Psychological distress as a crucial determinant for quality of life in patients with noncardiac chest pain in Central China

A cross-sectional study

Lei Zhang, MD\(^b\), Lei Tu, MD\(^a\), Jie Chen, PhD\(^a\), Tao Bai, MD\(^a\), Jun Song, MD\(^a\), Xuelian Xiang, MD\(^a\), Ruiyun Wang, MD\(^b\), Xiaohua Hou, MD, PhD\(^a\)*

Abstract

Increased psychiatric comorbidity, predominantly anxiety and depressive symptoms, and lower quality of life (QoL) are associated with noncardiac chest pain (NCCP). We aimed to investigate the roles of anxiety and depression in the impaired QoL of NCCP patients in Central China.

In this hospital-based cross-sectional study, 200 consecutive patients who complained of chest pain with normal coronary angiography were enrolled in the Department of Cardiology and Gastroenterology, Union Hospital, Wuhan, China. Meanwhile, 100 healthy controls, with age and sex-matched, were recruited. Upper gastrointestinal endoscopy was undergone and a standardized symptom questionnaire was completed in NCCP patients. Levels of anxiety and depression and QoL were assessed using locally translated and validated versions of the Hospital Anxiety and Depression Scale (HADS) and the 36-item Short Form Health Survey (SF-36), respectively.

The NCCP patients had poorer physical and mental QoL compared with the controls, and nearly half of them had anxiety (49.7%) and depression (40.1%). Those with anxiety and/or depression had lower physical (PCS) and mental (MCS) component summary score compared with those without anxiety and depression. Increased levels of anxiety and depression were associated with lower PCS \((r = -0.469 \text{ and } -0.523 \text{ respectively, } P < 0.001)\) and MCS \((r = -0.474 \text{ and } -0.440 \text{ respectively, } P < 0.001)\). The chest pain, heartburn, and anxiety were independent factors influence on both PCS and MCS. Moreover, psychological distress, besides directly acting on the QoL, may also mediate indirectly effects of physical symptoms on both the physical and mental QoL.

We demonstrated that anxiety and depression are important determinants for the QoL of NCCP patients. Therefore, interventions should emphasize on identifying and treating the psychological impact in NCCP.

Abbreviations: BMI = body mass index, CCP = cardiac chest pain, CFI = comparative fit index, CI = confidence interval, FD = functional dyspepsia, GERD = gastroesophageal reflux disease, HADS = the Hospital Anxiety and Depression Scale, MCS = mental component summary score, NCCP = noncardiac chest pain, NNFI = nonnormed fit index, OR = odds ratio, PCS = physical component summary score, QoL = quality of life, RMSEA = root mean square error of approximation, SD = standard deviation, SF-36 = the 36-item Short Form Health Survey, SRMR = standardized root mean square residual, VIF = variance inflation factor.

Keywords: anxiety, chest pain, depression, esophagus, quality of life

1. Introduction

Noncardiac chest pain (NCCP) is a common problem with the annual prevalence at approximately 23% in the western population and 13% to 15% in Chinese subjects\(^{[1,2]}\) which can be defined as the experience of recurrent substernal or angina-like chest pain in the absence of coronary artery disease or other apparent cardiac abnormalities evaluated by reasonable cardiac examination\(^{[3,4]}\).

NCCP is a benign condition with the estimated 10-year mortality of less than 1%\(^{[2,4,5]}\); however, it is one of the most frightening pains which may be a warning sign of coronary artery disease or myocardial infarction\(^{[6]}\). It leads to impaired quality of life (QoL) with daily disability and emotional distress, and increased health care costs due to repeat hospitalizations, emergency department visits and cardiac examinations\(^{[1,3,4,6]}\). Although gastroesophageal reflux disease (GERD), esophageal dysmotilities such as achalasia, diffuse esophageal spasm and nutcracker esophagus, and musculoskeletal disorders explain most cases of this disorder\(^{[1,3]}\), it is still inadequate to be responsible for the exaggerated symptoms of pain and obviously
decreased health-related QoL. Recently, increased psychological morbidity, such as panic disorders, unique perceptual, and coping style, have been reported in patients with NCCP.[7,8] Psychiatric symptoms may cause the chest pain alone, or along with the organic disorders, which may be the reason why the pain is difficult to cure or usually recurrent.

