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Title Page

Perceived Stress in Chinese Patients with Coronary Heart Disease: A cross-sectional study

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ABSTRACT

Objective Studies have shown that stress is closely linked to the occurrence and development of cardiovascular disease. To date, few studies have focused on perceived stress in CHD patients and the identification of high-stress individuals. This study aims to analyse the mental stress of patients with coronary heart diseases(CHD) and determine the individual attributes closely associated it.

Design A cross-sectional study.

Setting This study was conducted at a cardiac rehabilitation clinic of a tertiary hospital in Beijing.

Participants A total of 2215 CHD patients. Participants were categorised as either high stress or low stress (based on the Chinese version Perceived Stress Scale, CPSS-14).

Results The mean CPSS score of Chinese patients with CHD was 27.16 ± 6.35. Compared with participants who received senior middle school education or below, those with a university degree had a higher probability of high perceived stress (OR: 1.453, CI: 1.206-1.750); this was more evident in participants with a masters or doctoral degree (OR: 1.928, CI: 1.290-2.882). And engaging in mental labor (OR: 1.389, CI: 1.144-1.686), having children (OR: 2.226, CI: 1.098-4.515), and having a habit of risky alcohol consumption (OR:1.492, CI: 1.146-1.944) were associated with perceived stress.

Conclusion: Patients with CHD in China had a relative higher CPSS score. And

patients who had higher educational attainment, engaged in mental labor, had children, and had a habit of risky alcohol consumption may require more stress interventions.

Keywords
Perceived stress，Coronary heart disease，Cardiac rehabilitation

Word Count 4369 words

Strengths and limitations of this study

Few studies have focused on perceived stress in CHD patients and the identification of high-stress individuals.

Utilize the PSS for the accurate identification of stress-sensitive individuals among patients with coronary heart disease.

Given the cross-sectional nature of the study, we cannot infer causal relationships

INTRODUCTION

The incidence of coronary heart disease (CHD) has been rising steadily over the past few decades and the resulting burden of disease is an issue faced by developed and developing countries alike [1]. Because the established biological and medical risk factors cannot fully explain the occurrence of CHD-related adverse cardiac events, we propose that psychological and social factors play an important and independent role in the development of coronary heart disease [2-3].

Psychological stress (stress) refers to the psychological challenge or threat caused by various triggering events or adverse life factors, and usually manifests as emotional discomfort, pain, or anguish [4]. Under normal circumstances, a dynamic equilibrium exists between an organism and its external environment, and stress arises when this equilibrium is upset or is self-perceived as upset [5]. Stress is believed to be closely linked to the occurrence and development of cardiovascular disease, one of the most important psychosomatic diseases [6]. Although the biological mechanisms remain unclear, the current literature suggests that self-perceived stress may cause over-activation of the autonomic nervous system and elicit a stress response from the endocrine system, thereby inducing endothelial dysfunction, ultimately triggering cardiovascular events [7]. However, the process by which stressors exert their effects on an organism is not linear; instead, it arises through interactions [5]. The stress perceived by an individual reflects his/her subjective evaluation of the stressor and will partly depend on individual attributes. Studies have shown that different individuals faced with identical stressors may perceive considerably different levels of stress, with different effects on CHD occurrence and development, resulting in differences in the severity or prognosis of CHD[8]. Therefore, the accurate identification of high-stress individuals is of great significance for the precise assessment and subsequent treatment of CHD.

Assessments of psychological stress are generally performed using standard psychological instruments. Commonly used questionnaires include the Perceived Stress Scale (PSS), Stress Appraisal Measure (SAM), and Impact of Event Scale (IES). The PSS is the most widely used instrument because it is simple to implement and does not require professional intervention during administration. Developed by Cohen et al. in

1983 [9], the PSS measures the dimensions of uncontrollability and stressfulness, and assesses the stress levels of individuals based on their subjective perceptions of stressors. It has been translated into many languages and used widely in diverse populations around the world [10]. The version most used in Chinese populations is the Chinese Perceived Stress Scale (CPSS), which is a simplified-Chinese version translated by Yang (2007) [11]. The CPSS has demonstrated good validity and reliability in a series of studies on general Chinese populations[12].

Few studies published to date have utilized the PSS for the accurate identification of stress-sensitive individuals among patients with CHD, and stress detection in the Chinese population with CHD has not yet been reported.

We, therefore, analyzed the PSS scores of patients who visited the cardiac rehabilitation clinic at our hospital with the aim of investigating the self-perceived stress levels of Chinese patients with CHD and determining the individual attributes closely associated with perceived stress in Chinese society. The results of this study can serve as a scientific basis for the development of stress management programs for Chinese populations in general and for patients with CHD in particular.

METHODS

Study participants

A cross-sectional study design was adopted. Using the electronic medical records system of our hospital, we screened patients referred to the cardiac rehabilitation clinic between 2015 and 2020. Only those with a definitive diagnosis of CHD were included in the analysis. Based on the criteria of the CHD 2019 ESC Guidelines for the Diagnosis and Management of Chronic Coronary Syndromes, the inclusions were: one or more lesions with ⩾50% stenosis as shown by coronary angiography; stable angina (SA); unstable angina (USA); old myocardial infarction (OMI); acute myocardial infarction (AMI); post-percutaneous coronary intervention (PCI); post-coronary artery bypass graft (CABG); or ischemic cardiomyopathy (IC).

Demographic characteristics and medical history

The demographic characteristics and medical history of the participants were obtained from the cardiac rehabilitation medical records system and collated by a

cardiologist. The demographic characteristics analyzed included age, sex, educational level, marital status, family structure (with/without children), nature of work (mental/manual labor), the presence/absence of sleep disorders, and the following lifestyle factors: regular exercise, risky alcohol consumption, and smoking. The medical history data analyzed included history of cardiac revascularization and the presence/absence of other chronic diseases requiring long-term medication. Mental labor was defined as professional, managerial, or administrative work generally performed in an office or other administrative environment. Manual labor was defined as strenuous physical work or other types of work demanding physical exertion. Regular exercise was defined as ⩾30 min of low-intensity exercise >5 times per week or ⩾20 min of moderate-intensity exercise >3 times per week. Sleep disorders were defined as the occurrence of at least one of the following ⩾3 times per week for at least 1 month: inability to sleep after 30 min in bed, waking up ⩾2 times during the night, wake time >15%, dreamful sleep or total sleep time <6 hours, and waking up ≥2 hours ahead of schedule and subsequently unable to get back to sleep. Risky alcohol consumption was defined as the consumption of ⩾5 alcoholic drinks on a single occasion >12 times in the past year [13].

Stress assessment

The perceived stress of the study participants was assessed using the CPSS, which comprises 14 items intended to measure the dimensions of uncontrollability and stressfulness. Each item is rated on a 5-point scale (0 = never, 1 = rarely, 2 = sometimes, 3 = fairly often, 4 = very often), with items 4, 5, 6, 7, 9, 10, and 13 scored in the reverse direction. Total scores range from 0 to 56 points, with higher scores indicating higher psychological stress. Study participants were asked to provide responses based on their own perceptions. All patients who visited the cardiac rehabilitation clinic for the first time were requested to complete the CPSS on their own after receiving instructions on questionnaire completion from a nurse. The responses were collected and collated by a cardiologist .

Statistical analysis

Statistical analysis was performed using SPSS 23.0. Quantitative variables were

tested for normality. Normally distributed variables were expressed as mean ± standard deviation (x ± s); variables not normally distributed were expressed as median and interquartile range (IQR). Qualitative data were expressed as ratios or percentages. Factors associated with the CPSS scores of the study participants were analyzed from binary logistic regression.

Patient and public involvement

Public and patient involvement was not applicable in this research.

RESULTS

Demographic data of patients with CHD

Of the 3845 patients referred to the cardiac rehabilitation clinic during the study period, 2215 had CHD and were eventually included in the study. The mean age of the study participants was 59.57 ± 10.10 y, and the majority of the participants were male (79.64%), had a university degree or below (94.13%), married (99.05%), had children (97.97%), engaged in mental labor (69.07%), had sleep disorders (74.81%), and did not have a drinking habit (60.18%) Of the participants, 77.1% had previously undergone stent insertion, 56.2% had concomitant hypertension, 47.4% had concomitant hyperlipidemia, and 27% had concomitant diabetes mellitus (see **Table 1**).

Comparison of characteristics between groups

The mean CPSS score of all the patients with CHD was 27.16 ± 6.35. Using the median score of 27 as the cut-off point, the study participants were divided into a low-stress group (CPSS score ⩽27) and a high-stress group (CPSS score >27).

Participants who had children, engaged in mental labor, or had a habit of risky alcohol consumption had a higher probability of experiencing higher stress levels. (see **Table 2**).

Logistic regression

Binary logistic regression analysis was performed by setting the CPSS score as the dependent variable and the following as the independent variables: age, sex, educational level, marital status, family structure (with/without children), nature of work (mental/manual labor), number of stents, and the presence/absence of sleep disorders, other chronic diseases, and the following habits: regular exercise, risky alcohol

consumption, and smoking. Our results indicated that study participants who have children had a higher probability of high perceived stress, with the odds ratio (OR) being 2.226 (confidence interval [CI]: 1.098-4.515). Compared with participants who received middle school education or below, those with a university degree had a higher probability of high perceived stress (OR: 1.453, CI: 1.206-1.750); this was more evident in participants with a masters or doctoral degree (OR: 1.928, CI: 1.290-2.882). Participants who engaged in mental labor had a higher probability of high perceived stress than those who engaged in manual labor (OR: 1.389, CI: 1.144-1.686). Compared with participants who did not have a habit of risky alcohol consumption, those who had this habit had a higher probability of high perceived stress (OR:1.492, CI: 1.146-1.944) (see **Table 3**).

DISCUSSION

The relationship between psychological stress and cardiovascular disease has attracted increasing attention in recent years. Considering that psychological stress may play some role in the occurrence and development of CHD, a greater emphasis has been placed on stress management in comprehensive cardiac rehabilitation programs because it may potentially provide benefits, such as improving the long-term prognosis of patients with CHD [14]. Therefore, recent models of comprehensive cardiac rehabilitation require cardiac rehabilitation specialists to accurately assess and identify high-stress individuals for targeted, stratified management. The mean CPSS score of Chinese patients with CHD in our study was 27.16 ± 6.35, which was slightly higher than that of the normal population [11]. In addition, we found that patients who had higher educational attainment, engaged in mental labor, had children, and had a habit of risky alcohol consumption perceived higher levels of stress.

Analysis of the demographic characteristics of high-stress individuals among patients with CHD can support the clinical stratified management of patients according to stress level, which increases the efficiency of rehabilitation treatment and maximizes the clinical benefits to each individual.

Our results showed a strong correlation between perceived stress and educational level in Chinese patients with CHD. A higher educational level was associated with

higher perceived stress, with the risk of high perceived stress in participants with a university degree being 1.453 times (CI: 1.206-1.750) that of those who received senior middle school education or below, and the OR increased to 1.928 (CI: 1.290-2.882) among participants with a masters or doctoral degree. However, this result is contrary to the findings of studies conducted in other countries[15-16] which have indicated that individuals with lower educational attainment generally perceive higher stress. This may possibly be attributed to the long-standing, strong emphasis on educational attainment in Chinese society, which has led to the general view that individuals with higher educational levels should attain greater personal achievements and bear greater social responsibilities and expectations. However, it is not clear whether this unique sociocultural background has caused the aforementioned difference between Eastern and Western countries in the influence of educational level on perceived stress.

Perceived stress was also found to be strongly related to the nature of work in the Chinese population. Participants who engaged in mental labor had higher perceived stress than did those who engaged in manual labor; in other words, they had a higher probability of a high perceived stress score (OR: 1.389, CI: 1.144-1.686). Such a result is not in complete agreement with the findings of previous studies. A survey by Lesage et al.[17] revealed that differences in perceived stress among administrative, technical, and blue-collar workers were statistically insignificant. However, the 501 participants of Lesage's study were selected from individuals who attended occupational health centers in northern France, whereas the participants of our study had a greater diversity of occupations, including teachers, doctors, taxi drivers and gardeners. The greater diversity of occupations included in our study provides a better reflection of the actual range of perceived stress across occupations, thereby helping the occupational factor to reach significance. Dėdelė et al. [18] performed a cross-sectional study on perceived stress among 571 full-time workers in Lithuania and found that blue-collar workers who spent relatively more time engaging in physical work had a higher risk of high perceived stress than white-collar workers, which appears to contradict our results. However, the distribution of perceived stress across occupations may depend on the social environment. With China's vast population, Chinese workers are often faced with

complicated interpersonal relationships in their workplace. In general, workplace ecology is more complex among individuals engaged in mental labor than among manual workers, which may have partially contributed to the difference in perceived stress we observed between the two occupational categories.

The drinking habit of patients with CHD has also been identified as a potential factor associated with perceived stress. Our results indicated that participants with a habit of risky alcohol consumption had higher perceived stress (P = 0003). We also found that the probability that risky alcohol drinkers were assessed as having high stress was 1.492 times that of non-risky alcohol drinkers (CI: 1.146-1.944). These findings are consistent with those reported by Yoon et al. [19], who showed that the proportion of individuals with adverse drinking habits was higher in the population with high perceived stress than in the population with low perceived stress. Although the study by Yoon et al. did not investigate possible causal relationships between high stress and at-risk drinking, there is no doubt that patients with a habit of risky alcohol consumption can have higher perceived stress. Therefore, for such individuals, emphasis should be placed on appropriate stress interventions in the formulation of rehabilitation programs.

