USA) and a two-tailed *P* value of ≤0.05 was deemed as statistically significant.

Based on PHQ-9/GAD-7 scores, this patient cohort was divided into four groups of anxiety alone (GAD-7 score ≥10), major depression alone (PHQ-9 score ≥10), comorbidity (comorbid anxiety/depression) (PHQ-9 ≥10 and GAD-7 ≥10), and control (PHQ-9 score <10 and GAD-7 score <10). After tested by variance homogeneity test and normal distribution test, differences in baseline profiles, QOL, adverse events, and dynamic changes of PHQ-9/GAD-7 scores over a period of 12 months among four groups were examined by one-way analysis of variance (ANOVA) and Chi-squared tests for all dichotomous variables. Bonferroni post-hoc test for multiple comparisons was utilized for continuous variables. And Fisher exact probabilities were calculated when necessary.

The associations were also examined between depression, anxiety, comorbidity, QOL, and adverse events during 12-month follow-ups by comparing the outcomes of four groups after adjusting for covariates. Two multivariate logistic regression analyses were performed for examining depression, anxiety, and comorbid depression/anxiety as independent predictors of all-cause mortality, cardiac events, and QOL. Model 1 adjusted for age (<60 years *vs.* ≥60 years) and gender while model 2 adjusted for age (<60 years *vs.* ≥60 years), gender, LVEF (<50% *vs.* ≥50%), physical activity, smoking, diabetes mellitus, hypertension, hypercholesterolemia, and peripheral artery disease.

Results

Baseline profiles in four different mood groups of patients with ACS

A total of 647 eligible patients with ACS were enrolled, including 438 (67.7%) males and 209 (32.3%) females. The mean age was 63.4 ± 12.0 years. Follow-ups were completed by 531 patients (82.5%). Their baseline socio-demographic and clinical profiles were summarized in Table 1.

Among 647 participants, no significant differences existed in baseline age, education, gender, prevalence of drinking/smoking, cardiovascular risk factors, medications, and troponin I among four groups ($P > 0.05$). However, significant differences existed in prevalence of hypercholesterolemia, active physical activity and LVEF [Table 1].

Table 1: Baseline demographic data, medications, and coronary heart disease risk factors in patients with ACS stratified by depression/anxiety (*n* = 647).

Items	Depression group	Anxiety group	Comorbid group	Normal group	*F*	*P*
Patients, *n* (%)	53 (8.2)	68 (10.5)	50 (7.7)	476 (73.6)		—
Male gender, *n* (%)	36 (67.9)	42 (61.8)	34 (68.0)	326 (68.6)	1.39	0.73
Age (years)	65.9 ± 13.6	61.5 ± 12.8	61.2 ± 12.4	63.6 ± 11.6	2.01	0.10
Smoking, *n* (%)					1.78	0.43
Current	16 (30.2)	21 (30.9)	11 (22.5)	152 (32.6)		
Ever	8 (15.1)	16 (23.5)	12 (24.5)	115 (24.6)		
Never	29 (54.8)	31 (45.6)	26 (53.1)	200 (42.8)		
Drinking (cups/week)					1.97	0.63
0	26 (50.0)	42 (63.6)	29 (61.7)	282 (64.8)		
≤20	22 (42.3)	19 (28.8)	17 (36.2)	131 (30.1)		
21–40	3 (5.8)	4 (6.1)	1 (2.1)	17 (3.9)		
>40	1 (1.9)	1 (1.5)	0	5 (1.2)		
Education level, *n* (%)					1.41	0.45
<Primary	11 (22.0)	8 (13.8)	2 (4.6)	75 (16.4)		
<High school	25 (50.0)	30 (51.7)	29 (65.9)	225 (51.3)		
>University	14 (28.0)	20 (34.5)	13 (29.6)	142 (32.3)		
Regular exercise, *n* (%)	9 (17.3)	13 (20.3)	4 (9.1)*	125 (27.5)	5.46	0.005
BMI (kg/m^2)	24.66 ± 3.26	25.97 ± 4.86	24.54 ± 2.63	25.12 ± 3.33	1.98	0.19
Hypertension, *n* (%)	37 (69.8)	50 (74.6)	36 (73.5)	307 (65.9)	1.56	0.37
Diabetes mellitus, *n* (%)	23 (43.4)	25 (37.9)	18 (36.7)	183 (39.4)	1.73	0.91
Hypercholesterolemia, *n* (%)	26 (49.1)	36 (55.4)	26 (53.1)	176 (38.1)	6.34	0.01
Lipid-lowering, *n* (%)	43 (86.0)	56 (90.3)	37 (78.7)	381 (91.2)	2.23	0.053
Beta-blockers, *n* (%)	38 (74.5)	52 (80.0)	33 (73.3)	279 (66.6)	1.89	0.11
ACE inhibitors, *n* (%)	35 (68.6)	41 (63.1)	30 (65.2)	253 (60.4)	1.32	0.65
LVEF (%)	59.9 ± 1.5	53.9 ± 1.7	57.4 ± 1.6	59.8 ± 0.6	4.85	0.01
Troponin I (ng/dl)	11.60 ± 4.42	13.26 ± 5.00	9.98 ± 5.13	9.30 ± 1.67	1.67	0.86

