Original Article

Mental health is correlated with lipoprotein(a) levels in male patients with premature coronary heart disease

Jinlan Bao[1,2#], Shaoxin Zheng[1,2#], Jingjing Huang[1,2], Xiangkun Xie[1,2], Jinglu Zhang[3], Shiliang Yang[3], Xiaoying Wu[1,2], Yuling Zhang[1,2]

[1]Department of Cardiology, Sun Yat-sen Memorial Hospital, Sun Yat-sen University, Guangzhou, China; [2]Guangzhou Key Laboratory of Molecular Mechanism and Translation in Major Cardiovascular Disease, Sun Yat-Sen Memorial Hospital, Sun Yat-Sen University, Guangzhou, China; [3]Department of General Practice, Sun Yat-sen Memorial Hospital, Sun Yat-sen University, Guangzhou, China

Contributions: (I) Conception and design: J Bao, S Zheng; (II) Administrative support: Y Zhang; (III) Provision of study materials or patients: J Bao, J Huang, X Xie; (IV) Collection and assembly of data: J Bao, J Huang, J Zhang, S Yang; (V) Data analysis and interpretation: J Bao, S Zheng; (VI) Manuscript writing: All authors; (VII) Final approval of manuscript: All authors.

[#]These authors contributed equally to this work.

Correspondence to: Yuling Zhang. Sun Yat-sen Memorial Hospital, Sun Yat-sen University, No. 107, the West of Yanjiang Road, Guangzhou 510120, China. Email: zhyul@mail.sysu.edu.cn.

Background: High levels of lipoprotein(a) (Lp(a)) is an independent risk factor for premature coronary heart disease (PCHD). It is also considered a residual risk for controlled low density lipoprotein cholesterol (LDL-C). Dietary control, exercise, and drugs have limited effects on the levels of Lp(a). Recently, mental health was found to be associated with lipid levels and increased risk of PCHD. However, the relationship between mental health and Lp(a) is still unknown. This study explored the association between mental health and Lp(a) levels in men with PCHD.

Methods: A retrospective, observational study was conducted. A total of 226 male patients with PCHD, aged 49.65±3.68 years, was included in this study. The control group consisted of 230 age-matched healthy male volunteers. Serum Lp(a) levels ≥30 mg/dL, as measured by the immunoturbidimetry method, were considered high. All participants received health related quality of life (HRQoL) scores using the self-assessed 36-Item Short Form Health Survey (SF-36). The HRQoL includes both a physical component summary (PCS) and a mental component summary (MCS).

Results: Patients with PCHD were found to have higher levels of Lp(a) (51.61±33.39 *vs.* 26.42±21.93, P<0.001), and lower MCS (35.83±4.21 *vs.* 39.85±4.12) and PCS scores (38.02±3.73 *vs.* 39.63±3.21) compared to healthy volunteers. The MCS score was negatively correlated with Lp(a) levels in the PCHD group (R=–0.295, P<0.001), but no correlation was detected in the control group. There was no relationship between the PCS score and Lp(a) levels in neither the PCHD group nor the healthy control group. Multivariate logistic regression analysis indicated that the MCS and PCS scores were negatively correlated with the risk of PCHD.

Conclusions: These findings suggested that poor mental health may be associated with high levels of Lp(a) and increased risk of PCHD in men. Therefore, improving the mental state in men with PCHD may be crucial.

Keywords: Mental health; lipoprotein(a) levels (Lp(a) levels); premature coronary heart disease (PCHD)

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Introduction

Lipoprotein(a) (Lp(a)) is an independent risk factor for premature coronary heart disease (PCHD) (1-5). Risk factors for premature and late-onset coronary heart disease (CHD) are different; Smoking, family history of CHD and dyslipidemia were the main risk factors for PCHD, while hypertension and diabetes were the main risk factors for the late onset of CHD (6,7). Previous studies indicated that high levels of Lp(a) have an important influence on the progress of coronary heart disease (CHD) (8). The Prospective Cardiovascular Munster Study (PROCAM) identified Lp(a) as a risk factor for early onset (age <45 years) myocardial infarction (3,4). The Gottingen Risk Incidence and Prevalence Study (GRIP) also indicated that Lp(a) is a major cardiovascular risk factor for men aged 40 to 59 years (4,9). Recent studies have shown that high levels of Lp(a) remain a cardiovascular risk factor even when low density lipoprotein cholesterol (LDL-C) levels are less than 70 mg/dL (10-12). Therefore, these studies all suggest that the residual risk of cardiovascular disease is caused by high Lp(a) levels in patients with controlled LDL-C (10).

