

Clinical outcomes and survival analysis in patients with psycho-cardiological disease: a retrospective analysis of 132 cases

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Abstract

Objectives: The deleterious effects of psychological problems on coronary heart disease (CHD) are not satisfactorily explained. We explored influential factors associated with mortality in psycho-cardiological disease in a Chinese sample.

Methods: Of 7460 cardiac patients, we selected 132 patients with CHD and mental illness. Follow-up was conducted via telephone. We analyzed clinical characteristics, clinical outcomes, and survival.

Results: The clinical detection rate of psycho-cardiological disease in the overall patient population was 1.8%. Of these, 113 patients completed follow-up; 18 died owing to cardiovascular diseases during follow-up. Kaplan–Meier analysis showed dysphagia, limb function, self-care ability, percutaneous coronary intervention, low-density lipoprotein, total cholesterol, pro-brain natriuretic peptide and high-sensitivity (hs) troponin T had significant associations with cumulative survival. Cox regression analysis showed total cholesterol (hazard ratio [HR]: 2.765, 95% confidence interval [CI]: 1.001–7.641), hs troponin T (HR: 4.668, 95% CI: 1.293–16.854), and percutaneous coronary intervention (HR: 3.619, 95% CI: 1.383–9.474) were independently associated with cumulative survival.

Conclusions: The clinical detection rate of psycho-cardiological disease was far lower than expected. Normal total cholesterol and hs troponin T were associated with reduced cardiovascular disease mortality over 2 years. Percutaneous coronary intervention is a prognostic risk factor in patients with psycho-cardiological disease.

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Keywords

Coronary heart disease, mental illness, psycho-cardiological disease, survival, hs troponin T, percutaneous coronary intervention

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Introduction

Coronary heart disease (CHD) is the leading cause of death worldwide, representing a serious public health problem. In recent years, the interaction between psychological disorders and CHD has received widespread attention in the Chinese medical field. Although much progress has been made over the past two decades in the treatment of CHD, the rates of hospitalization and mortality remain high.¹ Cardiovascular diseases and mental illnesses have become the two main serious diseases affecting human physical and mental health. When present together, these are referred to as psycho-cardiological disease.

With development of the psycho-cardiology discipline, a large number of epidemiological studies have reported that even by controlling biological risks, such as cholesterol levels and blood pressure, other psychological risk factors such as anxiety, depression, and excessive stress are still considered to be important in the onset of CHD.^{2,3} These factors are also regarded as predictors for a decline in patients' quality of life or even death.⁴ In China, approximately 50% of patients with CHD have anxiety or depressive symptoms, and women and older patients are considered high-risk populations.⁵

Depression is a risk factor for morbidity and mortality in patients with CHD, especially following acute coronary syndrome.^{2,6} Depression is also a predictor of heart disease.⁴ Depressed patients have a 64% greater risk of heart disease than

those without depression.⁷ A large number of studies have shown that depression is an important factor influencing the prevalence of cardiovascular diseases, increased re-hospitalization rates, and increased mortality in patients with CHD.⁸ Depression is commonly seen among patients with CHD, and there is ample evidence that the prevalence of depression is 20% higher in patients with heart failure than in healthy individuals.^{9–11}

A systematic review including 12 studies evaluated clinical endpoints, such as myocardial infarction and cardiac death. Five studies reported significant associations, three studies reported marginally significant associations, and four studies reported no association between indexes of anxiety and patients with CHD.¹² In their meta-analysis, Roest et al. (2010) investigated the connection between anxiety and risk factors of coronary artery disease and found anxiety was an independent risk factor for CHD and cardiac death. The association between anxiety and CHD is somewhat less evident than the corresponding relationship between depression and CHD; however, this connection was stronger than the relationship between anger and CHD occurrence.¹³ According to a survey on physical and psychological symptoms of anxiety in patients with CHD, anxiety was correlated with physical factors, such as palpitations without engaging in any physical exercise, anger and redness in the face, abnormal heart beat, and muscle tension, which increase the risk of CHD, especially in women.¹⁴

In this 2-year follow-up study, we collected clinical data to explore relevant factors in patients with psycho-cardiological disease. We investigated and summarized risk factors of the disease to identify factors related to mortality among patients with psycho-cardiological disease.