Interestingly, we also found that patients with CHD with children were nearly twice as likely to belong to the high stress group as those without children, which is consistent with the findings of Lesage et al.[17]

Our results also showed that the perceived stress of patients with CHD was not correlated with age, sex or marital status. Previous studies have disagreed on these aspects. For instance, a study by Andreou et al. [20] indicated that younger individuals, women, and single or divorced individuals may have higher perceived stress. Cohen et al. [9] reported that perceived stress was higher in women, but unrelated to age; similar conclusions were reached in two other studies [21-22]. However, Dėdelė et al. [18] asserted that older individuals had higher perceived stress. A study by Leung et al. [12] indicated higher levels of perceived stress in women, but a contrary result was reported by Ojard et al. [23] Although the measurement of the perceived stress of an individual is based on his/her subjective perceptions, it may also be affected by objective environmental stressors. Therefore, differences in the findings of the aforementioned studies may be

related to differences in social background among different countries.

LIMITATIONS

This study has several limitations. First, some degree of bias may have resulted from enrolment being limited to a single center. Further multicenter studies with a larger sample size are therefore warranted to validate the accuracy and clinical value of the present results. Second, although we were able to screen factors that were possibly related to perceived stress, we were unable to infer causal relationships given the cross-sectional nature of the study. To address this limitation, we plan to conduct further prospective cohort studies to further investigate the effects of the relevant factors on perceived stress in patients.

CONCLUSIONS

In conclusion, the results of this study indicate that patients with CHD have a generally high perceived stress. Individuals who engaged in mental labor, had a habit of risky alcohol consumption, and had a higher level of educational attainment had a higher probability of scoring high on perceived stress. These results can provide a scientific basis for further investigation of the relationship between stress management and prognosis in patients with CHD. We recommend the formulation of individualized stress management programs in cardiac rehabilitation to provide additional care to individuals with the aforementioned characteristics.

Contributors

The study was initiated by JM and YX. YG performed the statistical analysis and drafted the manuscript. RH, YZ and MY were helpful for data collection. JM and YX contributed substantially to its revision. JM and YX took responsibility for the manuscript as a whole.

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Competing interests

None declared.

Patient consent for publication

Not required.

Ethics approval

This study was approved by the ethics committee of the Chinese PLA General Hospital(S2020-382-01)

Data availability statement

Data are available upon reasonable request. Given that the data is in Chinese, complete raw data are not available for sharing. Partial data sets used and/or analysed during the current study are available from the corresponding author on reasonable request.

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Table 1 Social Demography Factors of the subjects

social demography factor		n	%
age	＜45	160	7.2
	45-64	1317	59.5
	65-84	727	32.8
	⩾85	11	0.4
Gender	Male	1764	79.6
	Female	451	20.4
Education level	Senior high school and below	1107	50.0
	College	978	44.2
	Above college	130	5.9
Having children	Yes	2170	98.0
	No	45	2.0
Marital status	Married	2194	99.0
	Other (single, divorced, or widowed)	21	1.0
Occupation	Mental	1530	69.1
	Physical	685	30.9
Regular exercise	Yes	1630	73.6
	No	585	26.4
Risky alcohol drinking	Yes	298	13.5
	No	1917	86.5
Current Smoker	Yes	334	15.1
	No	1881	84.9
Comorbidity			
Number of stent	0	508	22.9
	1	901	40.7
	2	462	20.9
	⩾3	344	15.5
Hypertension	Yes	1245	56.2

	No	970	43.8
Hyperlipemia	Yes	1049	47.4
	No	1166	52.6
Diabetes	Yes	598	27.0
	No	1617	73.0
Other disease	Yes	158	7.1
	No	2057	92.9
Sleep disorder	Yes	1657	74.8
	No	558	25.2

Table 2 comparison of two groups with different CPSS score

Characteristics	Categories	High stress group (n=1190)		Low stress group (n=1025)		X^2	P value
		n	%	n	%		
age	＜45	89	7.5	71	6.9	0.358	0.949
	45-64	709	59.6	608	59.3		
	65-84	386	32.4	341	33.3		
	⩾85	6	0.5	5	0.5		
Gender	Male	966	81.2	798	77.9	3.750	0.053
	Female	224	18.8	227	22.1		
Education level	Senior high school and below	526	44.2	581	56.7	36.611	0.000
	College	578	48.6	400	39.0		
	Above college	86	7.2	44	4.3		
Having children	Yes	1173	98.6	997	97.3	4.698	0.030
	No	17	1.4	28	2.7		
Marital status	Married	1182	99.3	1012	98.7	2.083	0.149
	Other (single, divorced, or widowed)	8	0.7	13	1.3		
Occupation	Mental	881	74.0	649	63.3	29.605	0.000
	Physical	309	26.0	376	36.7		
Regular exercise	Yes	901	75.7	729	71.1	5.975	0.015
	No	289	24.3	296	28.9		
Risky alcohol drinking	Yes	188	15.8	110	10.7	12.141	0.000
	No	1002	84.2	915	89.3		

Current Smoker		Yes	182	15.3	152	14.8	0.093	0.760
		No	1008	84.7	873	85.2		
Number stent	of	0	280	23.5	228	22.2	0.820	0.845
		1	486	40.8	415	40.5		
		2	243	20.4	219	21.4		
		⩾3	181	15.2	163	15.9		
Chronic disease		Yes	965	81.1	831	81.1	0.000	0.991
		No	225	18.9	194	18.9		
Sleep disorder		Yes	889	74.7	768	74.9	0.014	0.905
		No	301	25.3	257	25.1		

Table 3 Logistics regression of CPSS score

	OR(95%CI)	P value
Kid		
Yes	1.000	
No	2.226（1.098-4.515）	0.027
Education level		
Senior high school and below	1.000	
College	1.453（1.206-1.750）	0.000
Above college	1.928（1.290-2.882）	0.001
Occupation		
Manual	1.000	
Mental	1.389（1.144-1.686）	0.001
Risky alcohol drinking		
No	1.000	0.003
Yes	1.492 (1.146-1.944)	

STROBE 2007 (v4) Statement—Checklist of items that should be included in reports of *cross-sectional studies*

Section/Topic	Item #	Recommendation	Reported on page #
Title and abstract	1	(*a*) Indicate the study's design with a commonly used term in the title or the abstract	1
		(*b*) Provide in the abstract an informative and balanced summary of what was done and what was found	1
Introduction			
Background/rationale	2	Explain the scientific background and rationale for the investigation being reported	3
Objectives	3	State specific objectives, including any prespecified hypotheses	4
Methods			
Study design	4	Present key elements of study design early in the paper	4
Setting	5	Describe the setting, locations, and relevant dates, including periods of recruitment, exposure, follow-up, and data collection	4
Participants	6	(*a*) Give the eligibility criteria, and the sources and methods of selection of participants	4
Variables	7	Clearly define all outcomes, exposures, predictors, potential confounders, and effect modifiers. Give diagnostic criteria, if applicable	4
Data sources/ measurement	8*	For each variable of interest, give sources of data and details of methods of assessment (measurement). Describe comparability of assessment methods if there is more than one group	4
Bias	9	Describe any efforts to address potential sources of bias	
Study size	10	Explain how the study size was arrived at	4
Quantitative variables	11	Explain how quantitative variables were handled in the analyses. If applicable, describe which groupings were chosen and why	5
Statistical methods	12	(*a*) Describe all statistical methods, including those used to control for confounding	5
		(*b*) Describe any methods used to examine subgroups and interactions	5
		(*c*) Explain how missing data were addressed	5
		(*d*) If applicable, describe analytical methods taking account of sampling strategy	5
		(*e*) Describe any sensitivity analyses	5
Results			

Participants	13*	(a) Report numbers of individuals at each stage of study—eg numbers potentially eligible, examined for eligibility, confirmed eligible, included in the study, completing follow-up, and analysed	6
		(b) Give reasons for non-participation at each stage	6
		(c) Consider use of a flow diagram	
Descriptive data	14*	(a) Give characteristics of study participants (eg demographic, clinical, social) and information on exposures and potential confounders	6
		(b) Indicate number of participants with missing data for each variable of interest	
Outcome data	15*	Report numbers of outcome events or summary measures	6
Main results	16	(*a*) Give unadjusted estimates and, if applicable, confounder-adjusted estimates and their precision (eg, 95% confidence interval). Make clear which confounders were adjusted for and why they were included	6
		(*b*) Report category boundaries when continuous variables were categorized	6
		(*c*) If relevant, consider translating estimates of relative risk into absolute risk for a meaningful time period	
Other analyses	17	Report other analyses done—eg analyses of subgroups and interactions, and sensitivity analyses	6
Discussion			
Key results	18	Summarise key results with reference to study objectives	
Limitations	19	Discuss limitations of the study, taking into account sources of potential bias or imprecision. Discuss both direction and magnitude of any potential bias	7-10
Interpretation	20	Give a cautious overall interpretation of results considering objectives, limitations, multiplicity of analyses, results from similar studies, and other relevant evidence	7-10
Generalisability	21	Discuss the generalisability (external validity) of the study results	7-10
Other information			
Funding	22	Give the source of funding and the role of the funders for the present study and, if applicable, for the original study on which the present article is based	10

*Give information separately for cases and controls in case-control studies and, if applicable, for exposed and unexposed groups in cohort and cross-sectional studies.

Note: An Explanation and Elaboration article discusses each checklist item and gives methodological background and published examples of transparent reporting. The STROBE checklist is best used in conjunction with this article (freely available on the Web sites of PLoS Medicine at http://www.plosmedicine.org/, Annals of Internal Medicine at http://www.annals.org/, and Epidemiology at http://www.epidem.com/). Information on the STROBE Initiative is available at www.strobe-statement.org.

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Title Page

Perceived Stress in Chinese Patients with Coronary Heart Disease: A cross-sectional study

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ABSTRACT

Objective Studies have shown that chronic stress is closely linked to the occurrence and development of cardiovascular disease. To date, few studies have focused on perceived stress in coronary heart diseases (CHD) patients and the possible factors influencing the stress. This study aims to investigate the mental stress of patients with CHD and determine the individual attributes closely associated it.

Methods A total of 2215 CHD patients were enrolled and chronic stress were assessed with Chinese version Perceived Stress Scale (CPSS). Participants were divided into 2 groups due to CPSS score and binary logistic regression was applied to analyze the factors that affected CPSS.

Results The mean CPSS score of Chinese patients with CHD was 27.16 ± 6.35 which is higher than the mean value in Chinese general population. Compared with participants who received senior middle school education or below, those with a university degree had a higher probability of high perceived stress (OR: 1.453, CI: 1.206-1.750); this difference was more evident in participants with a masters or doctoral degree (OR: 1.928, CI: 1.290-2.882). Also engaging in mental labor (OR: 1.389, CI: 1.144-1.686), having children (OR: 2.226, CI: 1.098-4.515), and having a habit of risky alcohol consumption (OR:1.492, CI: 1.146-1.944) were associated with perceived

stress.

Conclusion: Patients with CHD in China had a relative higher CPSS score. Patients who had higher educational attainment, engaged in mental labor, had children, and had a habit of risky alcohol consumption were much easier to perceive the stress.

Keywords
Perceived stress，Coronary heart disease，Influencing factor

Word Count 2992 words

Strengths and limitations of this study

In this study, we investigated the stress perception level in Chinese CHD population and explored the possible influencing factors associated with them.

The Chinese version Perceived Stress Scale (CPSS) was used to evaluate the chronic stress of CHD patients.

When screening influencing factors associated with CPSS score, the variables we included might not cover all the possible factors.

Our study didn't clarify whether the CPSS score would associate with the clinical outcome of CHD patients, which might be a candidate topic we should investigate further.

INTRODUCTION

The incidence of coronary heart disease (CHD) has been rising steadily over the past few decades and the resulting burden of disease is an issue faced by developed and developing countries alike[1]. Finding out the potential risk factors of coronary heart disease and subsequent targeted treatment is a severe challenge. Recent studies demonstrated that psychological and social factors play an important and independent role in the development of coronary heart disease.[2-4]

Psychological stress (stress) refers to the psychological challenge or threat caused by various triggering events or adverse life factors, and usually manifests as emotional discomfort, pain, or anguish[5]. Under normal circumstances, a dynamic equilibrium exists between an organism and its external environment, and stress arises when this equilibrium is upset or is self-perceived as upset[6]. Stress is believed to be closely linked to the occurrence and development of cardiovascular disease, one of the most important psychosomatic diseases[7]. Acute events such as sudden illnesses and car accidents may lead to an increase in acute stress causing Posttraumatic Stress Disorder (PTSD) symptoms. PTSD symptoms were reported to be moderately prevalent among acute coronary syndrome (ACS) patients, which in turn increase risk for recurrent cardiac events and mortality.[8 9] Meanwhile if certain acute stress becomes persistent, it will change to chronic stress. The current literature suggests that chronic stress may cause over-activation of the autonomic nervous system and elicit a stress response from the endocrine system, thereby inducing endothelial dysfunction, ultimately triggering cardiovascular events.[10] A latest study [11] revealed that amygdala, a stress-sensitive structure, may increase the incidence of cardiovascular diseases by improving the activity of the immune system, which might be a possible mechanism. It was also found that the process by which stressors exert their effects on an organism is not linear; instead, it arises through interactions[6]. The actual effect of chronic stress on different individuals depends on the stress they perceived. The stress perceived by an individual reflects his/her subjective evaluation of the stressor and will partly depend on individual attributes. Studies have shown that different individuals faced with identical stressors may perceive considerably different levels of stress, with different effects on CHD

occurrence and development, resulting in differences in the severity or prognosis of CHD.[12] Therefore, the accurate identification of individuals who are more likely to perceive stress is of great significance for the precise assessment and subsequent treatment of CHD.