Anxiety and depression are major comorbid psychological factors of NCCP.[9] It is understandable that patients coexisting with anxiety or depression may more concern about having a serious heart disease, and more likely to possess higher rate of seeking medical consultation and lower QoL.[10] However, much is still to be learned about the role of psychological impact on the health-related QoL in patients with NCCP, particularly in Chinese subjects. Furthermore, in many cases, more emphasis has been given on the treatment of really physical symptoms, but ignored the adjustment to the invisible psychological disorders in these subjects. This issue may provide a good starting point for interventions of NCCP, since psychiatric symptoms may relate to persistent chest pain and continuing physical and mental incapacity.

In this study, a standardized questionnaire contained items to assess the main physical symptoms, mental disorders (anxiety and depression) and health-related QoL was designed and conducted in NCCP patients in Central China. We aimed to identify the interactions among physical symptoms, psychological disorders, and the QoL in NCCP subjects, in particular, the roles of anxiety and depression in the impaired QoL in these subjects. This may be meaningful for the treatment of those with NCCP, while an individualized biopsychosocial model has been proposed.[9]

2. Methods

2.1. Subjects

In this cross-sectional study, consecutive patients were invited from those who seeking care for a chief complaint of chest pain and undergoing coronary angiography at the Division of Cardiology and Gastroenterology, Union Hospital, Wuhan, China. And the patients with normal or near normal electrocardiogram and coronary angiography, defined as epicardial coronary artery stenoses < 30%,[11] were enrolled. A final sample of 200 NCCP patients was received in this study. Meanwhile, 100 healthy controls, with age and sex-matched with the total NCCP patients, were recruited. Patients were invited for upper gastrointestinal endoscopy and a standardized questionnaire (as detailed below) was conducted. This study was approved by the Institutional Ethical Review Committee of Huazhong University of Science and Technology, China ([2011] No.025).

2.2. The questionnaire

2.2.1. Demographic characteristics. Demographic information was collected using a self-report questionnaire, including age, sex, height, weight, education and occupation, as well as living habits (smoking, alcohol, tea and coffee).

2.2.2. The Rose angina questionnaire. The frequency, severity, duration, and other characteristics of the chest pain were recorded using a Chinese version of the translated Rose angina questionnaire, which has a intraclass correlation coefficient at 0.91, and a sensitivity and specificity of 68% and 95% for the diagnosis of ischemic heart disease, respectively.[2] NCCP was defined as nonexertional chest pain according to the Rose angina questionnaire and had not been diagnosed as ischemic heart diseases by coronary angiography.[10] Musculoskeletal-like chest pain referred to chest pain worse on movement, breathing, or pressing on the chest wall.[5]

2.2.3. The gastrointestinal symptom questionnaire. Gastrointestinal symptoms were assessed, including esophageal symptoms (heartburn, acid regurgitation, dysphagia, regurgitation, odynophagia, and sense of obstruction when swallowing) and extraesophageal symptoms (chronic cough, hoarseness of voice, asthma, pneumonia, and oral discomfort) related to GERD, as well as symptoms associated with functional dyspepsia (FD). The severity and frequency gastrointestinal symptoms were graded on a 5-point Likert scale (1–5) as previously described.[15] GERD was defined as acid regurgitation and/or heartburn occurring at least weekly.[11] In addition, the history of esophageal, gastric, cardiac or pulmonary disease, and the medication were recorded.

2.2.4. The hospital anxiety and depression scale. The Hospital Anxiety and Depression Scale (HADS) is widely used scale for detecting depression and anxiety in the clinic setting, which comprises of 14 items with a scale of 0 to 3 for each items. There is a total score of 21 for anxiety (7 items) and depression (7 items), respectively. A cut-off point of 8 is deemed to have anxiety or depression, and it has an optimal balance between sensitivity and specificity, and 8 to 10 points is mildly abnormal, 11 to 14 points is moderately abnormal, 15 to 21 points is severe abnormal.[11]

2.2.5. The 36-item Short Form Health Survey. The health-related QoL was assessed using the 36-item Short Form Health Survey (SF-36), which consists of 8 dimensions and divides into two aspects, the physical component score (PCS, including physical function, role-physical, bodily pain, and general health) and the mental component score (MCS, including vitality, social functioning, role-emotional, and mental health).[12] It is well-documented according to validity and reliability in available language versions.[13] The scores range from 0 to 100, and higher scores indicating a better health-related QoL.[11,12]

2.2.6. Data collection and statistical analysis. Data of questionnaires were cleaned, coded, and double-entered using EpiData software 3.1. Statistical results were presented as the mean ±SD or number of patients (%). SPSS 18.0 and AMOS 18.0 (SPSS, Inc., Chicago, IL) were used for data analysis. Two-sided P < 0.05 was considered statistically significant.