Currently, there are few treatments available to effectively decrease Lp(a) levels (10,13). Dietary control, exercise, and drugs have limited effects on Lp(a) levels (4,13). Although Lp(a) levels have been reported to be associated with daily vitamin D supplements and monounsaturated fatty acids, there is no clinical association between lifestyle habits and Lp(a) levels (10,13,14). The improvement of Lp(a) level by exercise was not consistent (15,16). Exercise significantly promote serum Lp(a) concentration (15,16). Another study showed that serum Lp(a) concentration did not change significantly with dietary and physical activity (17). The JUPITER (Justification for the Use of Statins in Prevention: an Intervention Trial Evaluating Rosuvastatin) study reported no significant difference in the regulation of Lp(a) levels with statins compared to placebo (11). A meta-analysis indicated that statins decreased LDL-C by 39% but did not affect Lp(a) levels (18). In a recent study, the Lp(a) levels of 3,896 patients were measured pre- and post-statin treatment. The average Lp(a) level increased by 11% after statin treatment, although some other studies have shown the increase to be as high as 50% (10). Although, PCSK9 (proprotein convertase subtilisin/kexin type 9) inhibitors have been shown to lower LDL, studies have shown that it failed to reduce Lp(a) levels (19).

Interestingly, mental health has been associated with an increased risk of PCHD (5,20), and significantly increased cardiovascular morbidity and mortality (20,21). Psychological factors such as emotional state and stress can affect a patient's health-related behaviors and further lead to poor medication compliance (22). The INTERHEART study, which assessed risk factors for cardiovascular disease, found that psycho-social stress is an increased risk factor for acute myocardial infarction (23). Mental disorders can also affect lipid levels. A study consisting of 92 unmedicated bipolar depression patients and 195 unmedicated uni-polar depression patients found that the bipolar group had significantly lower lipid levels compared to the uni-polar group (24). Previous studies have confirmed that high levels of Lp(a) and poor HRQoL significantly increase the risk of PCHD; However, whether mental disorders affect Lp(a) levels is still unknown.

The health-related quality of life (HRQoL) assessment, as measured by the 36-Item Short Form Health Survey (SF-36) (25-27), is an individual's subjective assessment of their physical and mental health (26). The HRQoL is increasingly used as a method to evaluate the outcome of CHD (28). In patients with well-controlled traditional risk factors, low HRQoL scores significantly correlate with the increased morbidity and mortality of CHD (29). CHD patients had lower HRQoL scores compared to healthy controls. In addition, CHD patients who were well-managed had better HRQoL scores compared to untreated CHD patients (25,30). Indeed, the HRQoL goes beyond direct traditional measures of health risk factors and commonalities in predicting cardiovascular outcomes (26). This study aimed to investigate whether mental health is associated with Lp(a) levels in men with PCHD. We present the following article in accordance with the STROBE reporting checklist (available at https://dx.doi.org/10.21037/apm-21-1024).