Assessments of psychological stress are generally performed using standard psychological instruments. Commonly used questionnaires include the Perceived Stress Scale (PSS), Stress Appraisal Measure (SAM), and Impact of Event Scale (IES). The PSS is the ost widely used scale to assess chronic stress because it is easy to implement and does not require professional intervention during administration. Developed by Cohen et al. in 1983[13], the PSS measures the dimensions of uncontrollability and stressfulness, and assesses the stress levels of individuals based on their subjective perceptions of stressors. It has been translated into many languages and used widely in diverse populations around the world[14-20]. Blumenthal et al.[21] have used PSS as a tool to assess the chronic stress of CHD patients. The version most used in Chinese populations is the Chinese Perceived Stress Scale (CPSS), which is a simplified-Chinese version translated by Yang (2007)[22]. The CPSS has demonstrated good validity and reliability in a series of studies in different Chinese populations[23-25], especially in cardiac patients[26].

Few studies published to date have utilized the CPSS for the accurate identification of high perceived stress individuals among patients with CHD, and stress detection in the Chinese mainland population with CHD has not yet been reported. We, therefore, analyzed the CPSS scores of patients who visited the cardiac rehabilitation clinic at our hospital with the aim of investigating the self-perceived stress levels of Chinese patients with CHD and determining the individual attributes closely associated with perceived stress. The results of this study might help to stratify CHD patients according to stress perception level and supply the individualized stress management programs for Chinese populations with CHD.

METHODS

Study participants

A cross-sectional study design was adopted. Using the electronic medical records system of our hospital, we screened patients referred to the cardiac rehabilitation clinic between 2015 and 2020. All patients in the inpatient department of cardiology were recommended to the rehabilitation clinic regardless of whether they choose to receive the follow rehabilitation treatment or not. Only those with a definitive diagnosis of CHD were included in the analysis. Based on the criteria of the CHD 2019 ESC Guidelines for the Diagnosis and Management of Chronic Coronary Syndromes, the inclusions were: one or more lesions with ⩾50% stenosis as shown by coronary angiography; stable angina (SA); unstable angina (USA); old myocardial infarction (OMI); acute myocardial infarction (AMI); post-percutaneous coronary intervention (PCI); post-coronary artery bypass graft (CABG); or ischemic cardiomyopathy (IC). Those who are unwilling to take the scale will be excluded.

Demographic characteristics and medical history

The demographic characteristics and medical history of the participants were obtained from the cardiac rehabilitation medical records system and collated by a cardiologist. The demographic characteristics analyzed included age, sex, region (south /north, divided along the Qinling Mountains-Huaihe River line), educational level, marital status, family structure (with/without children), nature of work (mental/manual labor), the presence/absence of sleep disorders, and the following lifestyle factors: regular exercise, risky alcohol consumption, and smoking. The medical history data analyzed included history of cardiac revascularization and the presence/absence of other chronic diseases requiring long-term medication. Mental labor was defined as professional, managerial, or administrative work generally performed in an office or other administrative environment. Manual labor was defined as strenuous physical work or other types of work demanding physical exertion. Regular exercise was defined as ⩾30 min of low-intensity exercise >5 times per week or ⩾20 min of moderate-intensity exercise >3 times per week. Sleep disorders were defined as the occurrence of at least one of the following ⩾3 times per week for at least 1 month: inability to sleep after 30 min in bed, waking up ⩾2 times during the night, wake time >15%, dreamful sleep or total sleep time <6 hours, and waking up ≥2 hours ahead of schedule and

subsequently unable to get back to sleep. Risky alcohol consumption was defined as the consumption of ⩾5 alcoholic drinks on a single occasion >12 times in the past year.[27]

Stress assessment

The perceived stress of the study participants was assessed using the CPSS, which comprises 14 items intended to measure the dimensions of uncontrollability and stressfulness. Each item is rated on a 5-point scale (0 = never, 1 = rarely, 2 = sometimes, 3 = fairly often, 4 = very often), with items 4, 5, 6, 7, 9, 10, and 13 scored in the reverse direction. Total scores range from 0 to 56 points, with higher scores indicating higher psychological stress.

In addition to the CPSS, all the participates were asked to complete the Patient Health Questionnaire (PHQ-9) scale and the Generalized Anxiety Disorder (GAD-7) scale to assess preexisting mental health comorbidities. The PHQ-9 is a self-rating scale consisting of 9 items. A PHQ9 score greater than 5 indicates that the patient may be in a mild or more depressive state. The GAD-7 is a 7-item self-rating scale indicating a mild or more anxiety state when the score is greater than 5.

All the participants were asked to provide responses based on their own perceptions. All patients who visited the cardiac rehabilitation clinic for the first time were requested to complete the scales on their own after receiving instructions on questionnaire completion from a nurse. The responses were collected and collated by a cardiologist.

Statistical analysis

Statistical analysis was performed using SPSS 25.0. Quantitative variables were tested for normality. Normally distributed variables were expressed as mean ± standard deviation (x ± s); variables not normally distributed were expressed as median and interquartile range (IQR). Qualitative data were expressed as ratios or percentages. Factors associated with the CPSS scores of the study participants were analyzed from binary logistic regression.

Patient and public involvement

Public and patient involvement was not applicable in this research.

RESULTS

Demographic data of patients with CHD

Of the 3845 patients referred to the cardiac rehabilitation clinic during the study period, 1630 patients were excluded, of which 1428 did not meet the inclusion criteria, and 202 refused to be evaluated by CPSS. Eventually 2215 CHD patients were included in the study (Figure 1). The mean age of the study participants was 59.57 ± 10.10 y, and the majority of the participants were male (79.64%), had a university degree or below (94.13%), married (99.05%), had children (97.97%), engaged in mental labor (69.07%), had sleep disorders (74.81%), and did not have a drinking habit (60.18%) Of the participants, 77.1% had previously undergone stent insertion, 56.2% had concomitant hypertension, 47.4% had concomitant hyperlipidemia, and 27% had concomitant diabetes mellitus (see **Table 1**).

Comparison of characteristics between groups

The mean CPSS score of all the patients with CHD was 27.16 ± 6.35. Using the median score of 27 as the cut-off point, the study participants were divided into a low-stress group (CPSS score ⩽27) and a high-stress group (CPSS score >27).

Participants who had children, engaged in mental labor, or had a habit of risky alcohol consumption had a higher probability of experiencing higher stress perception levels. (see **Table 2**).

Logistic regression

Binary logistic regression analysis was performed in model 1 by setting the CPSS score as the dependent variable and the following as the independent variables: age, sex, educational level, marital status, family structure (with/without children), nature of work (mental/manual labor), number of stents, and the presence/absence of sleep disorders, other chronic diseases, and the following habits: regular exercise, risky alcohol consumption, and smoking. Our results indicated that study participants who have children had a higher probability of high perceived stress, with the odds ratio (OR) being 2.226 (confidence interval [CI]: 1.098-4.515). Compared with participants who received middle school education or below, those with a university degree had a higher probability of high perceived stress (OR: 1.453, CI: 1.206-1.750); this was more evident in participants with a masters or doctoral degree (OR: 1.928, CI: 1.290-2.882).

Participants who engaged in mental labor had a higher probability of high perceived stress than those who engaged in manual labor (OR: 1.389, CI: 1.144-1.686). Compared with participants who did not have a habit of risky alcohol consumption, those who had this habit had a higher probability of high perceived stress (OR:1.492, CI: 1.146-1.944). Model 2 was adjusted by GAD-7 and PHQ-9 scores, which has no major influence on the conclusion (see **Table 3**).

DISCUSSION

The relationship between psychological stress and cardiovascular disease has attracted increasing attention in recent years. Considering that psychological stress may play some role in the occurrence and development of CHD, a greater emphasis has been placed on stress management in comprehensive cardiac rehabilitation programs because it may potentially provide benefits, such as improving the long-term prognosis of patients with CHD.[21] In this study, we investigated the stress perception level in Chinese CHD population and explored the possible influencing factors associated with them. Our studied suggested that patients with CHD in China had a relative higher CPSS score. In addition, we found that patients who had higher educational attainment, engaged in mental labor, had children, and had a habit of risky alcohol consumption were much easier to perceive the stress.

The mean CPSS score of Chinese patients with CHD in our study was 27.16 ± 6.35, which was slightly higher than that of the normal population.[22] Yang et al.[22] conducted a CPSS assessment of the Chinese general population (n=3666), with an average score of 24. 22 ±5. 811. A summary independent-sample t test proves that the CPSS scores of the two groups are statistically different (P = 0.000).

Analysis of the demographic characteristics of high-stress individuals among patients with CHD can support the clinical stratified management of patients according to stress level, which increases the efficiency of rehabilitation treatment and maximizes the clinical benefits to each individual. Previous studies have shown that demographic characteristics such as age, sex, educational level, marital status, family structure (with/without children), nature of work (mental/manual labor), the presence/absence of mental health comorbidities, sleep disorders, other chronic diseases, and the following

habits: regular exercise, risky alcohol consumption, and smoking may have an impact on mental stress,[13, 17, 19, 26, 28-30] but the conclusion is not completely consistent. We also observed in the clinic that patients implanted with multiple stents tend to be more stressed.

Our results showed a strong correlation between perceived stress and educational level in Chinese patients with CHD. A higher educational level was associated with higher perceived stress, with the risk of high perceived stress in participants with a university degree being 1.453 times (CI: 1.206-1.750) that of those who received senior middle school education or below, and the OR increased to 1.928 (CI: 1.290-2.882) among participants with a masters or doctoral degree. However, this result is contrary to the findings of studies conducted in other countries[19, 31]which have indicated that individuals with lower educational attainment generally perceive higher stress. This may possibly be attributed to the long-standing, strong emphasis on educational attainment in Chinese society, which has led to the general view that individuals with higher educational levels should attain greater personal achievements and bear greater social responsibilities and expectations. However, it is not clear whether this unique sociocultural background has caused the aforementioned difference between Eastern and Western countries in the influence of educational level on perceived stress.

Perceived stress level was also found to be strongly related to the nature of work in the Chinese population. Participants who engaged in mental labor had higher perceived stress than did those who engaged in manual labor; in other words, they had a higher probability of a high perceived stress score (OR: 1.389, CI: 1.144-1.686). Such a result is not in complete agreement with the findings of previous studies. A survey by Lesage et al.[17] revealed that differences in perceived stress among administrative, technical, and blue-collar workers were statistically insignificant. However, the 501 participants of Lesage's study were selected from individuals who attended occupational health centers in northern France, whereas the participants of our study had a greater diversity of occupations, including teachers, doctors, taxi drivers and gardeners. The greater diversity of occupations included in our study provides a better reflection of the actual range of perceived stress across occupations, thereby helping

the occupational factor to reach significance. Dėdelė et al.[32] performed a cross-sectional study on perceived stress among 571 full-time workers in Lithuania and found that blue-collar workers who spent relatively more time engaging in physical work had a higher risk of high perceived stress than white-collar workers, which appears to contradict our results. However, the distribution of perceived stress across occupations may depend on the social environment. With China's vast population, Chinese workers are often faced with complicated interpersonal relationships in their workplace. In general, workplace ecology is more complex among individuals engaged in mental labor than among manual workers, which may have partially contributed to the difference in perceived stress we observed between the two occupational categories.

The drinking habit of patients with CHD has also been identified as a potential factor associated with perceived stress. Our results indicated that participants with a habit of risky alcohol consumption had higher perceived stress (P = 0003). We also found that the probability that risky alcohol drinkers were assessed as having high perceived stress was 1.492 times that of non-risky alcohol drinkers (CI: 1.146-1.944). These findings are consistent with those reported by Yoon et al.[29], who showed that the proportion of individuals with adverse drinking habits was higher in the population with high perceived stress than in the population with low perceived stress. Although the study by Yoon et al. did not investigate possible causal relationships between high stress and at-risk drinking, there is no doubt that patients with a habit of risky alcohol consumption can have higher perceived stress. Therefore, for such individuals, emphasis should be placed on appropriate stress interventions in the formulation of rehabilitation programs.

Interestingly, we also found that patients with CHD with children were nearly twice as likely to perceive the stress as those without children, which is consistent with the findings of Lesage et al.[17]

Our results also showed that the perceived stress of patients with CHD was not correlated with age, sex or marital status. There is no study to investigate the effect of this 3 factors on perceived stress level especially in CHD patients. For the general population, there is some inconsistent findings. A study by Andreou et al.[28] indicated

that younger individuals, women, and single or divorced individuals may have higher perceived stress. Cohen et al.[13] reported that perceived stress was higher in women, but unrelated to age; similar conclusions were reached in two other studies.[33,34] However, Dėdelė et al.[32] asserted that older individuals had higher perceived stress. A study by Leung et al.[26] indicated higher levels of perceived stress in women, but a contrary result was reported by Ojard et al.[35] In summary, we have to say research on this matter is far from conclusive. And the inconsistency of our study with other precious ones might attribute to the disease type, difference environmental and social background.

LIMITATIONS

This study has several limitations. First, we conducted the study in CHD patients referred to the cardiac rehabilitation center in our hospital, which might bring selection bias. Also, multi-center study to further evaluate the CPSS score in CHD patients all over China is ongoing. Second, when screening influencing factors associated with CPSS score, the variables we included might not cover all the possible factors. The effect size should be interpreted with caution due to the low variation of marital status and other potential missing covariates. Third, our study didn't clarify whether the CPSS score would associate with the clinical outcome of CHD patients, which might be a candidate topic we should investigate further.

CONCLUSIONS

In conclusion, the results of this study indicate that patients with CHD have a relative higher perceived stress level. Individuals who had higher educational attainment, engaged in mental labor, had children, and had a habit of risky alcohol consumption were much easier to perceive the stress. The results of this study might help to stratify CHD patients according to stress perception level and supply the individualized stress management programs for Chinese populations with CHD..

Contributors

The study was initiated by JM and YX. YG performed the statistical analysis and drafted the manuscript. RH, YZ and MY were helpful for data collection. JM and YX contributed substantially to its revision. JM and YX took responsibility for the

manuscript as a whole.