Sample size was calculated with 95% confidence level and 85% power with a P-value of 0.05. Continuous variables were analyzed by means of 1-way ANOVA or nonparametric Kruskal–Wallis test, followed by the least significant difference (LSD) test or Dunnett T3 test for multiple comparisons when required. Categorical variables were compared via Chi-square test or Fisher exact test as appropriate. Spearman correlation analysis was used to identify the correlations among somatic symptoms, psychological status, and the QoL. Multiple regression analysis was then performed to determine the independent factors effect on the QoL. The missing data were excluded. To find the best model, a stepwise procedure was carried out with the entry P < 0.05 and removal P > 0.10, and collinearity diagnostics indicated no marked multicollinearity with tolerance >0.1 and variance inflation factor (VIF) <5.

In order to test the multiple interactions between somatic symptoms and psychological disorders, and their direct and indirect effects on the QoL, a path analysis with a covariance matrix as input and full information maximum likelihood
estimation was conducted. Model modification was guided by the Wald statistics and modification indices. The goodness-of-fit indices, including comparative fit index (CFI) and nonnormed fit index (NNFI), as well as the root mean square error of approximation (RMSEA) and standardized root mean square residual (SRMR) were calculated to evaluate the model fit. A model with CFI > 0.95, RMSEA < 0.10, SRMR < 0.08 is indicative of good model fit.[14]

3. Results

3.1. Demographic characteristics of NCCP patients

Totally 200 NCCP patients (mean age, 58 years; range, 21–82 years; 113 male and 87 female) included in this study. The NCCP patients were divided into 4 subgroups according to the HADS-scores, that is, NCCP without anxiety or depression (contained patients without anxiety or depression, N = 88), NCCP with anxiety (contained patients with anxiety only and with both anxiety and depression N = 98), NCCP with depression (contained patients with depression only and with both depression and anxiety, N = 79), NCCP with anxiety and depression (contained patients with both anxiety and depression, N = 68). Subjects of NCCP with anxiety and/or depression were a little younger than those without anxiety or depression (52.9 ± 10.4 vs 48.9 ± 11.2, P = 0.040). However, there was no significant difference in gender, body mass index (BMI), education, occupation and living habits for smoking, alcohol, tea and coffee between subjects of NCCP with and without anxiety or depression (Table 1). Besides, the healthy controls were matched with the total NCCP group (age: 51.06 ± 10.22; female/male: 1/1.14; BMI: 22.87 ± 3.04; all P > 0.05).

3.2. Upper gastrointestinal endoscopy findings in NCCP patients

A total of 88 (44.0%) patients with NCCP completed the upper gastrointestinal endoscopy. In these patients, 33 (37.5%) cases were normal, 3 (3.4%) cases were Barrett esophagus, 5 (5.7%) cases were esophagitis, 46 (52.3%) cases were mild gastritis, and only 1 (1.1%) case was gastric ulcer. In patients with typical reflux symptoms, about 61.2% (60/98) completed the endoscopy and most of them were normal or just mild gastritis (88.3% (53/60)). About 42.7% (32/75) of NCCP patients with dyspepsia symptoms underwent endoscopy and 96.9% (31/32) of them were normal or mild gastritis.

3.3. Chest pain and other symptoms in NCCP patients

The proportions of patients with chest pain < once per month, ≥ once per month, and ≥ once per week were 29.0%, 31.5%, and 39.5%, respectively. And most of these patients had a moderate to severe chest pain (44.5% and 37.5%, respectively). 12.5% of NCCP subjects with a muscular chest pain. Nearly half (44.0%) of NCCP patients were diagnosed with GERD. Heartburn (43.5%) and acid regurgitation (44.5%) were chief esophageal symptoms, and 36.5% of subjects had extraesophageal symptoms. Moreover, a significant number (37.5%) of patients suffered symptoms associated with FD (Table 2).

3.4. Anxiety and depression in NCCP patients

Nearly half of the NCCP patients had anxiety (49.7%) and obviously higher than the controls (11.0%), the odds ratio (OR) was 5.197 (95% confidence interval (CI), 2.843–9.501, P < 0.001). The NCCP patients diagnosed as depression also more than the controls (40.1% vs 16.0%), the OR was 5.417 (95% CI, 2.843–9.501, P < 0.001). Moreover, most of the NCCP patients diagnosed as anxiety or depression were mild to moderate (Table 3).