Methods

Participants and recruitment

This retrospective study was approved by the Ethics Committee of Guangdong Provincial People's Hospital (GPPH) in China. Patients with CHD who had mental illness were enrolled, using the GPPH Hospital Information System, between January and December 2017. Two researchers assessed the information at the same time to address any inconsistencies. This retrospective study was approved by the ethics committee of GPPH. Patients participating in the study provided verbal informed consent.

The inclusion criteria were as follows: (1) patients with a diagnosis of CHD, (2) diagnosed with anxiety or depression, (3) cardiac function grade I–II, based on echocardiography, and (4) patients with any acute cardiovascular events in the past 6 months. Anxiety and depressive symptoms were measured using the Self-Rating Anxiety Scale (SAS)¹⁵ and Self-Rating Depression Scale (SDS),¹⁵ respectively. Both the SAS and SDS are 20-item self-report questionnaires used to measure anxiety and depression symptoms in the general population as well as in medically ill patients. We adopted a total sum score of 20 to 80 after multiplying by 1.25; higher scores indicate greater anxiety and depression symptoms. Cut-off points of 50 and 53 are generally used to define patients at risk for clinical anxiety and depression, respectively. Diagnoses were based on physicians' clinical experience. Exclusion criteria were

as follows: patients (1) diagnosed with cancer, and (2) those with other mental disorders, such as schizophrenia.

Follow-up method

Follow-up started in the third month after the patient was discharged and was conducted via telephone. All telephone follow-up sessions were completed by two researchers who understood the purpose, importance, and operating procedures of the entire project. During follow-up, a uniformly designed follow-up form was used, and the researchers asked participants about each item on the form. All follow-up calls were recorded so that they could be checked by the two researchers. If the researchers disagreed regarding the content of a call, a third senior researcher was asked to make a judgment to ensure consistency of the follow-up content. The Cronbach's alpha of the follow-up questionnaire was 0.947. Survival data were collected until July 2019. Nineteen patients were lost to follow-up owing to changing their telephone number. The rate of loss to follow-up was 14.4%. The patient flow diagram is shown in Figure 1.

Statistical analysis

We used IBM SPSS version 23.0 (IBM Corp., Armonk, NY, USA) to perform the statistical analysis, and the significance was defined as $P < 0.05$. Categorical variables are presented as percentages and were assessed using the chi-square test. Continuous variables are presented as mean \pm standard deviation and were assessed using a two-tailed t -test or analysis of variance test. Univariate survival analysis was performed using the Kaplan–Meier method, and multivariate survival analysis was performed using a Cox regression model. Factors with $P < 0.1$ in univariate survival analysis were included in the Cox

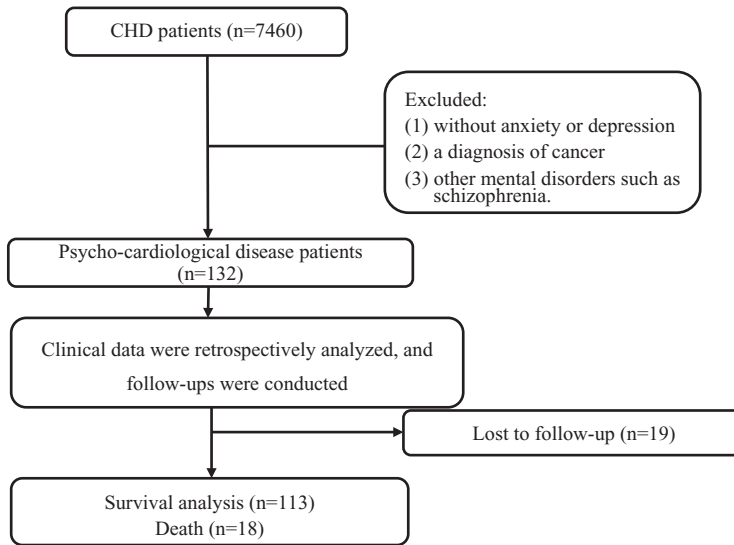


Figure 1. Flow chart of patients enrolled in the study.

regression model. The Mann–Whitney U test was used as a nonparametric test.