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Competing interests

None declared.

Patient consent for publication

Not required.

Ethics approval

This study was approved by the ethics committee of the Chinese PLA General Hospital(S2020-382-01)

Data availability statement

Data are available upon reasonable request. Given that the data is in Chinese, complete raw data are not available for sharing. Partial data sets used and/or analysed during the current study are available from the corresponding author on reasonable request.

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Table 1 Social Demography Factors of the subjects

social demography factor		n	%
age	＜45	160	7.2
	45-64	1317	59.5
	65-84	727	32.8
	⩾85	11	0.4
Gender	Male	1764	79.6
	Female	451	20.4
Region	North	1388	62.7
	South	827	37.3
Education level	Senior high school and below	1107	50.0
	College	978	44.2
	Above college	130	5.9
Having children	Yes	2170	98.0
	No	45	2.0
Marital status	Married	2194	99.0
	Other (single, divorced, or widowed)	21	1.0
Occupation	Mental	1530	69.1
	Physical	685	30.9
Regular exercise	Yes	1630	73.6
	No	585	26.4
Risky alcohol drinking	Yes	298	13.5
	No	1917	86.5
Current Smoker	Yes	334	15.1
	No	1881	84.9
Comorbidity			
Number of stent	0	508	22.9
	1	901	40.7
	2	462	20.9

	⩾3	344	15.5
Hypertension	Yes	1245	56.2
	No	970	43.8
Hyperlipemia	Yes	1049	47.4
	No	1166	52.6
Diabetes	Yes	598	27.0
	No	1617	73.0
Cerebrovascular	Yes	39	1.8
disease	No	2176	98.2
Other disease	Yes	119	7.1
	No	2096	92.9
Sleep disorder	Yes	1657	74.8
	No	558	25.2
Depressive state	Yes	817	36.9
	No	1398	63.1
Anxiety state	Yes	1113	50.2
	No	1102	49.8

516 Table 2 comparison of two groups with different CPSS score

Characteristics	Categories	High stress group (n=1190)		Low stress group (n=1025)		X^2	*P* value
		n	%	n	%		
age	＜45	89	7.5	71	6.9	0.358	0.949
	45-64	709	59.6	608	59.3		
	65-84	386	32.4	341	33.3		
	⩾85	6	0.5	5	0.5		
Gender	Male	966	81.2	798	77.9	3.750	0.053
	Female	224	18.8	227	22.1		
Education level	Senior high school and below	526	44.2	581	56.7	36.611	0.000
	College	578	48.6	400	39.0		
	Above college	86	7.2	44	4.3		
Having children	Yes	1173	98.6	997	97.3	4.698	0.030
	No	17	1.4	28	2.7		
Marital status	Married	1182	99.3	1012	98.7	2.083	0.149
	Other (single, divorced, or widowed)	8	0.7	13	1.3		
Occupation	Mental	881	74.0	649	63.3	29.605	0.000
	Physical	309	26.0	376	36.7		
Regular exercise	Yes	901	75.7	729	71.1	5.975	0.015
	No	289	24.3	296	28.9		
Risky alcohol drinking	Yes	188	15.8	110	10.7	12.141	0.000
	No	1002	84.2	915	89.3		

Current Smoker		Yes	182	15.3	152	14.8	0.093	0.760
		No	1008	84.7	873	85.2		
Number stent	of	0	280	23.5	228	22.2	0.820	0.845
		1	486	40.8	415	40.5		
		2	243	20.4	219	21.4		
		⩾3	181	15.2	163	15.9		
Chronic disease		Yes	965	81.1	831	81.1	0.000	0.991
		No	225	18.9	194	18.9		
Sleep disorder		Yes	889	74.7	768	74.9	0.014	0.905
		No	301	25.3	257	25.1		

Table 3 Logistics regression of CPSS score

	Model 1*		Model 2**	
	OR(95%CI)	*P* value	OR(95%CI)	*P* value
Kid				
Yes	1.000		1.000	
No	2.226(1.098-4.515)	0.027	2.338(1.258-4.345)	0.007
Education level				
Senior high school and below	1.000		1.000	
College	1.453(1.206-1.750)	0.000	1.478(1.231-1.776)	0.000
Above college	1.928(1.290-2.882)	0.001	1.936(1.306-2.870)	0.001
Occupation				
Manual	1.000		1.000	
Mental	1.389(1.144-1.686)	0.001	1.394(1.149-1.690)	0.001
Risky alcohol drinking				
No	1.000	0.003	1.000	0.001
Yes	1.492 (1.146-1.944)		1.516(1.175-1.958)	

*Adjusted by age, sex, educational level, marital status, family structure (with/without children), nature of work (mental/manual labor), number of stents, and the presence/absence of sleep disorders, other chronic diseases, and the following habits: regular exercise, risky alcohol consumption, and smoking.

*Adjusted by age, sex, educational level, marital status, family structure (with/without children), nature of work (mental/manual labor), number of stents, and the presence/absence of sleep disorders, other chronic diseases, the following habits: regular exercise, risky alcohol consumption, and smoking， PHQ9 scores and GAD7 scores.

OR: Odds Ratio

549

550 Figure 1 Flow diagram of the participants

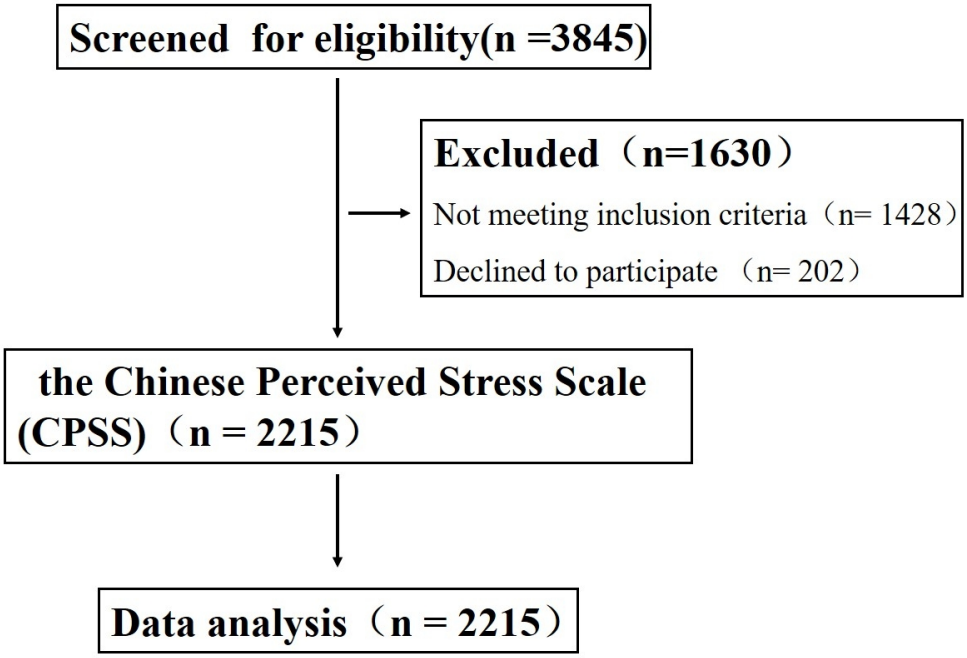

Figure 1 Flow diagram of the participants

203x136mm (150 x 150 DPI)

STROBE 2007 (v4) Statement—Checklist of items that should be included in reports of *cross-sectional studies*

Section/Topic	Item #	Recommendation	Reported on page #
Title and abstract	1	(*a*) Indicate the study's design with a commonly used term in the title or the abstract	1
		(*b*) Provide in the abstract an informative and balanced summary of what was done and what was found	1
Introduction			
Background/rationale	2	Explain the scientific background and rationale for the investigation being reported	3
Objectives	3	State specific objectives, including any prespecified hypotheses	4
Methods			
Study design	4	Present key elements of study design early in the paper	4
Setting	5	Describe the setting, locations, and relevant dates, including periods of recruitment, exposure, follow-up, and data collection	4
Participants	6	(*a*) Give the eligibility criteria, and the sources and methods of selection of participants	4
Variables	7	Clearly define all outcomes, exposures, predictors, potential confounders, and effect modifiers. Give diagnostic criteria, if applicable	4
Data sources/ measurement	8*	For each variable of interest, give sources of data and details of methods of assessment (measurement). Describe comparability of assessment methods if there is more than one group	4
Bias	9	Describe any efforts to address potential sources of bias	
Study size	10	Explain how the study size was arrived at	4
Quantitative variables	11	Explain how quantitative variables were handled in the analyses. If applicable, describe which groupings were chosen and why	5
Statistical methods	12	(*a*) Describe all statistical methods, including those used to control for confounding	5
		(*b*) Describe any methods used to examine subgroups and interactions	5
		(*c*) Explain how missing data were addressed	5
		(*d*) If applicable, describe analytical methods taking account of sampling strategy	5
		(*e*) Describe any sensitivity analyses	5
Results			

Participants	13*	(a) Report numbers of individuals at each stage of study—eg numbers potentially eligible, examined for eligibility, confirmed eligible, included in the study, completing follow-up, and analysed	6
		(b) Give reasons for non-participation at each stage	6
		(c) Consider use of a flow diagram	
Descriptive data	14*	(a) Give characteristics of study participants (eg demographic, clinical, social) and information on exposures and potential confounders	6
		(b) Indicate number of participants with missing data for each variable of interest	
Outcome data	15*	Report numbers of outcome events or summary measures	6
Main results	16	(*a*) Give unadjusted estimates and, if applicable, confounder-adjusted estimates and their precision (eg, 95% confidence interval). Make clear which confounders were adjusted for and why they were included	6
		(*b*) Report category boundaries when continuous variables were categorized	6
		(*c*) If relevant, consider translating estimates of relative risk into absolute risk for a meaningful time period	
Other analyses	17	Report other analyses done—eg analyses of subgroups and interactions, and sensitivity analyses	6
Discussion			
Key results	18	Summarise key results with reference to study objectives	
Limitations	19	Discuss limitations of the study, taking into account sources of potential bias or imprecision. Discuss both direction and magnitude of any potential bias	7-10
Interpretation	20	Give a cautious overall interpretation of results considering objectives, limitations, multiplicity of analyses, results from similar studies, and other relevant evidence	7-10
Generalisability	21	Discuss the generalisability (external validity) of the study results	7-10
Other information			
Funding	22	Give the source of funding and the role of the funders for the present study and, if applicable, for the original study on which the present article is based	10

*Give information separately for cases and controls in case-control studies and, if applicable, for exposed and unexposed groups in cohort and cross-sectional studies.

Note: An Explanation and Elaboration article discusses each checklist item and gives methodological background and published examples of transparent reporting. The STROBE checklist is best used in conjunction with this article (freely available on the Web sites of PLoS Medicine at http://www.plosmedicine.org/, Annals of Internal Medicine at http://www.annals.org/, and Epidemiology at http://www.epidem.com/). Information on the STROBE Initiative is available at www.strobe-statement.org.

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Title Page

Perceived Stress in Chinese Patients with Coronary Heart Disease: A cross-sectional study

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ABSTRACT

Objective Studies have shown that chronic stress is closely linked to the occurrence and development of cardiovascular disease. To date, few studies have focused on perceived stress in coronary heart diseases (CHD) patients and the possible factors influencing the stress. This study aims to investigate the mental stress of patients with CHD and determine the individual attributes closely associated with it.

Design A cross-sectional study.

Participates A total of 2215 CHD patients were enrolled and chronic stress was assessed with the Chinese version Perceived Stress Scale (CPSS). Participants were divided into 2 groups due to CPSS score and binary logistic regression was applied to analyze the factors that affected CPSS.

Results The mean CPSS score of Chinese patients with CHD was 27.16 ± 6.35 Compared with participants who received senior middle school education or below, those with a university degree had a higher probability of high perceived stress (OR: 1.453, CI: 1.206-1.750); this difference was more evident in participants with a master or doctoral degree (OR: 1.928, CI: 1.290-2.882). Also engaging in mental labor (OR: 1.389, CI: 1.144-1.686), having children (OR: 2.226, CI: 1.098-4.515), and having a habit of risky alcohol consumption (OR:1.492, CI: 1.146-1.944) were associated with

perceived stress.

Conclusion: Patients who had higher educational attainment, engaged in mental labor, had children, and had a habit of risky alcohol consumption were much easier to perceive the stress.

Keywords
Perceived stress, Coronary heart disease, Influencing factor

Word Count 3081 words

Strengths and limitations of this study

- Few studies have focused on perceived stress in CHD patients and the identification of high-stress individuals.
- Utilize the PSS for the accurate identification of stress-sensitive individuals among patients with coronary heart disease.
- Given the cross-sectional nature of the study, we cannot infer causal relationships

INTRODUCTION

The incidence of coronary heart disease (CHD) has been rising steadily over the past few decades and the resulting burden of disease is an issue faced by developed and developing countries alike[1]. Finding out the potential risk factors of coronary heart disease and subsequent targeted treatment is a severe challenge. Recent studies demonstrated that psychological and social factors play an important and independent role in the development of coronary heart disease.[2-4]

Psychological stress (stress) refers to the psychological challenge or threat caused by various triggering events or adverse life factors and usually manifests as emotional discomfort, pain, or anguish[5]. Under normal circumstances, a dynamic equilibrium exists between an organism and its external environment, and stress arises when this equilibrium is upset or is self-perceived as upset[6]. Stress is believed to be closely linked to the occurrence and development of cardiovascular disease, one of the most important psychosomatic diseases[7-8]. Acute mental stress caused by sudden accidents or illness may be a trigger for cardiac events such as myocardial ischemia or Takotsubo cardiomyopathy.[9-10] The process of seeking medical care for patients with an acute coronary event could be another stressor itself.[11] Meanwhile if certain acute stress becomes persistent, it will change to chronic stress. A meta-analysis[12] suggests that high stress is associated with a moderately increased risk of incident CHD. The current literature suggests that mental stress may cause over-activation of the autonomic nervous system and elicit a stress response from the endocrine system, thereby inducing endothelial dysfunction, ultimately triggering cardiovascular events.[13-15] A latest study[16] revealed that the amygdala, a stress-sensitive structure, may increase the incidence of cardiovascular diseases by improving the activity of the immune system, which might be a possible mechanism. Stress-induced platelet bioactivity increase and prolongation may also be involved in this process.[17]

It was also found that the process by which stressors exert their effects on an organism is not linear; instead, it arises through interactions[6]. The actual effect of chronic stress on different individuals depends on the stress they perceived. The stress perceived by an individual reflects his/her subjective evaluation of the stressor and will

partly depend on individual attributes. Studies have shown that different individuals faced with identical stressors may perceive considerably different levels of stress, with different effects on CHD occurrence and development, resulting in differences in the severity or prognosis of CHD.[18-19] Therefore, the accurate identification of individuals who are more likely to perceive stress is of great significance for the precise assessment and subsequent treatment of CHD.