3.5. Health-related QoL in NCCP patients

The NCCP patients had a poorer QoL compared with the controls, with a lower PCS (59.89 ± 10.15 vs 79.78 ± 15.96, P < 0.05), MCS (43.51 ± 23.61 vs 79.90 ± 18.87, P < 0.05), and total score (60.77 ± 2.10 vs 79.84 ± 15.20, P < 0.05) (Fig. 1). Compared with those without anxiety or depression, the PCS and MCS as well as total QoL score were much lower (all P < 0.01) in NCCP subjects with anxiety, with depression, and with both anxiety and depression (Table 4).

Table 1

| Characteristics of NCCP patients. | NCCP without anxiety or depression (N = 88) | NCCP with anxiety (N = 98) | NCCP with depression (N = 79) | NCCP with anxiety and depression (N = 68) | Total NCCP (N = 200) | P |
|-----------------------------------|--------------------------------------------|---------------------------|-------------------------------|-----------------------------------------|---------------------|---|
| Age (M ± SD), y                   | 48.92 ± 11.22                              | 52.62 ± 10.86             | 52.99 ± 10.15                 | 52.91 ± 10.67                           | 51.19 ± 10.91       | 0.040|
| Sex (female/male)                 | 49/39 (1.0:0.80)                           | 47/53 (1:1.09)            | 42/37 (1:1.08)                | 32/38 (1:1.23)                          | 87/113 (1:1.30)     | 0.636|
| BMI (M ± SD), kg/m²               | 23.20 ± 3.68                               | 22.71 ± 3.02              | 22.91 ± 2.83                  | 22.67 ± 2.94                            | 23.01 ± 3.27        | 0.704|

Table 1 Characteristics of NCCP patients.

BMI = body mass index, M ± SD = mean ± standard deviation, NCCP = noncardiac chest pain.

| Characteristics of NCCP patients. | NCCP without anxiety or depression (N = 88) | NCCP with anxiety (N = 98) | NCCP with depression (N = 79) | NCCP with anxiety and depression (N = 68) | Total NCCP (N = 200) | P |
|-----------------------------------|--------------------------------------------|---------------------------|-------------------------------|-----------------------------------------|---------------------|---|
| Age (M ± SD), y                   | 48.92 ± 11.22                              | 52.62 ± 10.86             | 52.99 ± 10.15                 | 52.91 ± 10.67                           | 51.19 ± 10.91       | 0.040|
| Sex (female/male)                 | 49/39 (1.0:0.80)                           | 47/53 (1:1.09)            | 42/37 (1:1.08)                | 32/38 (1:1.23)                          | 87/113 (1:1.30)     | 0.636|
| BMI (M ± SD), kg/m²               | 23.20 ± 3.68                               | 22.71 ± 3.02              | 22.91 ± 2.83                  | 22.67 ± 2.94                            | 23.01 ± 3.27        | 0.704|

| Characteristics of NCCP patients. | NCCP without anxiety or depression (N = 88) | NCCP with anxiety (N = 98) | NCCP with depression (N = 79) | NCCP with anxiety and depression (N = 68) | Total NCCP (N = 200) | P |
|-----------------------------------|--------------------------------------------|---------------------------|-------------------------------|-----------------------------------------|---------------------|---|
| Age (M ± SD), y                   | 48.92 ± 11.22                              | 52.62 ± 10.86             | 52.99 ± 10.15                 | 52.91 ± 10.67                           | 51.19 ± 10.91       | 0.040|
| Sex (female/male)                 | 49/39 (1.0:0.80)                           | 47/53 (1:1.09)            | 42/37 (1:1.08)                | 32/38 (1:1.23)                          | 87/113 (1:1.30)     | 0.636|
| BMI (M ± SD), kg/m²               | 23.20 ± 3.68                               | 22.71 ± 3.02              | 22.91 ± 2.83                  | 22.67 ± 2.94                            | 23.01 ± 3.27        | 0.704|

| Characteristics of NCCP patients. | NCCP without anxiety or depression (N = 88) | NCCP with anxiety (N = 98) | NCCP with depression (N = 79) | NCCP with anxiety and depression (N = 68) | Total NCCP (N = 200) | P |
|-----------------------------------|--------------------------------------------|---------------------------|-------------------------------|-----------------------------------------|---------------------|---|
| Age (M ± SD), y                   | 48.92 ± 11.22                              | 52.62 ± 10.86             | 52.99 ± 10.15                 | 52.91 ± 10.67                           | 51.19 ± 10.91       | 0.040|
| Sex (female/male)                 | 49/39 (1.0:0.80)                           | 47/53 (1:1.09)            | 42/37 (1:1.08)                | 32/38 (1:1.23)                          | 87/113 (1:1.30)     | 0.636|
| BMI (M ± SD), kg/m²               | 23.20 ± 3.68                               | 22.71 ± 3.02              | 22.91 ± 2.83                  | 22.67 ± 2.94                            | 23.01 ± 3.27        | 0.704|
3.6. Effects of physical symptoms, anxiety and depression on the QoL in NCCP patients