Data are expressed as *n* (%) or mean ± standard deviation. One-way ANOVA and post-hoc (Bonferroni test) for multiple comparisons for continuous variables and chi-square test for dichotomous variables. *$P < 0.05$ when comorbid group *vs.* depression, anxiety, and normal group, respectively. ACE: Angiotensin converting enzyme; ACS: Acute coronary syndrome; ANOVA: Analysis of variance; BMI: Body mass index; LVEF: Left ventricular ejection fraction.

The overall prevalence of depression/anxiety in patients with ACS stood at 26.5%, in which 7.7% for comorbid depression/anxiety. Considering 1-year dynamic changes of PHQ-9/GAD-7 scores, PHQ-9 score declined gradually and normalized during 12-month follow-ups in depression and comorbid depression/anxiety groups [Figure 1A]. In anxiety group, GAD-7 score dropped rapidly and normalized during 1-month follow-ups [Figure 1B]. Yet a more gradual decline in scores occurred in comorbid depression/anxiety group.

Effect of baseline depression/anxiety on QOL during 12 months post-ACS

Regarding QOL in patients with ACS of four separate groups, significant differences existed in baseline scores of SF-12, SF-MCS, and SF-PCS (all $P < 0.0001$) and the lowest was found in comorbid depression/anxiety group. The scores of SF-12, SF-MCS, and SF-PCS improved significantly during 12-month follow-ups in all groups. However, the lowest was found in comorbid depression/anxiety group [Table 2].

Two models of multivariate logistic regression revealed a strong relationship between baseline comorbidity and poor 12-month SF-12, SF-MCS, and SF-PCS [Table 3].

Effect of baseline depression/anxiety on all-cause mortality, non-fatal MI, and cardiac re-hospitalization during 12 months post-ACS

Ten deaths (10/531, 1.9%) occurred during 12-month follow-ups and three died of a cardiac event. No significant difference existed in all-cause mortality among four groups ($P = 0.22$) [Table 4]. Using two models of multivariate Logistic regression, baseline anxiety, and/or depression were not associated with 12-month all-cause mortality [Table 5].

Thirty-nine patients (39/531, 7.3%) experienced non-fatal MI prior to 12-month follow-ups. The prevalence of non-fatal MI was significantly different among depression, anxiety, comorbidity, and control groups with the highest prevalence in comorbidity group [Table 4]. Using two