Assessments of psychological stress are generally performed using standard psychological instruments. Commonly used questionnaires include the Perceived Stress Scale (PSS), Stress Appraisal Measure (SAM), and Impact of Event Scale (IES). The PSS is the most widely used scale to assess chronic stress because it is easy to implement and does not require professional intervention during administration. Developed by Cohen et al. in 1983[20], the PSS measures the dimensions of uncontrollability and stressfulness, and assesses the stress levels of individuals based on their subjective perceptions of stressors. It has been translated into many languages and used widely in diverse populations around the world[21-27]. Blumenthal et al.[28] have used PSS as a tool to assess the chronic stress of CHD patients. The version most used in Chinese populations is the Chinese Perceived Stress Scale (CPSS), which is a simplified-Chinese version translated by Yang (2007)[29]. The CPSS has demonstrated good validity and reliability in a series of studies in different Chinese populations[30-32], especially in cardiac patients[33].

Few studies published to date have utilized the CPSS for the accurate identification of high perceived stress individuals among patients with CHD, and stress detection in the Chinese mainland population with CHD has not yet been reported. We, therefore, analyzed the CPSS scores of patients who visited the cardiac rehabilitation clinic at our hospital with the aim of investigating the self-perceived stress levels of Chinese patients with CHD and determining the individual attributes closely associated with perceived stress. The results of this study might help to stratify CHD patients according to stress perception level and supply the individualized stress management programs for Chinese populations with CHD.

METHODS

Study participants

A cross-sectional study design was adopted. Using the electronic medical records system of our hospital, we screened patients referred to the cardiac rehabilitation clinic between 2015 and 2020. All patients in the inpatient department of cardiology were recommended to the rehabilitation clinic regardless of whether they choose to receive the following rehabilitation treatment or not. Only those with a definitive diagnosis of CHD were included in the analysis. Based on the criteria of the CHD 2019 ESC Guidelines for the Diagnosis and Management of Chronic Coronary Syndromes, the inclusions were: one or more lesions with ⩾50% stenosis as shown by coronary angiography; stable angina (SA); unstable angina (USA); old myocardial infarction (OMI); acute myocardial infarction (AMI); post-percutaneous coronary intervention (PCI); post-coronary artery bypass graft (CABG); or ischemic cardiomyopathy (IC). Those who are unwilling to take the scale will be excluded.

Demographic characteristics and medical history

The demographic characteristics and medical history of the participants were obtained from the cardiac rehabilitation medical records system and collated by a cardiologist. The demographic characteristics analyzed included age, sex, region (south /north, divided along the Qinling Mountains-Huaihe River line), educational level, marital status, family structure (with/without children), nature of work (mental/manual labor), the presence/absence of sleep disorders, and the following lifestyle factors: regular exercise, risky alcohol consumption, and smoking. The medical history data analyzed included a history of cardiac revascularization and the presence/absence of other chronic diseases requiring long-term medication. Mental labor was defined as professional, managerial, or administrative work generally performed in an office or other administrative environment. Manual labor was defined as strenuous physical work or other types of work demanding physical exertion. Regular exercise was defined as ⩾30 min of low-intensity exercise >5 times per week or ⩾20 min of moderate-intensity exercise >3 times per week. Sleep disorders were defined as the occurrence of

at least one of the following ⩾3 times per week for at least 1 month: inability to sleep after 30 min in bed, waking up ⩾2 times during the night, wake time >15%, dreamful sleep or total sleep time <6 hours, and waking up ≥2 hours ahead of schedule and subsequently unable to get back to sleep. Risky alcohol consumption was defined as the consumption of ⩾5 alcoholic drinks on a single occasion >12 times in the past year.[34]

Stress assessment

The perceived stress of the study participants was assessed using the CPSS, which comprises 14 items intended to measure the dimensions of uncontrollability and stressfulness. Each item is rated on a 5-point scale (0 = never, 1 = rarely, 2 = sometimes, 3 = fairly often, 4 = very often), with items 4, 5, 6, 7, 9, 10, and 13 scored in the reverse direction. Total scores range from 0 to 56 points, with higher scores indicating higher psychological stress.

In addition to the CPSS, all the participates were asked to complete the Patient Health Questionnaire (PHQ-9) scale and the Generalized Anxiety Disorder (GAD-7) scale to assess preexisting mental health comorbidities. The PHQ-9 is a self-rating scale consisting of 9 items. A PHQ9 score greater than 5 indicates that the patient may be in a mild or more depressive state. The GAD-7 is a 7-item self-rating scale indicating a mild or more anxiety state when the score is greater than 5.

All the participants were asked to provide responses based on their own perceptions. All patients who visited the cardiac rehabilitation clinic for the first time were requested to complete the scales on their own after receiving instructions on questionnaire completion from a nurse. The responses were collected and collated by a cardiologist.

Statistical analysis

Statistical analysis was performed using SPSS 25.0. Quantitative variables were tested for normality. Normally distributed variables were expressed as mean ± standard deviation (x ± s); variables not normally distributed were expressed as median and interquartile range (IQR). Qualitative data were expressed as ratios or percentages. Factors associated with the CPSS scores of the study participants were analyzed from binary logistic regression.

Patient and public involvement

Public and patient involvement was not applicable in this research.

RESULTS

Demographic data of patients with CHD

Of the 3845 patients referred to the cardiac rehabilitation clinic during the study period, 1630 patients were excluded, of which 1428 did not meet the inclusion criteria, and 202 refused to be evaluated by CPSS. Eventually, 2215 CHD patients were included in the study (Figure 1). The mean age of the study participants was 59.57 ± 10.10 y, and the majority of the participants were male (79.64%), had a university degree or below (94.13%), married (99.05%), had children (97.97%), engaged in mental labor (69.07%), had sleep disorders (74.81%), and did not have a drinking habit (60.18%) Of the participants, 77.1% had previously undergone stent insertion, 56.2% had concomitant hypertension, 47.4% had concomitant hyperlipidemia, and 27% had concomitant diabetes mellitus (see **Table 1**).

Comparison of characteristics between groups

The mean CPSS score of all the patients with CHD was 27.16 ± 6.35. Using the median score of 27 as the cut-off point, the study participants were divided into a low-stress group (CPSS score ⩽27) and a high-stress group (CPSS score >27).

Participants who had children, engaged in mental labor, or had a habit of risky alcohol consumption had a higher probability of experiencing higher stress perception levels. (see **Table 2**).

Logistic regression

Binary logistic regression analysis was performed in model 1 by setting the CPSS score as the dependent variable and the following as the independent variables: age, sex, educational level, marital status, family structure (with/without children), nature of work (mental/manual labor), number of stents, and the presence/absence of sleep disorders, other chronic diseases, and the following habits: regular exercise, risky alcohol consumption, and smoking. Our results indicated that study participants who have children had a higher probability of high perceived stress, with the odds ratio (OR) being 2.226 (confidence interval [CI]: 1.098-4.515). Compared with participants who

received middle school education or below, those with a university degree had a higher probability of high perceived stress (OR: 1.453, CI: 1.206-1.750); this was more evident in participants with a master or doctoral degree (OR: 1.928, CI: 1.290-2.882). Participants who engaged in mental labor had a higher probability of high perceived stress than those who engaged in manual labor (OR: 1.389, CI: 1.144-1.686). Compared with participants who did not have a habit of risky alcohol consumption, those who had this habit had a higher probability of high perceived stress (OR:1.492, CI: 1.146-1.944). Model 2 was adjusted by GAD-7 and PHQ-9 scores, which has no major influence on the conclusion (see **Table 3**).

DISCUSSION

The relationship between psychological stress and cardiovascular disease has attracted increasing attention in recent years. Considering that psychological stress may play some role in the occurrence and development of CHD, a greater emphasis has been placed on stress management in comprehensive cardiac rehabilitation programs because it may potentially provide benefits, such as improving the long-term prognosis of patients with CHD.[28] In this study, we investigated the stress perception level in the Chinese CHD population and explored the possible influencing factors associated with them. Our study suggested that patients with CHD in China had a relatively higher CPSS score. In addition, we found that patients who had higher educational attainment, engaged in mental labor, had children, and had a habit of risky alcohol consumption were much easier to perceive the stress.

The mean CPSS score of Chinese patients with CHD in our study was 27.16 ± 6.35. Yang et al.[29] conducted a CPSS assessment of the Chinese general population (n=3666), with an average score of 24. 22 ±5. 811. A summary independent-sample t-test proves that the CPSS scores of the two groups are statistically different (P = 0.000).

Analysis of the demographic characteristics of high-stress individuals among patients with CHD can support the clinical stratified management of patients according to the stress level, which increases the efficiency of rehabilitation treatment and maximizes the clinical benefits to each individual. Previous studies have shown that demographic characteristics such as age, sex, educational level, marital status, family

structure (with/without children), nature of work (mental/manual labor), the presence/absence of mental health comorbidities, sleep disorders, other chronic diseases, and the following habits: regular exercise, risky alcohol consumption, and smoking may have an impact on mental stress,[20, 24, 26, 33, 35-37] but the conclusion is not completely consistent. We also observed in the clinic that patients implanted with multiple stents tend to be more stressed. Our results showed a strong correlation between perceived stress and educational level in Chinese patients with CHD. A higher educational level was associated with higher perceived stress, with the risk of high perceived stress in participants with a university degree being 1.453 times (CI: 1.206-1.750) that of those who received senior middle school education or below, and the OR increased to 1.928 (CI: 1.290-2.882) among participants with a master or doctoral degree. However, this result is contrary to the findings of studies conducted in other countries[26, 38]which have indicated that individuals with lower educational attainment generally perceive higher stress. This may be attributed to the long-standing, strong emphasis on educational attainment in Chinese society, which has led to the general view that individuals with higher educational levels should attain greater personal achievements and bear greater social responsibilities and expectations. However, it is not clear whether this unique socio-cultural background has caused the aforementioned difference between Eastern and Western countries in the influence of educational level on perceived stress.

The perceived stress level was also found to be strongly related to the nature of work in the Chinese population. Participants who engaged in mental labor had higher perceived stress than did those who engaged in manual labor; in other words, they had a higher probability of a high perceived stress score (OR: 1.389, CI: 1.144-1.686). Such a result is not in complete agreement with the findings of previous studies. A survey by Lesage et al.[24] revealed that differences in perceived stress among administrative, technical, and blue-collar workers were statistically insignificant. However, the 501 participants of Lesage's study were selected from individuals who attended occupational health centers in northern France, whereas the participants of our study had a greater diversity of occupations, including teachers, doctors, taxi drivers, and

gardeners. The greater diversity of occupations included in our study provides a better reflection of the actual range of perceived stress across occupations, thereby helping the occupational factor to reach significance. Dėdelė et al.[39] performed a cross-sectional study on perceived stress among 571 full-time workers in Lithuania and found that blue-collar workers who spent relatively more time engaging in physical work had a higher risk of high perceived stress than white-collar workers, which appears to contradict our results. However, the distribution of perceived stress across occupations may depend on the social environment. With China's vast population, Chinese workers are often faced with complicated interpersonal relationships in their workplace. In general, workplace ecology is more complex among individuals engaged in mental labor than among manual workers, which may have partially contributed to the difference in perceived stress we observed between the two occupational categories.

The drinking habit of patients with CHD has also been identified as a potential factor associated with perceived stress. Our results indicated that participants with a habit of risky alcohol consumption had higher perceived stress (P = 0003). We also found that the probability that risky alcohol drinkers were assessed as having high perceived stress was 1.492 times that of non-risky alcohol drinkers (CI: 1.146-1.944). These findings are consistent with those reported by Yoon et al.[36], who showed that the proportion of individuals with adverse drinking habits was higher in the population with high perceived stress than in the population with low perceived stress. Although the study by Yoon et al. did not investigate possible causal relationships between high stress and at-risk drinking, there is no doubt that patients with a habit of risky alcohol consumption can have higher perceived stress. Therefore, for such individuals, emphasis should be placed on appropriate stress interventions in the formulation of rehabilitation programs.

Interestingly, we also found that patients with CHD with children were nearly twice as likely to perceive the stress as those without children, which is consistent with the findings of Lesage et al.[24]

Our results also showed that the perceived stress of patients with CHD was not correlated with age, sex, or marital status. There is no study to investigate the effect of

these 3 factors on perceived stress levels, especially in CHD patients. For the general population, there are some inconsistent findings. A study by Andreou et al.[35] indicated that younger individuals, women, and single or divorced individuals may have higher perceived stress. Cohen et al.[20] reported that perceived stress was higher in women but unrelated to age; similar conclusions were reached in two other studies.[40-41] However, Dėdelė et al.[39] asserted that older individuals had higher perceived stress. A study by Leung et al.[33] indicated higher levels of perceived stress in women, but a contrary result was reported by Ojard et al.[42] In summary, we have to say research on this matter is far from conclusive. And the inconsistency of our study with other precious ones might attribute to the disease type, difference in environmental and social background.