The correlation analysis suggested that severity (CPS) and frequency (CPF) of chest pain, esophageal symptoms (heartburn, acid regurgitation, dysphagia) were positive related to levels of anxiety and depression, while negative correlated with the PCS and MCS of NCCP patients. In addition, FD symptoms and extraesophageal symptoms also had significant positive correlations with both anxiety and depression, but only negative correlated to the MCS. Other symptoms, such as muscular chest pain, odynophagia, sense of obstruction when swallowing had no significant correlation to levels of anxiety and depression and health-related QoL (Table 5). Increased levels of anxiety and depression were associated with lower PCS ($r = -0.469$ and $-0.523$, respectively, $P < 0.001$) and MCS ($r = -0.474$ and $-0.440$, respectively, $P < 0.001$) (Table 5). Furthermore, the results of multiple regression analysis showed that CPF, CPS, heartburn, and anxiety were the independent factors effects on both the physical and mental QoL of NCCP patients (Table 6).

3.7. Direct and indirect effects of symptoms, anxiety and depression on the QoL in NCCP patients in a path model

A path model was established among symptoms, anxiety and depression and the QoL in NCCP patients as it is shown in Fig. 2. The final path model had a good fitness with $\chi^2(6) = 14.846, P = 0.021$; CFI = 0.979, NNFI = 0.907, SRMR = 0.030, RMSEA = 0.087 with 90% CI [0.031, 0.144]. It suggested that psychological impact could direct effects on the QoL, as well as the chest pain. Moreover, anxiety and depression may mediate the indirect effects of chest pain on the QoL (Fig. 2). CPS and CPF had indirect effects on PCS ($-0.135$, $P = 0.010$ and $-0.114$, $P = 0.022$, respectively) and MCS ($-0.103$, $P = 0.014$ and $-0.87$, $P = 0.027$, respectively) (Table 7). Relatively, the effects of esophageal and extraesophageal symptoms and FD symptoms seemed to be less direct but an indirect effects on the physical and mental QoL (Fig. 2).

4. Discussion

Chest pain is a common and alarm symptom that leads to serious psychological distress and decreasing in the QoL in western society, even though more than half of these patients are noncardiac origin,[1,4] It may also be true in Chinese populations. In this study, particularly, role of psychological distress in impaired health-related QoL of NCCP patients in Central China were assessed. The results revealed that high ratio of anxiety and depression, and poorer physical and mental QoL existed in NCCP subjects, moreover, anxiety and depression were closely associated with lower QoL. Psychological distress, besides directly acting on the QoL, may also mediate indirectly effects of physical symptoms on both the physical and mental QoL.

Impairment of QoL, both the physical and mental aspects, was evident in NCCP patients compared with the healthy subjects as we demonstrated. Moreover, it has been reported that NCCP patients were generally accompanied by poorer QoL and more frequent of work absenteeism, similarly as it was in cardiac chest pain (CCP) patients.[2,15] We further confirmed that chest pain, heartburn, and anxiety are major independent influencing factors on the QoL of NCCP patients. It suggested that the symptoms of
illness and the psychological distress may be main factors to be responsible for the poor QoL.

In our patients, the chest pain had a strong negative correlation with both the mental and physical QoL. It was no doubt that physical illness play an important role in the determination of physical and mental well-being. Esophageal and gastric abnormalities are main symptoms overlapped with NCCP, especially the GERD-related symptoms. About 44.0% of NCCP patients were diagnosed with GERD according to the GERD questionnaire with typical symptoms, based on our results. It was consistent with the report that GERD is the most common cause of NCCP.[16,17] A range of 22% to 80% of those with NCCP had pathological acid reflux on 24-hour esophageal pH monitoring.[18] The major reflux symptoms, including heartburn, acid regurgitation, and dysphagia, were negatively related to the mental and physical QoL. Besides, extraesophageal symptoms