Methods

Study population

A total of 456 males who were treated in the Department of Cardiology of the Sun Yat-sen Memorial Hospital from January 2017 to January 2020 were enrolled in this retrospective study. All patients were aged 18–55 years and underwent coronary angiography. There were 226 patients diagnosed with PCHD (the PCHD group), defined as having at least one major coronary vessel stenosis

Table 1 HRQoL scores in patients with PCHD and healthy control subjects

Variable	PCHD group N=226	Healthy control group, N=230	P
MCS	35.83±4.21	39.85±4.12	<0.001
Vitality	9.47±1.38	10.15±1.12	<0.001
Social function	9.85±1.38	10.22±1.19	0.003
Role emotional	7.48±2.37	9.17±2.68	<0.001
Mental health	9.02±1.38	10.32±1.07	<0.001
PCS	38.02±3.73	39.63±3.21	<0.001
Physical function	10.04±0.98	10.31±0.97	0.002
Role physical	8.33±2.38	9.0±1.81	0.001
Body pain	9.83±1.18	10.01±1.12	0.113
General health	9.83±1.27	10.32±1.12	<0.001
HRQoL	73.86±6.12	79.49±6.18	<0.001

HRQoL score includes both PCS and MCS, each composed of four parts. The total HRQoL score ranges from 0 (worst) to 100 (best) and includes 8 items, each of which ranges from 0 (worst) to 100 (best). The weighted standard of all 8 items are converted into a total HRQoL score out of 100, with an average of 50±10. HRQoL, health related quality of life; PCHD, premature coronary heart disease; PCS, physical component summary; MCS, mental component summary.

≥50% (31). The average age in the PCHD group was 49.65±3.68 years. The healthy control group included 230 healthy males without coronary vessel stenosis ≥50%. The two groups were matched by age. Patients were excluded if they presented any of the following: congenital heart disease, cardiomyopathy, myocarditis, infective endocarditis, rheumatic heart disease, serious valvular disease, liver failure, or kidney failure. Patient characteristics including clinical history, biochemical markers, and coronary angiogram results were collected. Patient HRQoL scores were assessed using the SF-36 survey. This research conformed with the Declaration of Helsinki (as revised in 2013) and was approved by the Ethics Committee of the Sun Yat-sen Memorial Hospital, Sun Yat-sen University. Because of the retrospective nature of the research, the requirement for informed consent was waived.

HRQoL and SF-36

HRQoL was assessed using the SF-36 program for self-assessment of health status over a 4-week period (26,32). The HRQoL score includes both the physical component summary (PCS) and the mental component summary (MCS), with each comprising of 4 parts (*Table 1*). The HRQoL assesses 8 items, with each item scoring between 0 (worst) and 100 (best). The weighted standard of the 8 items is then converted into the total HRQoL score ranging from 0 (worst) to 100 (best), with an average of 50±10 (Table S1) (27,33).

Measurement of Lp(a) levels

After fasting for 8 hours, 3–5 mL upper limb venous blood was extracted from the patient. Lp(a) levels were then measured by immunoturbidimetry within 2 hours, as previously described (34). Measurements ≥30 mg/dL are regarded as high levels of Lp(a) (35,36).

Diagnosis of other risk factors

Patients were defined as hypertensive if treatment was required or if at the second examination, mean systolic pressure was ≥140 mmHg and/or mean diastolic pressure was ≥90 mmHg. According to the 2004 Standard of the Chinese Medical Association, hyperlipidemia was defined as total cholesterol (TC) >5.18 mmol/L, LDL >3.37 mmol/L, and/or accepted lipid-lowering drug therapy. Diabetes mellitus (DM) was defined as fasting plasma glucose (FPG) ≥7.0 mmol/L, plasma glucose 2 hours after a meal ≥11.1 mmol/L, and/or accepted hypoglycemic therapy. Body mass index (BMI) was calculated as weight (kg) divided by height square (m^2) and

BMI >28.0 kg/m^2 was considered obese.

Statistical analysis

Continuous normal distribution variables were expressed as mean ± standard deviation and independent sample *T*-tests were used for comparison between two groups. Continuous non-normal distribution variables were expressed as median and interquartile range (IQR) and the Mann-Whitney test was used for comparison between these groups. The categorical variables were represented by numbers and percentages n (%) and the Pearson chi-square test was used for comparison between groups. Spearman linear correlation was used to study the correlation between Lp(a) levels and HRQoL scores in the PCHD and healthy control groups. The multivariable logistic regression model was used to confirm the correlation between Lp(a) level, HROoL score, and PCHD risk, adjusted for diabetes, smoking, TC, LDL-C, apoliproprotein A1 (apoA1), apolipoprotein B (apoB), FBG, and BMI. Results were considered statistically significant when P<0.05. Statistical analyses were performed using the SPSS 23.0 statistical software.