LIMITATIONS

This study has several limitations. First, we conducted the study in CHD patients referred to the cardiac rehabilitation center in our hospital, which might bring selection bias and the stress levels in the general population only had historical control. Also, a multi-center study to further evaluate the CPSS score in CHD patients and the general population all over China is ongoing. Second, when screening influencing factors associated with the CPSS score, the variables we included might not cover all the possible factors. The effect size should be interpreted with caution due to the low variation of marital status and other potential missing covariates. Third, our study didn't clarify whether the CPSS score would associate with the clinical outcome of CHD patients, which might be a candidate topic we should investigate further.

CONCLUSIONS

In conclusion, individuals who had higher educational attainment, engaged in mental labor, had children and had a habit of risky alcohol consumption were much easier to perceive the stress. The results of this study might help to stratify CHD patients according to stress perception level and supply the individualized stress management programs for Chinese populations with CHD.

Contributors

The study was initiated by JM and YX. YG performed the statistical analysis and

drafted the manuscript. RH, YZ, and MY were helpful for data collection. JM and YX contributed substantially to its revision. JM and YX took responsibility for the manuscript as a whole.

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Competing interests

None declared.

Patient consent for publication

Not required.

Ethics approval

This study was approved by the ethics committee of the Chinese PLA General Hospital(S2020-382-01)

Data availability statement

Data are available upon reasonable request. Given that the data is in Chinese, complete raw data are not available for sharing. Partial data sets used and/or analyzed during the current study are available from the corresponding author on reasonable request.

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485 Table 1 Social Demography Factors of the subjects

social demography factor		n	%
age	＜45	160	7.2
	45-64	1317	59.5
	65-84	727	32.8
	⩾85	11	0.4
Gender	Male	1764	79.6
	Female	451	20.4
Region	North	1388	62.7
	South	827	37.3
Education level	Senior high school and below	1107	50.0
	College	978	44.2
	Above college	130	5.9
Having children	Yes	2170	98.0
	No	45	2.0
Marital status	Married	2194	99.0
	Other (single, divorced, or widowed)	21	1.0
Occupation	Mental	1530	69.1
	Physical	685	30.9
Regular exercise	Yes	1630	73.6
	No	585	26.4
Risky alcohol drinking	Yes	298	13.5
	No	1917	86.5
Current Smoker	Yes	334	15.1
	No	1881	84.9
Comorbidity			
Number of stent	0	508	22.9
	1	901	40.7
	2	462	20.9

	⩾3	344	15.5
Hypertension	Yes	1245	56.2
	No	970	43.8
Hyperlipemia	Yes	1049	47.4
	No	1166	52.6
Diabetes	Yes	598	27.0
	No	1617	73.0
Cerebrovascular	Yes	39	1.8
disease	No	2176	98.2
Other diseases	Yes	119	7.1
	No	2096	92.9
Sleep disorder	Yes	1657	74.8
	No	558	25.2
Depressive state	Yes	817	36.9
	No	1398	63.1
Anxiety state	Yes	1113	50.2
	No	1102	49.8

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487 Table 2 Comparison of two groups with different CPSS scores

Characteristics	Categories	High-stress group (n=1190)		Low stress group (n=1025)		X^2	*P* value
		n	%	n	%		
age	＜45	89	7.5	71	6.9	0.358	0.949
	45-64	709	59.6	608	59.3		
	65-84	386	32.4	341	33.3		
	⩾85	6	0.5	5	0.5		
Gender	Male	966	81.2	798	77.9	3.750	0.053
	Female	224	18.8	227	22.1		
Education level	Senior high school and below	526	44.2	581	56.7	36.611	0.000
	College	578	48.6	400	39.0		
	Above college	86	7.2	44	4.3		
Having children	Yes	1173	98.6	997	97.3	4.698	0.030
	No	17	1.4	28	2.7		
Marital status	Married	1182	99.3	1012	98.7	2.083	0.149
	Other (single, divorced, or widowed)	8	0.7	13	1.3		
Occupation	Mental	881	74.0	649	63.3	29.605	0.000
	Physical	309	26.0	376	36.7		
Regular exercise	Yes	901	75.7	729	71.1	5.975	0.015
	No	289	24.3	296	28.9		
Risky alcohol drinking	Yes	188	15.8	110	10.7	12.141	0.000
	No	1002	84.2	915	89.3		

Current Smoker	Yes	182	15.3	152	14.8	0.093	0.760
	No	1008	84.7	873	85.2		
Number of stent	0	280	23.5	228	22.2	0.820	0.845
	1	486	40.8	415	40.5		
	2	243	20.4	219	21.4		
	⩾3	181	15.2	163	15.9		
Chronic disease	Yes	965	81.1	831	81.1	0.000	0.991
	No	225	18.9	194	18.9		
Sleep disorder	Yes	889	74.7	768	74.9	0.014	0.905
	No	301	25.3	257	25.1		
Depressive state	Yes	626	52.6	487	47.5	5.713	0.017
	No	564	47.4	538	52.5		
Anxiety state	Yes	470	39.5	347	33.9	7.530	0.006
	No	720	60.5	678	66.1		

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Table 3 Logistics regression of CPSS score

	Model 1*		Model 2**	
	OR(95%CI)	*P* value	OR(95%CI)	*P* value
Kid				
Yes	1.000		1.000	
No	2.226(1.098-4.515)	0.027	2.338(1.258-4.345)	0.007
Education level				
Senior high school and below	1.000		1.000	
College	1.453(1.206-1.750)	0.000	1.478(1.231-1.776)	0.000
Above college	1.928(1.290-2.882)	0.001	1.936(1.306-2.870)	0.001
Occupation				
Manual	1.000		1.000	
Mental	1.389(1.144-1.686)	0.001	1.394(1.149-1.690)	0.001
Risky alcohol drinking				
No	1.000	0.003	1.000	0.001
Yes	1.492 (1.146-1.944)		1.516(1.175-1.958)	

*Adjusted by age, sex, educational level, marital status, family structure (with/without children), nature of work (mental/manual labor), number of stents, and the presence/absence of sleep disorders, other chronic diseases, and the following habits: regular exercise, risky alcohol consumption, and smoking.

*Adjusted by age, sex, educational level, marital status, family structure (with/without children), nature of work (mental/manual labor), number of stents, and the presence/absence of sleep disorders, other chronic diseases, the following habits: regular exercise, risky alcohol consumption, and smoking, PHQ9 scores and GAD7 scores.OR: Odds Ratio

Figure 1 Flow diagram of the participants

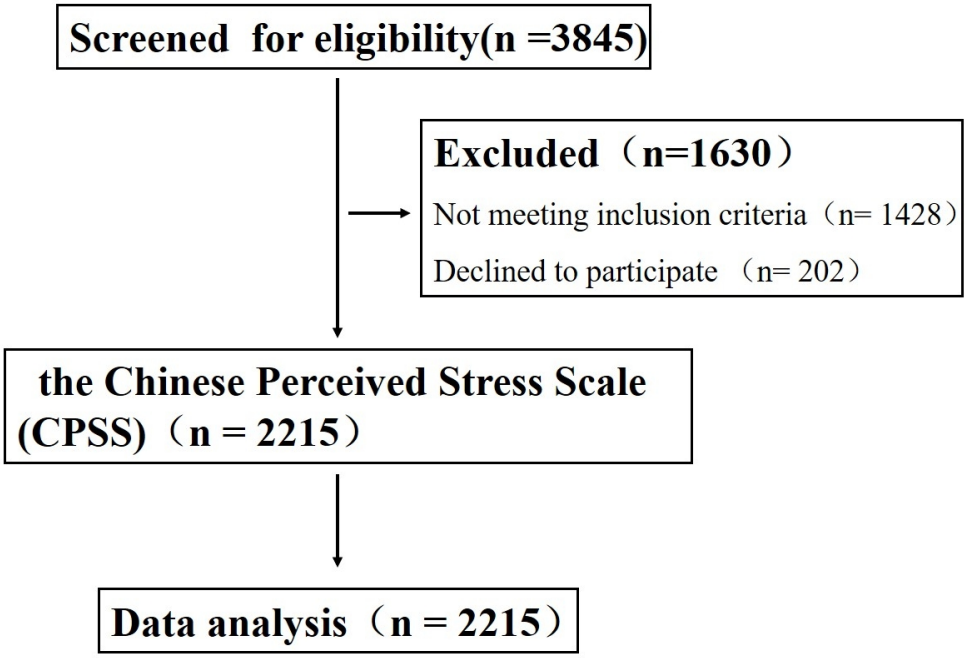

Figure 1 Flow diagram of the participants

203x136mm (150 x 150 DPI)

STROBE 2007 (v4) Statement—Checklist of items that should be included in reports of *cross-sectional studies*

Section/Topic	Item #	Recommendation	Reported on page #
Title and abstract	1	(*a*) Indicate the study's design with a commonly used term in the title or the abstract	1
		(*b*) Provide in the abstract an informative and balanced summary of what was done and what was found	1
Introduction			
Background/rationale	2	Explain the scientific background and rationale for the investigation being reported	3
Objectives	3	State specific objectives, including any prespecified hypotheses	4
Methods			
Study design	4	Present key elements of study design early in the paper	4
Setting	5	Describe the setting, locations, and relevant dates, including periods of recruitment, exposure, follow-up, and data collection	4
Participants	6	(*a*) Give the eligibility criteria, and the sources and methods of selection of participants	4
Variables	7	Clearly define all outcomes, exposures, predictors, potential confounders, and effect modifiers. Give diagnostic criteria, if applicable	4
Data sources/ measurement	8*	For each variable of interest, give sources of data and details of methods of assessment (measurement). Describe comparability of assessment methods if there is more than one group	4
Bias	9	Describe any efforts to address potential sources of bias	
Study size	10	Explain how the study size was arrived at	4
Quantitative variables	11	Explain how quantitative variables were handled in the analyses. If applicable, describe which groupings were chosen and why	5
Statistical methods	12	(*a*) Describe all statistical methods, including those used to control for confounding	5
		(*b*) Describe any methods used to examine subgroups and interactions	5
		(*c*) Explain how missing data were addressed	5
		(*d*) If applicable, describe analytical methods taking account of sampling strategy	5
		(*e*) Describe any sensitivity analyses	5
Results			

Participants	13*	(a) Report numbers of individuals at each stage of study—eg numbers potentially eligible, examined for eligibility, confirmed eligible, included in the study, completing follow-up, and analysed	6
		(b) Give reasons for non-participation at each stage	6
		(c) Consider use of a flow diagram	
Descriptive data	14*	(a) Give characteristics of study participants (eg demographic, clinical, social) and information on exposures and potential confounders	6
		(b) Indicate number of participants with missing data for each variable of interest	
Outcome data	15*	Report numbers of outcome events or summary measures	6
Main results	16	(*a*) Give unadjusted estimates and, if applicable, confounder-adjusted estimates and their precision (eg, 95% confidence interval). Make clear which confounders were adjusted for and why they were included	6
		(*b*) Report category boundaries when continuous variables were categorized	6
		(*c*) If relevant, consider translating estimates of relative risk into absolute risk for a meaningful time period	
Other analyses	17	Report other analyses done—eg analyses of subgroups and interactions, and sensitivity analyses	6
Discussion			
Key results	18	Summarise key results with reference to study objectives	
Limitations	19	Discuss limitations of the study, taking into account sources of potential bias or imprecision. Discuss both direction and magnitude of any potential bias	7-10
Interpretation	20	Give a cautious overall interpretation of results considering objectives, limitations, multiplicity of analyses, results from similar studies, and other relevant evidence	7-10
Generalisability	21	Discuss the generalisability (external validity) of the study results	7-10
Other information			
Funding	22	Give the source of funding and the role of the funders for the present study and, if applicable, for the original study on which the present article is based	10

*Give information separately for cases and controls in case-control studies and, if applicable, for exposed and unexposed groups in cohort and cross-sectional studies.

Note: An Explanation and Elaboration article discusses each checklist item and gives methodological background and published examples of transparent reporting. The STROBE checklist is best used in conjunction with this article (freely available on the Web sites of PLoS Medicine at http://www.plosmedicine.org/, Annals of Internal Medicine at http://www.annals.org/, and Epidemiology at http://www.epidem.com/). Information on the STROBE Initiative is available at www.strobe-statement.org.

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Perceived Stress in Chinese Patients with Coronary Heart Disease: A cross-sectional study

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Title Page

Perceived Stress in Chinese Patients with Coronary Heart Disease: A cross-sectional study

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ABSTRACT

Objective Studies have shown that chronic stress is closely linked to the occurrence and development of cardiovascular disease. To date, few studies have focused on perceived stress in coronary heart diseases (CHD) patients and the possible factors influencing the stress. This study aims to investigate the perceived stress of patients with CHD and determine the individual attributes closely associated with it.

Design A cross-sectional study.

Participates A total of 2215 CHD patients were enrolled and perceived stress was assessed with the Chinese version Perceived Stress Scale (CPSS). Participants were divided into 2 groups due to CPSS score and binary logistic regression was applied to analyze the factors that affected perceived stress level.

Results The mean CPSS score of Chinese patients with CHD was 27.16 ± 6.35 Compared with participants who received senior middle school education or below, those with a university degree had a higher probability of high perceived stress (OR: 1.453, CI: 1.206-1.750); this difference was more evident in participants with a master or doctoral degree (OR: 1.928, CI: 1.290-2.882). Also engaging in mental labor (OR: 1.389, CI: 1.144-1.686), having children (OR: 2.226, CI: 1.098-4.515), and having a habit of risky alcohol consumption (OR:1.492, CI: 1.146-1.944) were associated with

perceived stress.