### Table 4
Quality of life in NCCP patients.

|                          | NCCP without anxiety or depression (N = 88) | NCCP with anxiety (N = 98) | NCCP with depression (N = 79) | NCCP with anxiety and depression (N = 68) | Total NCCP (N = 200) |
|--------------------------|--------------------------------------------|----------------------------|--------------------------------|------------------------------------------|----------------------|
| Physical Component summary score (PCS) | 70.90 ± 18.21                              | 50.81 ± 19.36**            | 47.81 ± 18.35**                | 46.69 ± 18.93**                          | 59.69 ± 20.86**      |
| Mental Component summary score (MCS) | 74.92 ± 20.71                              | 53.52 ± 22.19**            | 52.51 ± 22.16**                | 51.02 ± 22.4**                           | 63.51 ± 23.61**      |
| SF-36 total score        | 71.25 ± 21.42                              | 52.17 ± 18.95**            | 50.16 ± 18.65**                | 48.86 ± 19.20**                          | 60.77 ± 22.10**      |

Data are shown as means ± standard deviation.

NCCP = noncardiac chest pain, SF-36 = the 36-item Short Form Health Survey.

* P < 0.05.

** P < 0.01, compare with NCCP patients without anxiety or depression.

### Table 5
Correlations analyses among physical symptoms, psychological state, and quality of life in NCCP patients (N = 197).

|                          | Anxiety, r | Depression, r | PCS, r | MCS, r |
|--------------------------|------------|---------------|--------|--------|
| Chest pain frequency     | 0.300**    | 0.182         | -0.301** | -0.357** |
| Chest pain severity      | 0.303**    | 0.266**       | -0.407** | -0.505** |
| Muscular chest pain      | -0.078     | 0.066         | -0.046 | -0.038 |
| Esophageal symptom       |            |               |        |        |
| Heartburn                | 0.181*     | 0.128         | -0.234** | -0.218** |
| Acid regurgitation       | 0.205**    | 0.146         | -0.209** | -0.251** |
| Regurgitation            | -0.020     | -0.047        | -0.141 | -0.147 |
| Dysphagia                | 0.187**    | 0.196         | -0.187** | -0.189** |
| Sense of obstruction when swallowing | 0.091 | -0.004 | -0.116 | -0.139 |
| Odynophagia              | 0.149      | 0.056         | -0.179 | -0.110 |
| Extraesophageal symptom  | 0.133*     | -0.137*       | -0.076 | -0.144* |
| FD symptom               | 0.293**    | 0.308**       | -0.122 | -0.213** |
| HADS anxiety             | 0.115      | 0.534**       | -0.469** | -0.474** |
| HADS depression          | 0.354**    | -0.523**      | -0.440** | -0.440** |

FD = functional dyspepsia, HADS = Hospital Anxiety and Depression Scale, MCS = mental component summary score, NCCP = noncardiac chest pain, PCS = physical component summary score.

* P < 0.05.

** P < 0.01.

### Table 6
Multiple linear regression analyses of the influence of physical symptoms and psychological state on quality of life in NCCP patients.

|                          | Unstandardized coefficients | Standardized coefficients (beta) | t      | P      | Tolerance | VIF |
|--------------------------|-----------------------------|---------------------------------|--------|--------|-----------|-----|
|                          | B                           | Std. err                        |        |        |           |     |
| PCS                      | Constant                    | 94.510                          | 4.677  |        | 20.207    | 0.000|
|                          | CFP                         | -4.413                          | 1.502  | -0.174 | -2.937    | 0.004|
|                          | CPS                         | -7.103                          | 1.611  | -0.264 | -4.409    | 0.000|
|                          | Heartburn                   | -6.523                          | 2.450  | -0.155 | -2.663    | 0.008|
|                          | Anxiety                     | -8.865                          | 1.410  | -0.376 | -6.287    | 0.000|
| MCS                      | Constant                    | 112.989                         | 5.109  |        | 22.116    | 0.000|
|                          | CFP                         | -6.906                          | 1.641  | -0.240 | -4.208    | 0.000|
|                          | CPS                         | -11.707                         | 1.760  | -0.384 | -6.653    | 0.000|
|                          | Heartburn                   | -6.051                          | 2.676  | -0.127 | -2.262    | 0.025|
|                          | Anxiety                     | -7.112                          | 1.540  | -0.266 | -4.618    | 0.000|