Results

Clinical and biochemical characteristics

Patients in the PCHD group and the healthy control group were age matched. The levels of Lp(a) in patients in the PCHD group were significantly higher compared to that observed in patients in the healthy control group (51.61±33.39 *vs.* 26.42±21.93, P<0.001). In addition, patients in the PCHD group had higher BMI, TC, LDL-C, apoA1, apoB, and FBG compared to healthy controls. There were also more smokers and more diabetic patients in the PCHD group compared to the healthy control group (*Table 2*).

HRQoL scores in the PCHD group and the health control group

HRQoL was assessed using the SF-36 survey, which consisted of the MCS and PCS scores (*Table 1*). Patients in the PCHD group had lower MCS and PCS scores compared to healthy participants, with the exception of body pain.

Linear correlation between Lp(a) levels and HRQoL scores

Spearman linear correlation analysis showed that Lp(a) levels were negatively correlated with MCS scores in PCHD patients (R=–0.305, P<0.001; *Figure 1*). After adjusting for risk factors, multiple linear regression analysis revealed that the MCS score was negatively correlated with Lp(a) levels in the PCHD group (R=–0.295, P<0.001), but there was no association in the healthy controls (*Table 3*).

Relationship between Lp(a) levels, HRQoL, and PCHD risk

Multivariate logistic regression analysis showed that high HRQoL scores significantly reduced the risk of PCHD [odds ratio (OR) =0.873, 95% confidence interval (CI): 0.838 to 0.910, P<0.001]. However, Lp(a) levels (OR =1.033, 95% CI: 1.024 to 1.043, P<0.001), Fasting blood glucose (OR =1.279, 95% CI: 1.030 to 1.588, P=0.026), and smoking (OR =2.178, 95% CI: 1.298 to 3.652, P=0.003) increased the risk of PCHD (*Table 4*). After adjusting for risk factors, MCS (OR =0.811, 95% CI: 0.760 to 0.860, P<0.001) and PCS scores (OR =0.874, 95% CI: 0.820 to 0.932, P<0.001) both significantly decreased the risk of PCHD (*Table 5*).

Discussion

Previous studies reported that high Lp(a) levels was an important independent risk factor for PCHD (1-5). The PROCAM study showed that Lp(a) was a hazard factor for early-onset (under 45 years old) myocardial infarction (MI) (3,4). The GRIP study also confirmed that high Lp(a) levels significantly increased cardiovascular events in men (4). Unfortunately, to date, there are few effective ways to reduce Lp(a) levels. In line with previous reports, this present study found that Lp(a) levels were higher in patients in the PCHD group compared to healthy subjects. Other common risk factors for PCHD in women were TC, LDL-C, autosomal dominant hyperlipidemia, PCHD family history and overweight (37,38). Smoking, dyslipidemia, metabolic syndrome, and PCHD family history are the main risk factors for men (39).

Diet, exercise, and lipid-regulating drugs have limited effects on Lp(a) levels (4). While statins have been shown to decrease LDL-C by 39%, there was little effect on Lp(a) levels (18). PCSK9 inhibitors also failed to reduce Lp(a) levels in the PCSK9 phase II trial (19). A meta-analysis including 2,337 patients reported that ezetimibe (10 mg) significantly reduced plasma Lp(a) compared with placebo (40). However, another meta-analysis of 10 randomized placebo-