Results

Clinical characteristics

Among 7460 patients with CHD, we enrolled 178 who had mental illness. The incidence of psycho-cardiological diseases among these 7460 patients was 1.8%. Of these, 46 cases were duplicated; finally, 132 patients were included, 67 men and 65 women, with an average age of 73.39 ± 13.30 years. Follow-up was conducted in 113 patients (follow-up rate: 85.6%), 46 men and 48 women, with average age 70.98 ± 13.13 years. Among them, 18 patients died owing to cardiovascular disease during the follow-up period (2017–2019). The 2-year mortality rate was 15.9%. Among the 113 patients with psycho-cardiology diseases, 67.3% were diagnosed with anxiety, 21.2% were diagnosed with depression, and 11.5% were diagnosed with both anxiety and depression. Of these 113 patients,

66.4% were diagnosed with hypertension and 32.8% had diabetes. A total of 20.4% patients had sleep disorders and 30.1% had limb weakness.

Univariate analysis

The results of univariate analysis revealed significant differences in age ($t = -2.089$, $P = 0.039$), urination ($\chi^2 = 5.937$, $P = 0.010$), limb weakness ($\chi^2 = 6.601$, $P = 0.010$), self-care ability ($\chi^2 = 19.524$, $P < 0.01$), percutaneous coronary intervention (PCI) ($\chi^2 = 4.972$, $P = 0.026$), total cholesterol (TC) ($\chi^2 = 6.476$, $P = 0.011$), pro-brain natriuretic peptide (pro-BNP) ($\chi^2 = 5.838$, $P = 0.016$), and high-sensitivity troponin T (hs-TnT) ($\chi^2 = 12.001$, $P = 0.001$) (Table 1).

Survival analysis

Kaplan–Meier analysis showed that dysphagia, limb function, self-care ability, PCI, low-density lipoprotein, TC, pro-BNP, and hs-TnT had significant associations with cumulative survival ($P < 0.1$, Table 2). Cox regression analysis showed

Table 1. Baseline characteristics of decedents and survivors

Characteristics	Survivors (n = 95)	Decedents (n = 18)	t/χ^2	P
Male sex, %	40.7	9.7	0.975	0.323
Age, y	72.43 ± 13.03	79.50 ± 13.89	-2.089	0.039
Education, %			1.890	0.596
Primary or below	10.6	1.8		
Secondary	40.7	5.3		
College/undergraduate	28.3	8.0		
Graduate degree	4.4	0.9		
Marital status, %			0.077	0.962
Unmarried	4.4	0.9		
Married	73.5	14.2		
Widowed	6.2	0.9		
Self-feeding, %			2.416	0.120
Yes	76.1	12.4		
No	8.0	3.5		
Dysphagia, %	10.6	4.4	2.716	0.099
Sleep, %			2.047	0.563
Normal	68.1	11.5		
Insomnia	6.2	2.7		
Wakes up early	1.8	0.0		
Needs to take sleeping pills	8.0	1.8		
Defecation, %			1.774	0.412
Normal	78.8	14.2		
Constipation	3.5	1.8		
Diarrhea	1.8	0.0		
Abnormal urination, %	4.4	3.5	5.937	0.015
Limb weakness, %	21.2	8.8	6.601	0.010
Self-care ability, %			19.524	<0.01
Self-care	69.9	6.2		
Partial self-care	5.3	6.2		
No ability	8.8	3.5		
Smoking or alcohol use, %	9.7	1.8	0.003	0.955
Hypertension, %	55.8	10.6	0.001	0.977
Diabetes, %	26.5	8.0	2.272	0.132
Mental illness, %			4.091	0.129
Anxiety	59.3	8.0		
Depression	15.0	6.2		
Mixed anxiety and depression	9.7	1.8		
PCI, %	16.8	7.1	4.972	0.026
Abnormal HDLC, %	58.4	11.5	0.054	0.816
Abnormal LDLC, %	7.1	3.5	3.037	0.081
Abnormal TC, %	8.8	5.3	6.476	0.011
Abnormal TRIG, %	21.2	7.1	2.743	0.098
Abnormal LVEF, %	4.4	0.9	0.003	0.960
Abnormal pro-BNP, %	44.2	13.3	5.838	0.016
Abnormal hs-TnT, %	32.7	13.3	12.001	0.001