CPF = chest pain frequency, CPS = chest pain severity, MCS = mental component summary score, NCCP = noncardiac chest pain, PCS = physical component summary score, VIF = variance inflation factor.
CPS with the anxiety-based theories of NCCP. Those with anxiety and depression were significant QoL compared with those without anxiety and depression of QoL levels. The reasons were as follows: NCCP patients psychological impact plays an important role in the determination of QoL levels. Moreover, many patients with NCCP who do not meet criteria for psychiatric disorders still experience significant psychological disorder. Functional disability, such as panic, catastrophizing, and somatization, physical symptoms, such as chest pain, heartburn, acid regurgitation, and dysphagia, were closely related to the psychologic state in patients with NCCP as we shown. However, the causality between each other is complicated and inconclusive. NCCP patients with psychological distress experienced more severe and frequent chest pain and more concern about pain. On the contrary, patients with nonlethal chest pain may experience more disease conviction, higher levels of depression and anxiety, more cardioprotective behavior, such as avoiding activities that they thought might be harmful to their heart. This may be especially true in the patients with Type D personality which is the independent factor affected on the presence of psychopathology in NCCP patients. Our further study exhibited that the chest pain could indirectly effects on both physical and mental QoL in NCCP patients through increasing the anxiety and depression. In this sense, psychological burden, such as anxiety and depression, may be an important determinant of QoL in patients with NCCP. Therefore, identification of psychological disorders seems especially important, since higher levels of depression and anxiety lead NCCP patients to repeatedly seek for medical consultation and intervention, accompanied by reductions in QoL.

This study also had several limitations. First, although the path model suggested that physical symptoms could act on psychological states, through which indirectly influence on the QoL, the prospective studies are still required to examine and confirm the cause–effect relationships among each other. Second, although the HADS and SF-36 questionnaire were widely used in clinics for assessment of anxiety/depression and health-related QoL, it need further evaluating the applicability of translated version of these self-reported questionnaires on Chinese NCCP subjects. Third, we did not follow-up with our NCCP patients, thus, it should be our subsequent works to follow-up the patients and verify our conclusions.

In summary, high proportion of anxiety and depression were closely associated with the poor QoL in NCCP patients. Besides the directly effects on the QoL, anxiety and depression may also mediate the indirect effects of chest pain on the physical and mental QoL in NCCP patients, which indicated that psychological distress was the crucial determinants of QoL in patients with NCCP. Therefore, we suggested that, in addition to therapies targeting the physical illness, interventions to identify and treat the psychological impact may be of great benefit to NCCP patients.

| Table 7 | Direct and anxiety/depression-mediated indirect effects of chest pain on quality of life in NCCP patients. |
|---------|----------------------------------------------------------------------------------------------------------------|
| **Effects** | **PCS** | **MCS** |
|          | Estimated | Std. err | P  | Estimated | Std. err | P  |
| CPF Total | −0.234 | 0.079 | 0.003 | −0.345 | 0.077 | 0.007 |
| Direct    | −0.120 | 0.076 | 0.012 | −0.238 | 0.073 | 0.001 |
| Indirect  | −0.114 | 0.050 | 0.022 | −0.107 | 0.040 | 0.020 |
| CPS Total | −0.426 | 0.082 | 0.000 | −0.459 | 0.080 | 0.000 |
| Direct    | −0.291 | 0.079 | 0.000 | −0.356 | 0.076 | 0.000 |
| Indirect  | −0.135 | 0.053 | 0.010 | −0.103 | 0.042 | 0.014 |

CPF = chest pain frequency, CPS = chest pain severity, MCS = mental component summary score, NCCP = noncardiac chest pain, PCS = physical component summary score.  
Based on standardized path coefficients.
Acknowledgments

The authors express their gratitude to all the participants, and also would like to thank Chuang Sun for the statistical assistance and Sheng-Yang Chen for the language polishing.