Table 2 Clinical characteristics of patients with PCHD and healthy volunteers

Characteristic	PCHD group, N=226	Healthy control group, N=230	P
Age, years	49.65±3.68	49.50±4.24	0.635
BMI (kg/m2)	23.58±1.27	23.31±1.65	0.044
Hypertension, n (%)	78 (34.51%)	65 (28.3%)	0.159
Diabetes, n (%)	54 (23.89%)	35 (15.2%)	0.024
Hyperlipidemia, n (%)	23 (10.18%)	23 (10%)	1
Hyperuricemia, n (%)	24 (10.62%)	20 (8.7%)	0.746
Smoking, n (%)	77 (34.07%)	49 (21.3%)	0.002
Alcohol, n (%)	16 (7.08%)	16 (7.0%)	1
PCHD family history, n (%)	18 (7.96%)	15 (6.5%)	0.591
Cholesterol therapy, n (%)	24 (10.62%)	21 (9.1%)	0.639
TC (mmol/L)	5.61±1.30	4.95±1.19	<0.001
TG (mmol/L)	1.66±0.83	1.59±0.99	0.433
HDL-C (mmol/L)	1.32±0.36	1.26±0.31	0.121
LDL-C (mmol/L)	3.56±0.92	3.08±0.90	<0.001
apoA1 (g/L)	1.35±0.30	1.28±0.25	0.006
apoB (g/L)	1.02±0.26	0.90±0.25	<0.001
apoE (mg/L)	37.49±11.59	37.44±13.72	0.973
Lp(a) (mg/dL)	51.61±33.39	26.42±21.93	<0.001
Creatinine (μmol/L)	82.73±24.04	83.45±26.92	0.762
Uric acid (μmol/L)	370.14±100.11	379.72±114.0	0.341
FPG (mmol/L)	5.95±1.59	5.57±1.34	0.005

Results are considered statistically significant when P<0.05. PCHD, premature coronary heart disease; BMI, body mass index; TC, total cholesterol; TG, triglycerides; LDL-C, low density lipoprotein cholesterol; HDL-C, high density lipoprotein cholesterol; FBG, fasting blood glucose ; apoA1, apolipoprotein A1; apoB, apolipoprotein B; apoE, apolipoprotein E.

controlled clinical trials (15 treatment arms) showed that ezetimibe therapy had no effect on Lp(a) levels (41). In the amipomersen phase III trials, amipomersen decreased Lp(a) levels at 28 weeks, but it had obvious side effects, including injection site reactions, as well as hepatic steatosis and hepatic enzyme elevation (13). While reports have shown that cholesterylester transfer protein (CETP) inhibitors can reduce Lp(a) levels by 25–40%, it is difficult to use in clinical practice (13,42,43). Although other studies have reported that daily supplements of vitamin D and monounsaturated fatty acids can help to decrease Lp(a) levels, there was no association between lifestyle habits and Lp(a) levels (13). Therefore, neither drugs nor lifestyle changes appear to be effective at reducing the levels of Lp(a). Of course, the role of omega-3 polyunsaturated fatty acids in the prevention of coronary heart disease remains controversial (44). Seafood and plant sources of omega-3 fatty acids concentrations of biomarkers related to reduce the incidence of fatal CHD (44); However, a study confirmed that serum fatty acid levels were not associated with coronary heart disease risk in people with low consumption of omega-3 polyunsaturated fatty acids (45).

Previous research have shown that CHD patients have lower HRQoL scores compared to healthy controls, and well-managed CHD patients have better HRQoL scores than untreated CHD patients (25,30). Mental disorders were found to significantly increase the risk of PCHD (5,20). Furthermore, psychological intervention could effectively decrease cardiovascular mortality and morbidity (46,47).