PCI, percutaneous coronary intervention; HDLC, high-density lipoprotein; LDLC, low-density lipoprotein; TC, total cholesterol; TRIG, triglyceride; LVEF, left ventricular ejection fraction; pro-BNP, pro-brain natriuretic peptide; hs-TnT, high-sensitivity troponin T.

Table 2. Survival analysis using Kaplan–Meier and Cox regression analyses.

Risk factors	Kaplan–Meier analysis		Cox regression analysis	
	MST (months)	<i>P</i>	HR (95% CI)	<i>P</i>
Self-feeding		0.086		
Yes	26.19 ± .73			
No	21.08 ± .72			
Dysphagia	20.47 ± .50	0.071		
Limb function, limb weakness	23.51 ± .84	0.011		
Self-care ability		<0.01		
Self-care	27.10 ± .70			
Partial self-care	23.13 ± 2.62			
No ability	18.50 ± .37			
PCI	22.03 ± .15	0.020	3.619 (1.383–9.474)	0.009
Anormal LDLC	19.67 ± 2.62	0.056		
Anormal TC	19.87 ± 2.34	0.10	3.856 (1.044–7.818)	0.041
Anormal pro-BNP	24.71 ± .25	0.014		
Anormal hs-TnT	23.54 ± .49	0.001	4.668 (1.293–16.854)	0.019

Note: All values are mean ± standard deviation, unless otherwise noted.

MST, mean survival time; PCI, percutaneous coronary intervention; LDLC, low-density lipoprotein; TC, total cholesterol; pro-BNP, pro-brain natriuretic peptide; hs-TnT, high-sensitivity troponin T.

that hs-TnT (hazard ratio [HR]: 4.668, 95% confidence interval [CI]: 1.293–16.854) (Figure 2), TC (HR: 2.765, 95% CI: 1.001–7.641) (Figure 3), and PCI (HR: 3.619, 95% CI: 1.383–9.474) (Figure 4) had independent associations with cumulative survival ($P < 0.05$, Table 2).

Discussion

With the development of life sciences over the past decade, the understanding of human disease and health has increased to a high level, and the simple biomedical model has gradually turned into a bio-psycho-social medical model. The most common chronic physical diseases (e.g., cardiovascular disease) are often complicated by psychiatric symptoms or emotional/psychological subjective symptoms.^{16,17} Risk factors related to CHD include hypertension, diabetes, and impaired glucose tolerance, smoking history, obesity, type A personality, and psychological factors

(e.g., anxiety, depression). Among these, psychological factors are present throughout the onset, development, and outcome in patients with CHD and have an important role in the progression and prognosis of patients with CHD.¹⁸ Therefore, attention is needed with respect to the impact of these psychological risk factors on the disease. There is increasing interest in the relationship between mental illnesses and heart diseases. The psycho-cardiology discipline¹⁹ refers to specialists in not only cardiovascular diseases but also patients' psychological illness. In the present research, the clinical detection rate of mental illness in patients with CHD was 1.8%, which was much lower than that of a study by Deng et al. (2010).⁵ The present study was based on medical diagnoses, with less focus on the psychological and mental problems of patients with CHD, resulting in a lower detection rate of mental illness in this retrospective analysis.