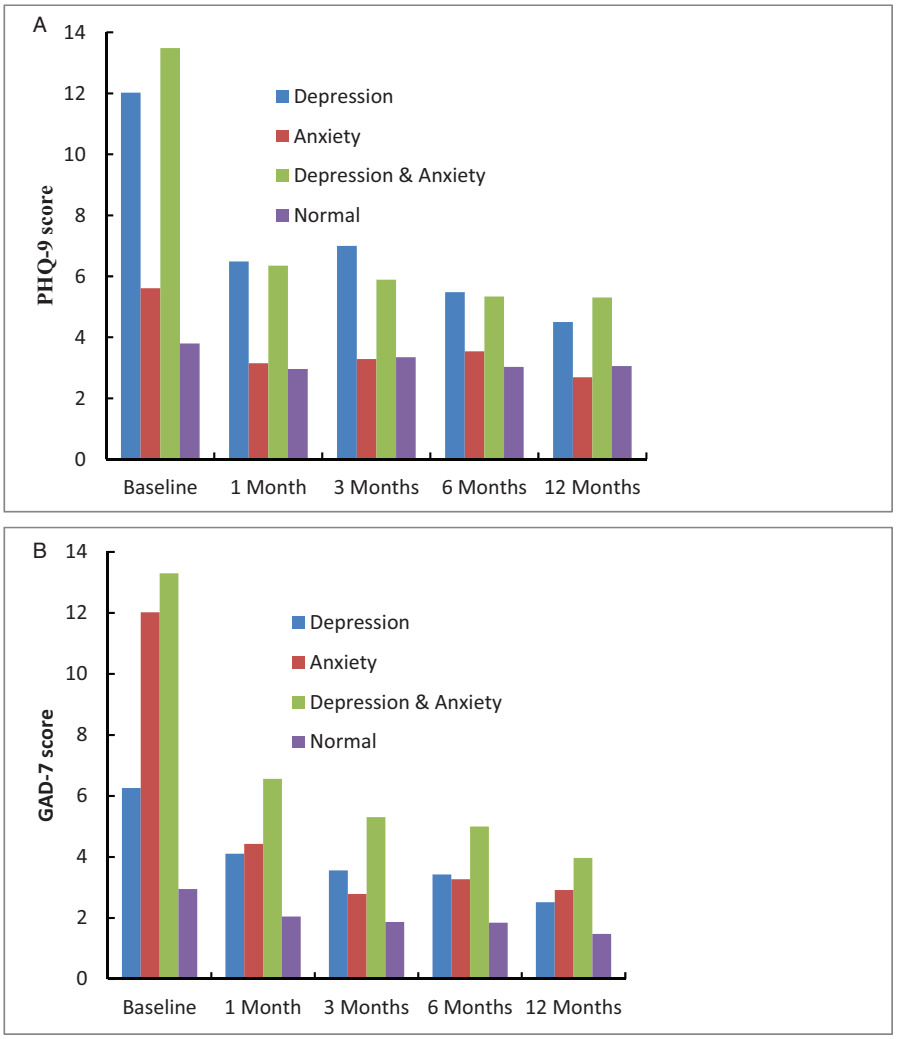

Figure 1: Changes of PHQ-9 score (A) and GAD-7 score (B) in patients with ACS over 1-year follow-ups and different psychological status. ACS: Acute coronary syndrome; PHQ-9: Patient health questionnaire.

Table 2: QOL at baseline and during 12-month follow-ups in patients with ACS stratified by depression/anxiety ($n = 531$).

Items	Depression group ($n = 44$)	Anxiety group ($n = 49$)	Comorbid group ($n = 46$)	Normal group ($n = 392$)	*F*	*P*
SF-12						
Baseline	50.62 ± 2.36	55.44 ± 2.07	42.84 ± 2.41*	65.40 ± 0.78	8.32	<0.0001
Follow-up	69.17 ± 2.70†	76.50 ± 2.37	69.94 ± 2.55†	75.08 ± 0.86	4.19	0.04
MCS						
Baseline	55.53 ± 2.49	62.21 ± 2.18	45.91 ± 2.54	73.14 ± 0.83	7.99	<0.0001
Follow-up	74.92 ± 19.55	80.19 ± 14.20	72.94 ± 18.59	80.65 ± 15.06	6.02	0.004
PCS						
Baseline	45.71 ± 2.87	48.67 ± 2.51	39.77 ± 2.92*	57.65 ± 0.95	10.11	<0.0001
Follow-up	63.43 ± 3.42†	72.81 ± 3.00	66.94 ± 3.23†	69.53 ± 1.09	1.69	0.18