References

[1] Eslick GD, Jones MP, Talley NJ. Non-cardiac chest pain: prevalence, risk factors, impact and consulting—a population-based study. Aliment Pharmacol Ther 2003;17:1115–24.
[2] Wong WM, Lam KF, Cheng C, et al. Population based study of noncardiac chest pain in southern Chinese: prevalence, psychosocial factors and health care utilization. World J Gastroenterol 2004;10:707–12.
[3] Fang J, Bjorkman D. A critical approach to noncardiac chest pain: pathophysiology, diagnosis, and treatment. Am J Gastroenterol 2001;96:958–68.
[4] White KS, McDonnell CJ, Gervino EV. Alexithymia and anxiety sensitivity in patients with non-cardiac chest pain. J Behav Ther Exp Psychiatry 2011;42:432–9.
[5] Cheung TK, Hou X, Lam KF, et al. Quality of life and psychological impact in patients with noncardiac chest pain. J Clin Gastroenterol 2009;43:13–8.
[6] Eslick GD, Talley NJ. Natural history and predictors of outcome for non-cardiac chest pain: a prospective 4-year cohort study. Neurogastroenterol Motil 2008;20:989–97.
[7] García-Campayo J, Rosel F, Serrano P, et al. Different psychological profiles in non-cardiac chest pain and coronary artery disease: a controlled study. Rev Esp Cardiol 2010;63:357–61.
[8] Cheng C, Wong WM, Lai KC, et al. Psychosocial factors in patients with noncardiac chest pain. Psychosom Med 2003;65:443–9.
[9] Chambers JB, Marks EM, Russell V, et al. A multidisciplinary, biopsychosocial treatment for non-cardiac chest pain. Int J Clin Pract 2015;69:922–7.
[10] Lampe FC, Walker M, Lennon LT, et al. Validity of a self-reported history of doctor-diagnosed angina. J Clin Epidemiol 1999;52:73–81.
[11] Kuipers PM, Denollet J, Lousberg R, et al. Validity of the hospital anxiety and depression scale for use with patients with noncardiac chest pain. Psychosomatics 2003;44:329–35.
[12] Hadlandsmyth K, White KS, Krone RJ. Quality of life in patients with non-CAD chest pain: associations to fear of pain and psychiatric disorder severity. J Clin Psychol Med Settings 2013;20:284–93.
[13] Thumboo J, Wu Y, Tai ES, et al. Reliability and validity of the English (Singapore) and Chinese (Singapore) versions of the Short-Form 36 version 2 in a multi-ethnic urban Asian population in Singapore. Qual Life Res 2013;22:2501–8.
[14] Ling J, Robbins LB, McCarthy VL, et al. Psychosocial determinants of physical activity in children attending afterschool programs: a path analysis. Nurs Res 2013;62:190–9.
[15] Eslick GD, Talley NJ. Non-cardiac chest pain: predictors of health care seeking, the types of health care professional consulted, work absenteeism and interruption of daily activities. Aliment Pharmacol Ther 2004;20:909–15.
[16] Hershkovitz T, Achem SR, Jha EK, et al. Systematic review: the treatment of noncardiac chest pain. Aliment Pharmacol Ther 2012;35:5–14.
[17] Park SH, Choi JY, Park EJ, et al. Prevalence of gastrointestinal diseases and treatment status in noncardiac chest pain patients. Korean Circ J 2013;45:469–72.
[18] Kim BJ, Choi SC, Kim JJ, et al. Pathological bolus exposure plays a significant role in eliciting non-cardiac chest pain. J Gastroenterol Hepatol 2010;25:1855–60.
[19] Rasmussen S, Jensen TH, Henriksen SL, et al. Overlap of symptoms of gastroesophageal reflux disease, dyspepsia and irritable bowel syndrome in the general population. Scand J Gastroenterol 2015;50:162–9.
[20] Esler JL, Bock BC. Psychological treatments for noncardiac chest pain: recommendations for a new approach. J Psychosom Res 2004;56:263–9.
[21] Rosenbaum DL, White KS, Gervino EV. The impact of perceived stress and perceived control on anxiety and mood disorders in noncardiac chest pain. J Health Psychol 2012;17:1183–92.
[22] Webster R, Norman P, Goodacre S, et al. The prevalence and correlates of psychological outcomes in patients with acute non-cardiac chest pain: a systematic review. Emerg Med J 2012;29:267–73.
[23] Fass R, Achem SR. Noncardiac chest pain: epidemiology, natural course and pathogenesis. J Neurogastroenterol Motil 2011;17:110–23.
[24] White KS, Craft JM, Gervino EV. Anxiety and hypervigilance to cardiopulmonary sensations in non-cardiac chest pain patients with and without psychiatric disorders. Behav Res Ther 2010;48:394–401.
[25] Shelby RA, Somers TJ, Keefe EF, et al. Pain catastrophizing in patients with noncardiac chest pain: relationships with pain, anxiety, and disability. Psycosom Med 2009;71:861–8.
[26] Kuipers PM, Denollet J, Wellens HJ, et al. Noncardiac chest pain in the emergency department: the role of cardiac history, anxiety or depression and Type D personality. Eur J Cardiovasc Prev Rehabil 2007;14:273–9.
[27] Kessing BF, Bredenoord AJ, Saleh CM, et al. Effects of anxiety and depression in patients with gastroesophageal reflux disease. Clin Gastroenterol Hepatol 2015;13:1089.e1–95.e1.
[28] Husser D, Bollmann A, Kühne C, et al. Evaluation of noncardiac chest pain: diagnostic approach, coping strategies and quality of life. Eur J Pain 2006;10:51–5.