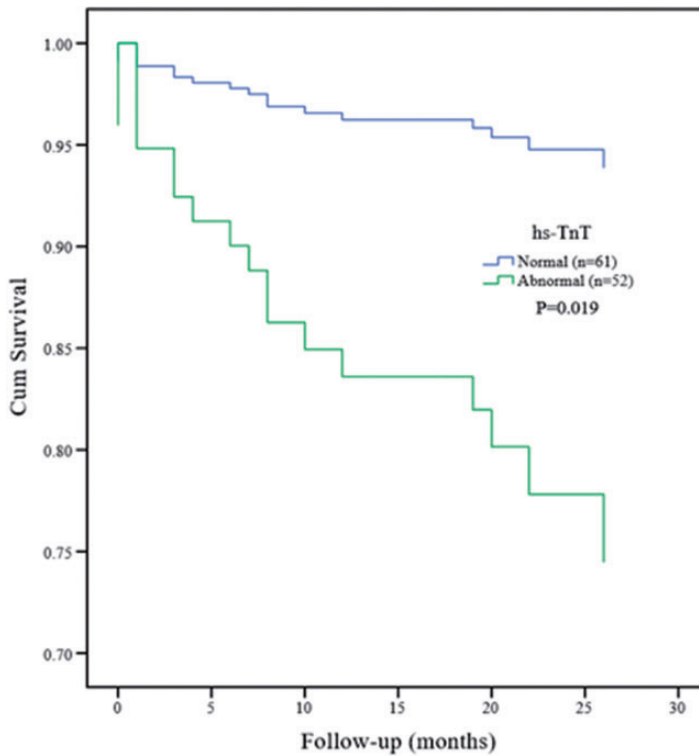


Figure 2. Cox regression analysis of patients with normal hs-TnT vs. abnormal hs-TnT. hs-TnT, high-sensitivity troponin T.

In this research, patients with CHD and mental illness were mainly older adults. Zhang et al. (2018) found that experiencing adverse life events is considered a risk factor for depressive symptoms in older people but that physical exercise and high levels of social support and self-evaluation are protective in this population. Education, monthly income, medical insurance, and the number of chronic diseases are also factors that influence anxiety in older people. Empty nest syndrome in older adults is another important risk factor for depression.²⁰ The American Heart Association recently published a Science Advisory with the recommendation that patients with CHD should be screened for depressive symptoms and depression.²¹ Luttik et al. (2010)²² suggested that routine screening

increases the demand for psychosocial diagnoses and treatment; therefore, the availability of qualified professionals should be guaranteed in advance.

Although nearly 15.9% of patients died during the follow-up period, the survival time until death or censoring was within the range of reports in the literature.¹⁹ Although unable to be inferred directly from our data, a number of factors (e.g., physical function and blood parameters) underlie prolonged patient survival. In Table 2, the results of Kaplan–Meier analysis showed that dysphagia, limb function, self-care ability, low-density lipoprotein, and pro-BNP were significantly associated with cumulative survival. These factors showed no significance in Cox regression analysis; however, there was still a certain