Data are expressed as mean ± standard deviation. One-way ANOVA and post-hoc (Bonferroni test) for multiple comparisons for continuous variables. *$P < 0.05$ comorbid group versus anxiety alone, depression alone and normal groups separately for baseline data; †$P < 0.05$ comorbid group or depression alone group *vs.* anxiety alone and normal groups separately for follow-up data. ACS: Acute coronary syndrome; ANOVA: Analysis of variance; MCS: Mental component summary; PCS: Physical component summary; QOL: Quality-of-life; SF-12: 12-Item short form health survey.

Table 3: Association between anxiety/depression and QOL adjusted by two multivariate logistic regression models.

Variables	Model 1 ($n = 531$)			Model 2 ($n = 531$)		
	OR	95% CI	*P*	OR	95% CI	*P*
12-month SF-12 score <50						
Normal group (reference)	0			0		
Depression group	1.24	0.81–1.82	0.30	1.09	0.70–1.63	0.68
Anxiety group	1.11	0.77–1.56	0.55	1.06	0.73–1.51	0.74
Comorbid group	1.74	1.22–2.44	0.003	1.77	1.22–2.52	0.003
12-month PCS score <50						
Normal group (reference)	0			0		
Depression group	1.44	0.95–2.11	0.09	1.34	0.86–2.00	0.19
Anxiety group	1.00	0.70–1.41	0.96	0.96	0.66–1.37	0.85
Comorbid group	1.59	1.12–2.22	0.01	1.62	1.12–2.29	0.01
12-month MCS score <50						
Normal group (reference)	0			0		
Depression group	1.46	0.99–2.06	0.06	0.95	0.61–1.42	0.82
Anxiety group	1.01	0.70–1.43	0.92	1.13	0.78–1.62	0.49
Comorbid group	1.41	0.99–1.94	0.05	1.75	1.20–2.47	0.004

Poor QOL was defined as SF-12 score, PCS score, and MCS score <50. Model 1: Adjusting for age (<60 years *vs.* ≥60 years) and gender. Model 2: Adjusting for age (<60 years *vs.* ≥60 years), gender, LVEF (<50% *vs.* ≥50%), smoking, physical activity, diabetes mellitus, hypertension, hypercholesterolemia, and PAD; CI: Confidence interval; MCS: Mentaxl component summary; OR: Odds ratio; PCS: Physical component summary; QOL: Quality-of-life; SF-12:12-Item short form health survey.

models of multivariate logistic regression, baseline anxiety, depression, and comorbidity were significantly associated with 12-month non-fatal MI and the highest odds ratio (OR) was found in comorbidity group [Table 5].

Another 190 patients (190/531, 35.8%) experienced cardiac re-hospitalization during follow-ups, and the higher prevalence occurred in comorbidity and anxiety alone groups than control group [Table 4]. Using two models of multivariate logistic regression, baseline anxiety, depression, and comorbidity were significantly associated with 12-month cardiac re-hospitalization and the highest OR was found in comorbidity group [Table 5].

Health consumption in different mood status groups

Table 4 showed that number of re-hospitalization stay, admission frequency within 12 months, non-scheduled outpatient or emergency visit, and medical cost within 2 months were all the highest in comorbid patients with ACS.

Discussion

The present study has mobilized the first large-scale cohort for exploring the associations between depression, anxiety, comorbidity, QOL, adverse outcomes, and medical expenditure in Chinese patients with ACS. Although baseline major depression, anxiety, and comorbidity were all independent predictors of 12-month non-fatal MI and cardiac re-hospitalization, comorbidity had the highest predictive value. Regarding medical expenditure and QOL, baseline comorbidity but not major depression or anxiety alone consumed much greater medical resources as compared with normal mood status. And also baseline comorbidity but not major depression or anxiety alone

Table 4: Different prevalence of adverse events in four groups ($n = 531$).