Conclusion: Patients who had higher educational attainment, engaged in mental labor, had children, and had a habit of risky alcohol consumption were much easier to perceive the stress.

Keywords
Perceived stress, Coronary heart disease, Influencing factor

Word Count 2979 words

Strengths and limitations of this study

- Few studies have focused on perceived stress in CHD patients and the identification of high perceived stress individuals.
- Utilize the PSS for the accurate identification of stress-sensitive individuals among patients with coronary heart disease.
- Given the cross-sectional nature of the study, we cannot infer causal relationships.

INTRODUCTION

The incidence of coronary heart disease (CHD) has been rising steadily over the past few decades and the resulting burden of disease is an issue faced by developed and developing countries alike[1]. Finding out the potential risk factors of coronary heart disease and subsequent targeted treatment is a severe challenge. Recent studies demonstrated that psychological and social factors play an important and independent role in the development of coronary heart disease.[2-4]

Psychological stress (stress) refers to the psychological challenge or threat caused by various triggering events or adverse life factors and usually manifests as emotional discomfort, pain, or anguish[5]. Under normal circumstances, a dynamic equilibrium exists between an organism and its external environment, and stress arises when this equilibrium is upset or is self-perceived as upset[6]. Stress is believed to be closely linked to the occurrence and development of cardiovascular disease, one of the most important psychosomatic diseases[7-8]. Acute mental stress caused by sudden accidents or illness may be a trigger for cardiac events such as myocardial ischemia or Takotsubo cardiomyopathy.[9-10] The process of seeking medical care for patients with an acute coronary event could be another stressor itself.[11] Meanwhile if certain acute stress becomes persistent, it will change to chronic stress. A meta-analysis[12] suggests that high stress is associated with a moderately increased risk of incident CHD. The current literature suggests that mental stress may cause over-activation of the autonomic nervous system and elicit a stress response from the endocrine system, thereby inducing endothelial dysfunction, ultimately triggering cardiovascular events.[13-15] A latest study[16] revealed that the amygdala, a stress-sensitive structure, may increase the incidence of cardiovascular diseases by improving the activity of the immune system, which might be a possible mechanism. Stress-induced platelet bioactivity increase and prolongation may also be involved in this process.[17]

It was also found that the process by which stressors exert their effects on an organism is not linear; instead, it arises through interactions[6]. The actual effect of chronic stress on different individuals depends on the stress they perceived. The stress perceived by an individual reflects his/her subjective evaluation of the stressor and will

partly depend on individual attributes. Studies have shown that different individuals faced with identical stressors may perceive considerably different levels of stress, with different effects on CHD occurrence and development, resulting in differences in the severity or prognosis of CHD.[18-19] Therefore, the accurate identification of individuals who are more likely to perceive stress is of great significance for the precise assessment and subsequent treatment of CHD.

Assessments of psychological stress are generally performed using standard psychological instruments. Commonly used questionnaires include the Perceived Stress Scale (PSS), Stress Appraisal Measure (SAM), and Impact of Event Scale (IES). The PSS is the most widely used scale to assess chronic stress because it is easy to implement and does not require professional intervention during administration. Developed by Cohen et al. in 1983[20], the PSS measures the dimensions of uncontrollability and stressfulness, and assesses the stress levels of individuals based on their subjective perceptions of stressors. It has been translated into many languages and used widely in diverse populations around the world[21-27]. Blumenthal et al.[28] have used PSS as a tool to assess the chronic stress of CHD patients. The version most used in Chinese populations is the Chinese Perceived Stress Scale (CPSS), which is a simplified-Chinese version translated by Yang (2007)[29]. The CPSS has demonstrated good validity and reliability in a series of studies in different Chinese populations[30-32], especially in cardiac patients[33].

Few studies published to date have utilized the CPSS for the accurate identification of high perceived stress individuals among patients with CHD, and perceived stress detection in the Chinese mainland population with CHD has not yet been reported. We, therefore, analyzed the CPSS scores of patients who visited the cardiac rehabilitation clinic at our hospital with the aim of investigating the self-perceived stress levels of Chinese patients with CHD and determining the individual attributes closely associated with perceived stress. The results of this study might help to stratify CHD patients according to stress perception level and supply the individualized stress management programs for Chinese populations with CHD.

METHODS

Study participants

A cross-sectional study design was adopted. Using the electronic medical records system of our hospital, we screened patients referred to the cardiac rehabilitation clinic between 2015 and 2020. All patients in the inpatient department of cardiology were recommended to the rehabilitation clinic regardless of whether they choose to receive the following rehabilitation treatment or not. Only those with a definitive diagnosis of CHD were included in the analysis. Based on the criteria of the CHD 2019 ESC Guidelines for the Diagnosis and Management of Chronic Coronary Syndromes, the inclusions were: one or more lesions with ⩾50% stenosis as shown by coronary angiography; stable angina (SA); unstable angina (USA); old myocardial infarction (OMI); acute myocardial infarction (AMI); post-percutaneous coronary intervention (PCI); post-coronary artery bypass graft (CABG); or ischemic cardiomyopathy (IC). Those who are unwilling to take the scale will be excluded.

Demographic characteristics and medical history

The demographic characteristics and medical history of the participants were obtained from the cardiac rehabilitation medical records system and collated by a cardiologist. The demographic characteristics analyzed included age, sex, region (south /north, divided along the Qinling Mountains-Huaihe River line), educational level, marital status, family structure (with/without children), nature of work (mental/manual labor), the presence/absence of sleep disorders, and the following lifestyle factors: regular exercise, risky alcohol consumption, and smoking. The medical history data analyzed included a history of cardiac revascularization and the presence/absence of other chronic diseases requiring long-term medication. Mental labor was defined as professional, managerial, or administrative work generally performed in an office or other administrative environment. Manual labor was defined as strenuous physical work or other types of work demanding physical exertion. Regular exercise was defined as ⩾30 min of low-intensity exercise >5 times per week or ⩾20 min of moderate-intensity exercise >3 times per week. Sleep disorders were defined as the occurrence of

at least one of the following ⩾3 times per week for at least 1 month: inability to sleep after 30 min in bed, waking up ⩾2 times during the night, wake time >15%, dreamful sleep or total sleep time <6 hours, and waking up ≥2 hours ahead of schedule and subsequently unable to get back to sleep. Risky alcohol consumption was defined as the consumption of ⩾5 alcoholic drinks on a single occasion >12 times in the past year.[34]

Stress assessment

The perceived stress of the study participants was assessed using the CPSS, which comprises 14 items intended to measure the dimensions of uncontrollability and stressfulness. Each item is rated on a 5-point scale (0 = never, 1 = rarely, 2 = sometimes, 3 = fairly often, 4 = very often), with items 4, 5, 6, 7, 9, 10, and 13 scored in the reverse direction. Total scores range from 0 to 56 points, with higher scores indicating higher psychological stress.

In addition to the CPSS, all the participates were asked to complete the Patient Health Questionnaire (PHQ-9) scale and the Generalized Anxiety Disorder (GAD-7) scale to assess preexisting mental health comorbidities. The PHQ-9 is a self-rating scale consisting of 9 items. A PHQ9 score greater than 5 indicates that the patient may be in a mild or more depressive state. The GAD-7 is a 7-item self-rating scale indicating a mild or more anxiety state when the score is greater than 5.

All the participants were asked to provide responses based on their own perceptions. All patients who visited the cardiac rehabilitation clinic for the first time were requested to complete the scales on their own after receiving instructions on questionnaire completion from a nurse. The responses were collected and collated by a cardiologist.

Statistical analysis

Statistical analysis was performed using SPSS 25.0. Quantitative variables were tested for normality. Normally distributed variables were expressed as mean ± standard deviation (x ± s); variables not normally distributed were expressed as median and interquartile range (IQR). Qualitative data were expressed as ratios or percentages. Factors associated with the CPSS scores of the study participants were analyzed from binary logistic regression.

Patient and public involvement

Public and patient involvement was not applicable in this research.

RESULTS

Demographic data of patients with CHD

Of the 3845 patients referred to the cardiac rehabilitation clinic during the study period, 1630 patients were excluded, of which 1428 did not meet the inclusion criteria, and 202 refused to be evaluated by CPSS. Eventually, 2215 CHD patients were included in the study (**Figure 1**). The mean age of the study participants was 59.57 ± 10.10 y, and the majority of the participants were male (79.64%), had a university degree or below (94.13%), married (99.05%), had children (97.97%), engaged in mental labor (69.07%), had sleep disorders (74.81%), and did not have a drinking habit (60.18%) Of the participants, 77.1% had previously undergone stent insertion, 56.2% had concomitant hypertension, 47.4% had concomitant hyperlipidemia, and 27% had concomitant diabetes mellitus (see **Table 1**).

Table 1 Social Demography Factors of the subjects

Social demography factor		n	%
age	＜45	160	7.2
	45-64	1317	59.5
	65-84	727	32.8
	⩾85	11	0.4
Gender	Male	1764	79.6
	Female	451	20.4
Region	North	1388	62.7
	South	827	37.3
Education level	Senior high school and below	1107	50.0
	College	978	44.2
	Above college	130	5.9
Having children	Yes	2170	98.0
	No	45	2.0

Marital status	Married	2194	99.0
	Other (single, divorced, or widowed)	21	1.0
Occupation	Mental	1530	69.1
	Physical	685	30.9
Regular exercise	Yes	1630	73.6
	No	585	26.4
Risky alcohol drinking	Yes	298	13.5
	No	1917	86.5
Current Smoker	Yes	334	15.1
	No	1881	84.9
Comorbidity			
Number of stent	0	508	22.9
	1	901	40.7
	2	462	20.9
	⩾3	344	15.5
Hypertension	Yes	1245	56.2
	No	970	43.8
Hyperlipemia	Yes	1049	47.4
	No	1166	52.6
Diabetes	Yes	598	27.0
	No	1617	73.0
Cerebrovascular disease	Yes	39	1.8
	No	2176	98.2
Other diseases	Yes	119	7.1
	No	2096	92.9
Sleep disorder	Yes	1657	74.8
	No	558	25.2
Depressive state	Yes	817	36.9
	No	1398	63.1

Anxiety state	Yes	1113	50.2
	No	1102	49.8

Comparison of characteristics between groups

The mean CPSS score of all the patients with CHD was 27.16 ± 6.35. Using the median score of 27 as the cut-off point, the study participants were divided into a low perceived stress group (CPSS score ⩽27) and a high perceived stress group (CPSS score >27). Yang et al.[29] conducted a CPSS assessment of the Chinese general population (n=3666), with an average score of 24. 22 ±5. 811. A summary independent-sample t-test proves that the CPSS scores of the two groups are statistically different (P = 0.000).Participants who had children, engaged in mental labor, or had a habit of risky alcohol consumption had a higher probability of experiencing higher stress perception levels. (see **Table 2**).

Table 2 Comparison of two groups with different CPSS scores

Characteristics	Categories	High-stress group (n=1190)		Low stress group (n=1025)		X^2	*P* value
		n	%	n	%		
age	＜45	89	7.5	71	6.9	0.358	0.949
	45-64	709	59.6	608	59.3		
	65-84	386	32.4	341	33.3		
	⩾85	6	0.5	5	0.5		
Gender	Male	966	81.2	798	77.9	3.750	0.053
	Female	224	18.8	227	22.1		
Education level	Senior high school and below	526	44.2	581	56.7	36.611	0.000
	College	578	48.6	400	39.0		
	Above college	86	7.2	44	4.3		

Having children	Yes	1173	98.6	997	97.3	4.698	0.030
	No	17	1.4	28	2.7		
Marital status	Married	1182	99.3	1012	98.7	2.083	0.149
	Other (single, divorced, or widowed)	8	0.7	13	1.3		
Occupation	Mental	881	74.0	649	63.3	29.605	0.000
	Physical	309	26.0	376	36.7		
Regular exercise	Yes	901	75.7	729	71.1	5.975	0.015
	No	289	24.3	296	28.9		
Risky alcohol drinking	Yes	188	15.8	110	10.7	12.141	0.000
	No	1002	84.2	915	89.3		
Current Smoker	Yes	182	15.3	152	14.8	0.093	0.760
	No	1008	84.7	873	85.2		
Number of stent	0	280	23.5	228	22.2	0.820	0.845
	1	486	40.8	415	40.5		
	2	243	20.4	219	21.4		
	⩾3	181	15.2	163	15.9		
Chronic disease	Yes	965	81.1	831	81.1	0.000	0.991
	No	225	18.9	194	18.9		
Sleep disorder	Yes	889	74.7	768	74.9	0.014	0.905
	No	301	25.3	257	25.1		
Depressive state	Yes	626	52.6	487	47.5	5.713	0.017
	No	564	47.4	538	52.5		
Anxiety state	Yes	470	39.5	347	33.9	7.530	0.006
	No	720	60.5	678	66.1		

Logistic regression

Binary logistic regression analysis was performed in model 1 by setting the CPSS

score as the dependent variable and the following as the independent variables: age, sex, educational level, marital status, family structure (with/without children), nature of work (mental/manual labor), number of stents, and the presence/absence of sleep disorders, other chronic diseases, and the following habits: regular exercise, risky alcohol consumption, and smoking. Our results indicated that study participants who have children had a higher probability of high perceived stress, with the odds ratio (OR) being 2.226 (confidence interval [CI]: 1.098-4.515). Compared with participants who received middle school education or below, those with a university degree had a higher probability of high perceived stress (OR: 1.453, CI: 1.206-1.750); this was more evident in participants with a master or doctoral degree (OR: 1.928, CI: 1.290-2.882). Participants who engaged in mental labor had a higher probability of high perceived stress than those who engaged in manual labor (OR: 1.389, CI: 1.144-1.686). Compared with participants who did not have a habit of risky alcohol consumption, those who had this habit had a higher probability of high perceived stress (OR:1.492, CI: 1.146-1.944). Model 2 was adjusted by GAD-7 and PHQ-9 scores, which has no major influence on the conclusion (see **Table 3**).