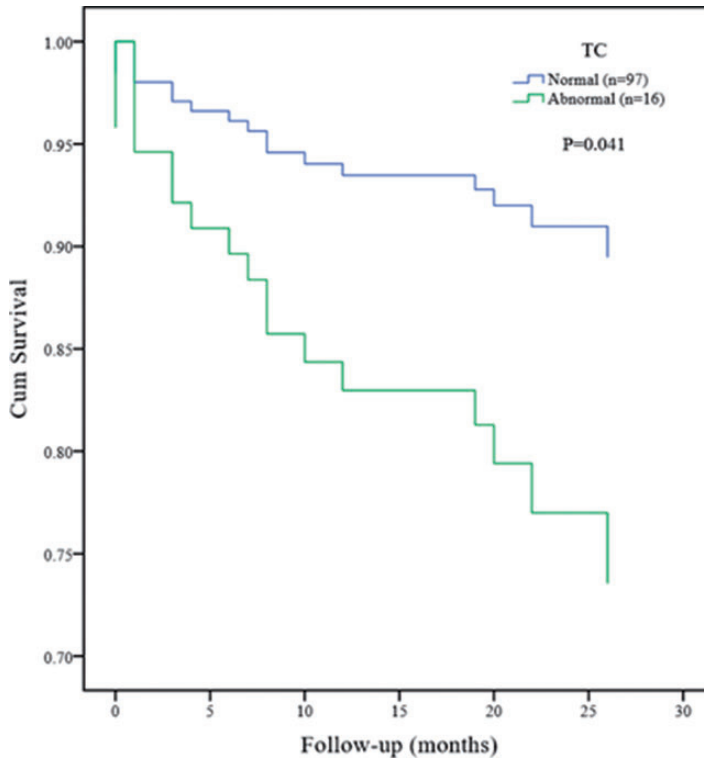


Figure 3. Cox regression analysis of patients with normal TC vs. abnormal TC
TC, total cholesterol.

correlation between patients' clinical outcomes. One study²³ found that patients with CHD who had good social support were less likely to be emotional and less likely to focus on their own disease within 4 months of discharge, in comparison with those who did not have social support. Additionally, patients with initial onset of heart disease are more urgently in need of social support than those with a previous hospitalization history. Another study²⁴ found that loneliness was an important risk factor for heart failure; also, the greater the patient's feelings of loneliness, the more serious the degree of heart failure. Moreover, living alone for a long time has been associated with negative emotions in patients with CHD.²⁵ Recent findings show that one in four patients with CHD

has a distressed (type D) personality, which is characterized by two stable traits: social inhibition and negative affectivity.²⁶ Dritto et al. (2015)²⁷ suggested that patients with CHD who have type D personality tend to experience difficulties with emotional well-being. From an emotional point of view, symptoms of depressed mood are often accompanied by other negative emotions, like anxiety and anger. Type D personality also predicts the occurrence of major cardiac events in patients with CHD.²⁸ Some studies²⁹ have found that marital relationships overlap with parent-child and friend relationships to a certain extent, but significant differences are observed at the same time. Compared with friends, mutual care is more intense in married couples, for example, by providing affection and paying

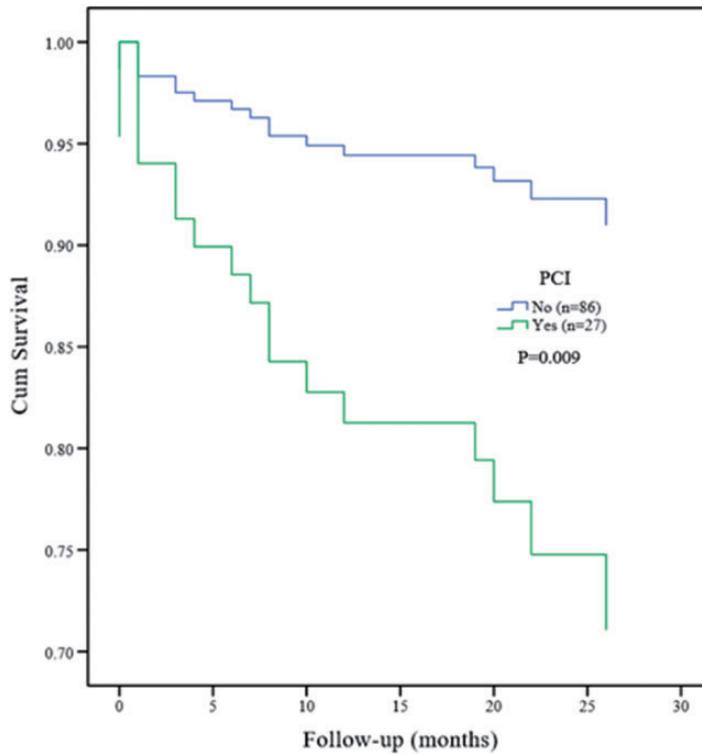


Figure 4. Cox regression analysis of patients with PCI vs. patients without PCI. PCI, percutaneous coronary intervention.

greater attention to a partner who is ill. Compared with parent–child relationships, there is greater understanding and tolerance in marital relationships, which might be owing to long-term and stable experiences shared in married life.