Items	Depression group ($n = 44$)	Anxiety group ($n = 49$)	Comorbid group ($n = 46$)	Normal group ($n = 392$)	F	P
12-month all-cause mortality, *n* (%)	2 (4.5)	2 (4.1)	1 (2.2)	4 (1.0)	1.98	0.22
12-month non-fatal MI, *n* (%)	5 (11.4)	10 (20.4)	15 (32.6)*	9 (2.3)	5.86	<0.0001
12-month cardiac rehospitalization, *n* (%)	16 (36.4)	31 (63.3)†	26 (56.5)*	117 (29.8)	6.32	<0.0001
Hospitalization stay within 1 year (days)	11.07 ± 1.62	10.84 ± 1.23	15.77 ± 1.45*	6.53 ± 0.48	8.79	<0.0001
Number of readmissions within 1 year (*n*)	1.46 ± 0.26	1.61 ± 0.19	2.65 ± 0.23*	0.73 ± 0.08	10.03	<0.0001
Number of non-scheduled outpatient or emergency clinic	3.92 ± 0.71	3.78 ± 0.52	4.76 ± 0.61*	1.90 ± 0.20	5.64	<0.0001
Medical expenditure within the last 2 months (RMB Yuan)	1032.69 ± 205.82	928.75 ± 151.48	1405.18 ± 170.25*	877.16 ± 60	3.67	0.03

Data are expressed as *n* (%) or mean ± standard deviation. One-way ANOVA and post-hoc (Bonferroni test) for multiple comparisons for continuous variables and chi-square test for dichotomous variables. *$P < 0.05$ comorbid group *vs.* depression and normal groups separately; †$P < 0.05$ anxiety group *vs.* depression and normal groups separately. ANOVA: Analysis of variance.

Table 5: Association between anxiety/depression and adverse events adjusted by two multivariate logistic regression models.

	Model 1			Model 2		
Variables	OR	95% CI	P	OR	95% CI	P
12-month all-cause mortality						
Normal group	0			0		
Depression group	3.18	0.40–18.30	0.24	2.33	0.17–21.67	0.49
Anxiety group	5.24	0.63–37.50	0.12	3.44	0.28–38.2	0.31
Comorbid group	1.54	0.08–11.58	0.72	0.68	0.02–8.09	0.79
12-month non-fatal MI						
Normal group	0			0		
Depression group	4.09	1.21–12.22	0.02	5.22	1.42–17.57	0.03
Anxiety group	4.51	1.63–12.08	0.005	4.47	1.50–13.00	0.01
Comorbid group	9.62	3.76–24.89	<0.0001	14.08	4.99–41.66	<0.0001
12-month re-hospitalization						
Normal group	0			0		
Depression group	1.95	0.81–4.36	0.13	2.58	1.02–6.15	0.05
Anxiety group	2.79	1.36–5.58	0.006	2.83	1.33–5.89	0.007
Comorbid group	5.17	2.52–10.64	<0.0001	6.33	2.96–13.79	<0.0001

Model 1: Adjusting for age (<60 years *vs.* ≥60 years) and gender. Model 2: Adjusting for age (<60 years *vs.* ≥60 years), gender. LVEF (<50% *vs.* ≥50%), smoking, physical activity, diabetes, hypertension, hypercholesterolemia, and PAD. CI: Confidence interval; MI: Myocardial infarction; OR: Odds ratio.

could predict 12-month poor QOL in Chinese patients with ACS.

As depression and anxiety are closely correlated, comorbid depression with anxiety has been known to be associated with a greater severity of depressive disorders and a worse response to anti-depressive treatments.[7,9,10] Based on previous findings that comorbidity associated with adverse outcomes in hypertensive patients or healthy population,[12-14] a more severe prognosis was associated with comorbidity in patients with ACS compared with depression/anxiety alone. Our study confirmed this assumption. A strong relationship existed between depression, anxiety, non-fatal MI, and cardiac re-hospitalization in our study. The highest predictive value was found in comorbidity group when compared with major depression/anxiety alone groups, indicating that comorbidity should be a new subtype of depression and more attention devoted to ACS. There was no association between depression, anxiety, and mortality. The reason might lie in that MI intervention technology has improved dramatically in recent years leading to long-term patient survivals. Hereafter, non-fatal MI may be the major adverse outcome for patients with ACS and depression, and/or anxiety. Several studies reported that depression/anxiety associated with cardiac outcomes in patients with CAD may be mediated by high-risk health behaviors, such as sedentary lifestyle, delayed treatment, smoking, and non-adherence to secondary preventive measures.[22,23] Our study found that the prevalence of regular exercise was the lowest in comorbid patients and might partly explain the worse prognosis in comorbid patients with ACS.