Table 3 Logistics regression of CPSS score

	Model 1*		Model 2**	
	OR(95%CI)	*P* value	OR(95%CI)	*P* value
Kid				
Yes	1.000		1.000	
No	2.226(1.098-4.515)	0.027	2.338(1.258-4.345)	0.007
Education level				
Senior high school and below	1.000		1.000	
College	1.453(1.206-1.750)	0.000	1.478(1.231-1.776)	0.000
Above college	1.928(1.290-2.882)	0.001	1.936(1.306-2.870)	0.001
Occupation				
Manual	1.000		1.000	

Mental	1.389(1.144-1.686)	0.001	1.394(1.149-1.690)	0.001
Risky alcohol drinking				
No	1.000	0.003	1.000	0.001
Yes	1.492 (1.146-1.944)		1.516(1.175-1.958)	

*Adjusted by age, sex, educational level, marital status, family structure (with/without children), nature of work (mental/manual labor), number of stents, and the presence/absence of sleep disorders, other chronic diseases, and the following habits: regular exercise, risky alcohol consumption, and smoking.

*Adjusted by age, sex, educational level, marital status, family structure (with/without children), nature of work (mental/manual labor), number of stents, and the presence/absence of sleep disorders, other chronic diseases, the following habits: regular exercise, risky alcohol consumption, and smoking, PHQ9 scores and GAD7 scores.OR: Odds Ratio

DISCUSSION

The relationship between psychological stress and cardiovascular disease has attracted increasing attention in recent years. Considering that perceived stress may play some role in the occurrence and development of CHD, a greater emphasis has been placed on stress management in comprehensive cardiac rehabilitation programs because it may potentially provide benefits, such as improving the long-term prognosis of patients with CHD.[28] In this study, we investigated the stress perception level in the Chinese CHD population and explored the possible influencing factors associated with them. Our study suggested that patients with CHD in China had a relatively higher perceived stress level. In addition, we found that patients who had higher educational attainment, engaged in mental labor, had children, and had a habit of risky alcohol consumption were much easier to perceive the stress.

Analysis of the demographic characteristics of high-stress individuals among patients with CHD can support the clinical stratified management of patients according

to the perceived stress level, which increases the efficiency of rehabilitation treatment and maximizes the clinical benefits to each individual. Previous studies have shown that demographic characteristics such as age, sex, educational level, marital status, family structure (with/without children), nature of work (mental/manual labor), the presence/absence of mental health comorbidities, sleep disorders, other chronic diseases, and the following habits: regular exercise, risky alcohol consumption, and smoking may have an impact on perceived stress,[20, 24, 26, 33, 35-37] but the conclusion is not completely consistent. We also observed in the clinic that patients implanted with multiple stents tend to be more stressed.

Our results showed a strong correlation between perceived stress and educational level in Chinese patients with CHD. A higher educational level was associated with higher perceived stress However, this result is contrary to the findings of studies conducted in other countries[26, 38]which have indicated that individuals with lower educational attainment generally perceive higher stress. This may be attributed to the long-standing, strong emphasis on educational attainment in Chinese society, which has led to the general view that individuals with higher educational levels should attain greater personal achievements and bear greater social responsibilities and expectations. However, it is not clear whether this unique socio-cultural background has caused the aforementioned difference between Eastern and Western countries in the influence of educational level on perceived stress.

The perceived stress level was also found to be strongly related to the nature of work in the Chinese population. Participants who engaged in mental labor had higher perceived stress than did those who engaged in manual labor. Such a result is not in complete agreement with the findings of previous studies. A survey by Lesage et al.[24] revealed that differences in perceived stress among administrative, technical, and blue-collar workers were statistically insignificant. However, the 501 participants of Lesage's study were selected from individuals who attended occupational health centers in northern France, whereas the participants of our study had a greater diversity of occupations, including teachers, doctors, taxi drivers, and gardeners. The greater

diversity of occupations included in our study provides a better reflection of the actual range of perceived stress across occupations, thereby helping the occupational factor to reach significance. Dėdelė et al.[39] performed a cross-sectional study on perceived stress among 571 full-time workers in Lithuania and found that blue-collar workers who spent relatively more time engaging in physical work had a higher risk of high perceived stress than white-collar workers, which appears to contradict our results. However, the distribution of perceived stress across occupations may depend on the social environment. With China's vast population, Chinese workers are often faced with complicated interpersonal relationships in their workplace. In general, workplace ecology is more complex among individuals engaged in mental labor than among manual workers, which may have partially contributed to the difference in perceived stress we observed between the two occupational categories.

The drinking habit of patients with CHD has also been identified as a potential factor associated with perceived stress. Our results indicated that participants with a habit of risky alcohol consumption had higher perceived stress. . These findings are consistent with those reported by Yoon et al.[36], who showed that the proportion of individuals with adverse drinking habits was higher in the population with high perceived stress than in the population with low perceived stress. Although the study by Yoon et al. did not investigate possible causal relationships between high stress and at-risk drinking, there is no doubt that patients with a habit of risky alcohol consumption can have higher perceived stress. Therefore, for such individuals, emphasis should be placed on appropriate stress interventions in the formulation of rehabilitation programs.

Interestingly, we also found that patients with CHD with children were nearly twice as likely to perceive the stress as those without children, which is consistent with the findings of Lesage et al.[24]

Our results also showed that the perceived stress of patients with CHD was not correlated with age, sex, or marital status. There is no study to investigate the effect of these 3 factors on perceived stress levels, especially in CHD patients. For the general population, there are some inconsistent findings. A study by Andreou et al.[35] indicated that younger individuals, women, and single or divorced individuals may have higher

perceived stress. Cohen et al.[20] reported that perceived stress was higher in women but unrelated to age; similar conclusions were reached in two other studies.[40-41] However, Dėdelė et al.[39] asserted that older individuals had higher perceived stress. A study by Leung et al.[33] indicated higher levels of perceived stress in women, but a contrary result was reported by Ojard et al.[42] In summary, we have to say research on this matter is far from conclusive. And the inconsistency of our study with other precious ones might attribute to the disease type, difference in environmental and social background.

LIMITATIONS

This study has several limitations. First, we conducted the study in CHD patients referred to the cardiac rehabilitation center in our hospital, which might bring selection bias and the stress levels in the general population only had historical control. Also, a multi-center study to further evaluate the CPSS score in CHD patients and the general population all over China is ongoing. Second, when screening influencing factors associated with the CPSS score, the variables we included might not cover all the possible factors. The effect size should be interpreted with caution due to the low variation of marital status and other potential missing covariates. Third, our study didn't clarify whether the CPSS score would associate with the clinical outcome of CHD patients, which might be a candidate topic we should investigate further.

CONCLUSIONS

In conclusion, individuals who had higher educational attainment, engaged in mental labor, had children and had a habit of risky alcohol consumption were much easier to perceive the stress. The results of this study might help to stratify CHD patients according to stress perception level and supply the individualized stress management programs for Chinese populations with CHD.

Contributors

The study was initiated by JM and YX. YG performed the statistical analysis and drafted the manuscript. RH, YZ, and MY were helpful for data collection. JM and YX contributed substantially to its revision. JM and YX took responsibility for the manuscript as a whole.

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Competing interests

None declared.

Patient consent for publication

Not required.

Ethics approval

This study was approved by the ethics committee of the Chinese PLA General Hospital(S2020-382-01)

Data availability statement

Data are available upon reasonable request. Given that the data is in Chinese, complete raw data are not available for sharing. Partial data sets used and/or analyzed during the current study are available from the corresponding author on reasonable request.

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Figure 1 Flow diagram of the participants

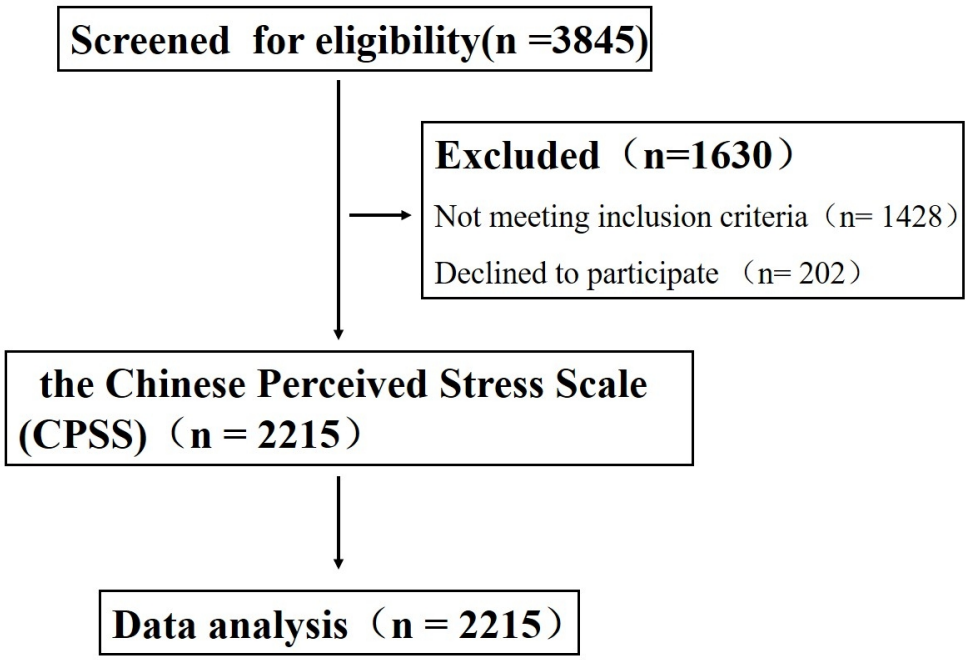

Figure 1 Flow diagram of the participants

203x136mm (150 x 150 DPI)

STROBE 2007 (v4) Statement—Checklist of items that should be included in reports of *cross-sectional studies*

Section/Topic	Item #	Recommendation	Reported on page #
Title and abstract	1	(*a*) Indicate the study's design with a commonly used term in the title or the abstract	1
		(*b*) Provide in the abstract an informative and balanced summary of what was done and what was found	1
Introduction			
Background/rationale	2	Explain the scientific background and rationale for the investigation being reported	3
Objectives	3	State specific objectives, including any prespecified hypotheses	4
Methods			
Study design	4	Present key elements of study design early in the paper	4
Setting	5	Describe the setting, locations, and relevant dates, including periods of recruitment, exposure, follow-up, and data collection	4
Participants	6	(*a*) Give the eligibility criteria, and the sources and methods of selection of participants	4
Variables	7	Clearly define all outcomes, exposures, predictors, potential confounders, and effect modifiers. Give diagnostic criteria, if applicable	4
Data sources/ measurement	8*	For each variable of interest, give sources of data and details of methods of assessment (measurement). Describe comparability of assessment methods if there is more than one group	4
Bias	9	Describe any efforts to address potential sources of bias	
Study size	10	Explain how the study size was arrived at	4
Quantitative variables	11	Explain how quantitative variables were handled in the analyses. If applicable, describe which groupings were chosen and why	5
Statistical methods	12	(*a*) Describe all statistical methods, including those used to control for confounding	5
		(*b*) Describe any methods used to examine subgroups and interactions	5
		(*c*) Explain how missing data were addressed	5
		(*d*) If applicable, describe analytical methods taking account of sampling strategy	5
		(*e*) Describe any sensitivity analyses	5
Results			

Participants	13*	(a) Report numbers of individuals at each stage of study—eg numbers potentially eligible, examined for eligibility, confirmed eligible, included in the study, completing follow-up, and analysed	6
		(b) Give reasons for non-participation at each stage	6
		(c) Consider use of a flow diagram	
Descriptive data	14*	(a) Give characteristics of study participants (eg demographic, clinical, social) and information on exposures and potential confounders	6
		(b) Indicate number of participants with missing data for each variable of interest	
Outcome data	15*	Report numbers of outcome events or summary measures	6
Main results	16	(*a*) Give unadjusted estimates and, if applicable, confounder-adjusted estimates and their precision (eg, 95% confidence interval). Make clear which confounders were adjusted for and why they were included	6
		(*b*) Report category boundaries when continuous variables were categorized	6
		(*c*) If relevant, consider translating estimates of relative risk into absolute risk for a meaningful time period	
Other analyses	17	Report other analyses done—eg analyses of subgroups and interactions, and sensitivity analyses	6
Discussion			
Key results	18	Summarise key results with reference to study objectives	
Limitations	19	Discuss limitations of the study, taking into account sources of potential bias or imprecision. Discuss both direction and magnitude of any potential bias	7-10
Interpretation	20	Give a cautious overall interpretation of results considering objectives, limitations, multiplicity of analyses, results from similar studies, and other relevant evidence	7-10
Generalisability	21	Discuss the generalisability (external validity) of the study results	7-10
Other information			
Funding	22	Give the source of funding and the role of the funders for the present study and, if applicable, for the original study on which the present article is based	10

*Give information separately for cases and controls in case-control studies and, if applicable, for exposed and unexposed groups in cohort and cross-sectional studies.

Note: An Explanation and Elaboration article discusses each checklist item and gives methodological background and published examples of transparent reporting. The STROBE checklist is best used in conjunction with this article (freely available on the Web sites of PLoS Medicine at http://www.plosmedicine.org/, Annals of Internal Medicine at http://www.annals.org/, and Epidemiology at http://www.epidem.com/). Information on the STROBE Initiative is available at www.strobe-statement.org.