The survival rate of patients with normal hs-TnT and abnormal hs-TnT was 51.3% and 32.7% and mean survival time (MST) was 27.82 ± 0.67 months and 23.54 ± 1.49 months, respectively. Cox regression analysis showed that hs-TnT (HR: 4.668, 95% CI: 1.293–16.854) was independently associated with cumulative survival. Therefore, hs-TnT blood test results are an effective and important means for predicting patients' clinical outcomes. Hs-TnT³⁰ is a marker of myocardial injury and necrosis and has clinical importance in the diagnosis

and risk stratification of acute myocardial infarction. Elevated troponin values suggest myocardial damage, which can be seen in acute myocardial infarction, unstable angina, pulmonary infarction, and heart failure. Our findings are consistent with those of a pilot study³¹ and a cohort study³² reporting hs-TnT as a good prognostic marker for mortality. Moreover, hs-TnT can be used to detect subclinical cardiac disease.

Cox regression analysis also showed that TC (HR: 2.765, 95% CI: 1.001–7.641) was an independent factor associated with cumulative survival. The survival rate of patients with normal and abnormal TC was 75.2% and 8.8% and the average survival time was 27.11 ± 0.82 months and 19.88 ± 2.34 months, respectively. Similarly,

we searched PubMed in December 2014 for cohort studies reporting the relationship between TC and CHD and total stroke. Data from 97 cohorts with 1,022,276 individuals, and 20,176 cases of CHD and 13,067 of stroke were included. The results revealed that increased levels of TC were considered a strong risk factor for CHD. However, it remains unknown whether psychological differences existed in the relationship between TC and CHD outcomes in our study.

In this study, 23.9% of patients received PCI and 76.1% did not receive PCI; the MST was 22.03 ± 2.15 months and 27.47 ± 0.78 months, respectively. Cox regression analysis showed that PCI (HR: 3.619, 95% CI: 1.383–9.474) was independently associated with cumulative survival. Although PCI has been proven to be an effective way to treat CHD, anxiety and depression were still prevalent among patients who underwent PCI, and the levels were unaffected by participation in cardiac rehabilitation.³³ Postoperative complications are also considered strong risk factors in patients with CHD and mental illness.

Limitations

Despite its clinical importance, the current study included some limitations. The main limitation of this retrospective study was that the grouping of participants was not randomized. In addition, owing to its retrospective nature, the data were limited in some respects; further research is needed, with an expanded horizontal survey and cohort study of the sample. Further, although the status of patients' anxiety or depressive symptoms were known in this study, the severity of anxiety and depression was unknown. Anxiety and depression have an important role in the pathogenesis of CHD, and although not yet proven, these might have an impact on patient

prognoses, based on the etiology of CHD. Finally, owing to a lack of attention paid to patients with mental health problems and CHD, there is no established standardized treatment or nursing protocol at our hospital; therefore, it was difficult to analyze the impact of different treatment or nursing strategies on the survival of our patients. Awareness of these limitations will assist in designing future studies on psychocardiological disease, ultimately benefitting patients with this disease.

Conclusions

The clinical detection rate of psychocardiological disease in patients with CHD and mental illness was far lower than expected, which might be owing to the limitations of our retrospective analysis. Normal TC and hs-TnT were associated with reduced cardiovascular disease deaths over a 2-year period. However, PCI was found to be a prognostic risk factor in patients with psychocardiological disease. The mechanism underlying this requires further exploration. However, this finding suggests that clinical medical staff should pay greater attention to patients with characteristics of psychocardiological disease in the future.

Authors' contributions

All authors contributed to the data analysis and to drafting and critically revising the paper. All the authors gave their final approval of the version to be published and agree to be accountable for all aspects of the work.

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Declaration of conflicting interest

The authors declare that there is no conflict of interest.

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