Although mortality has remained a key outcome in managing CVD, cardiologists are beginning to embrace other outcomes, especially QOL.[24] QOL outcomes may also be prognostic in predicting subsequent morbidity and mortality in patients with ACS.[25] Some studies indicated that depression could predict the outcome of QOL during 12-month follow-ups.[26-28] Other studies reported that baseline anxiety but not depression predicted QOL during 7 to 12-month follow-ups.[29-31] Our study found that baseline comorbidity, but not major depression or anxiety alone, predicted QOL during 12-month follow-ups. It seems that the results of previous studies diverged from our findings. The reason was probably due to the fact that previous studies made no distinction of comorbidity from depression or anxiety alone. The prevalence of comorbidity was bound to vary widely in different cohorts. Yet all studies agreed that baseline mood status could predict long-term QOL in patients with ACS. Screening and interventions for depression comorbid with anxiety should be implemented for improving outcomes and QOL for patients with ACS.

Few studies have investigated the relationship between depression, anxiety, and medical expenditure in Chinese patients with ACS. Both anxiety and depression were independent predictors of frequent visits to outpatient cardiac clinic or re-hospitalizations due to cardiac events and higher medical expenditure.[32,33] And previous studies made no effort of separately exploring the impact of comorbidity on medical expenditure. Different effects of depression, anxiety, and comorbidity on medical expenditure were examined in our study. Among Chinese patients with ACS, re-hospitalization, cardiac or emergency clinic visit, and medical cost within 2 months increased significantly in comorbidity group and yet insignificantly in depression or anxiety alone group as compared with control group. Our study indicated that comorbidity but not major depression or anxiety alone increased medical expenditure. Although more data are required for confirming this result, comorbidity deserves more attention of clinicians. In light of medical expenditure becoming an overwhelming financial burden in China, depression/anxiety screening and intervention should be emphasized in patients with ACS to arrest this rising trend.

To our knowledge, fewer studies have addressed the appropriate intervention timing of anxiety/depression after ACS. Consistent with previous studies, our results confirmed that baseline depression/anxiety significantly increased the long-term risks of cardiac events and QOL in patients with ACS.[34,35] And depression/anxiety screening and intervention should be emphasized in patients with ACS. Yet clinicians remain ambivalent about which mood status should be tackled in an early stage. In our study, GAD-7 scores declined rapidly and normalized during 1-month follow-ups in patients with ACS while PHQ-9 scores decreased gradually and recovered to a normal level at 12 months. And the slowest decreases of PHQ-9/GAD-7 occurred in patients with comorbid depression/anxiety. It suggested that depression or depression comorbid with anxiety recovered more slowly than anxiety alone. In light of the effect of comorbidity on cardiac outcomes and QOL, greater attention should be devoted to patients with ACS with comorbid depression/anxiety during an early stage.

The limitations of our study included using only one instrument for assessing specific symptoms of depression/anxiety. Our sampling was sourced only from North China so that the results might not be extrapolated to patients of other ethnicities and regions. However, practical merits would justify our pioneering efforts of conducting the first-ever large-scale domestic longitudinal study for examining different effects of major depression, anxiety, and comorbidity on cardiac events, medical expenditure, and QOL.

Conclusions

Major depression and anxiety can predict 12-month non-fatal MI and cardiac re-hospitalization. However, comorbidity has the highest predictive value with greater medical expenditure and worse QOL in Chinese patients with ACS. And depression with comorbid anxiety may be a new target of mood status in patients with ACS.

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Conflicts of interest

None.

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