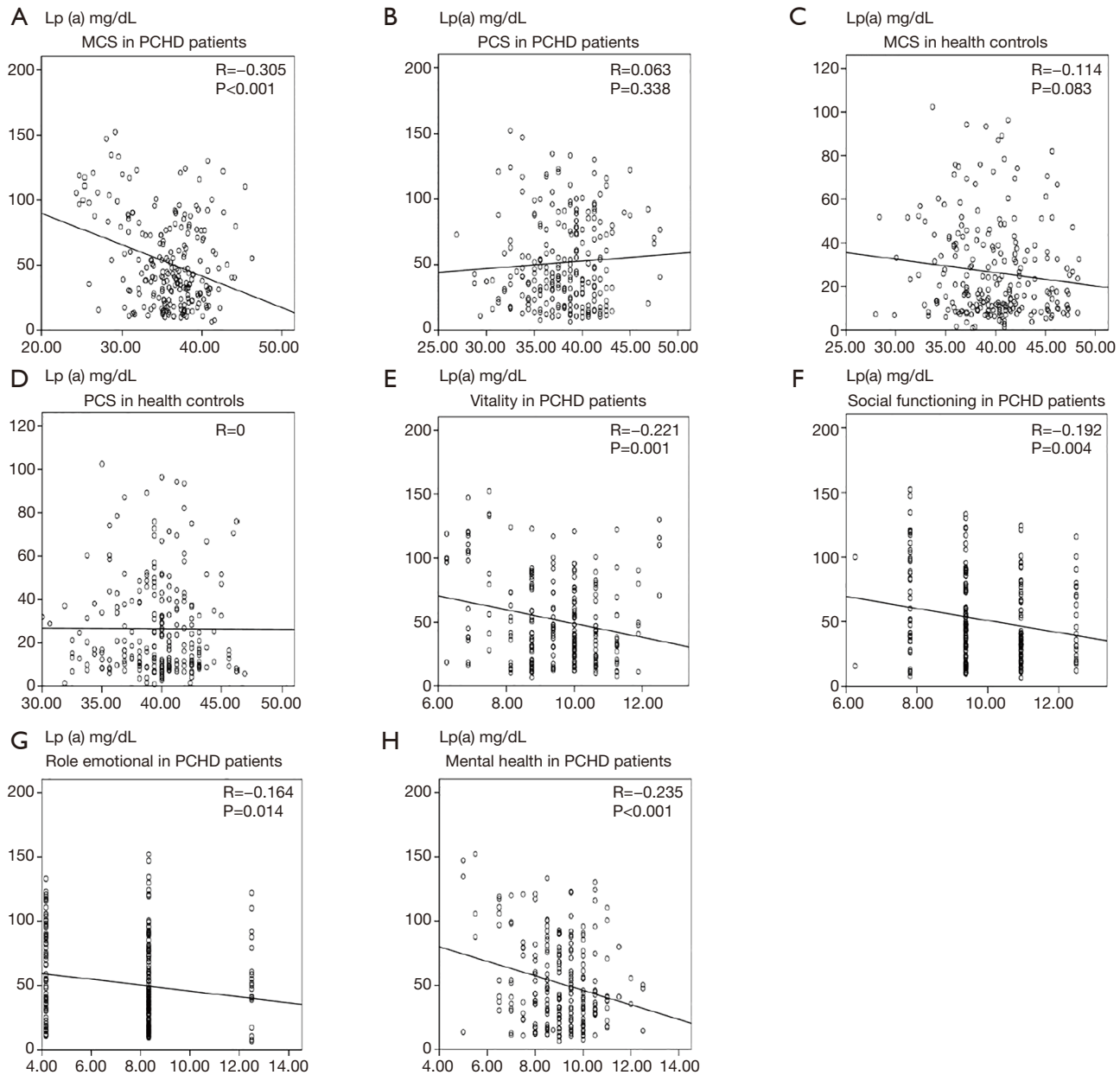

Figure 1 The linear correlation between Lp(a) and HRQoL. (A,B) In PCHD patients, Lp(a) was linearly correlated with MCS, but no correlation was observed with PCS. (C,D) In healthy control volunteers, there was no linear correlation between Lp(a) and MCS nor PCS. (E-H) In PCHD patients, Lp(a) was linearly correlated with vitality, social function, role emotional, and mental health status. Lp(a), lipoprotein(a); HRQoL, health related quality of life; PCHD, premature coronary heart disease; MCS, mental component summary; PCS; physical component summary.

In this present study, PCHD patients had lower MCS and PCS scores compared to healthy controls, which was in agreement with the former studies (5,20,25,30). Although CHD is a candidate risk factor for dementia or cognitive impairment, there is a lack of valid evidence (48). In a meta-analysis of 10 prospective cohort studies, CHD was associated with an increased risk of cognitive impairment or dementia (49).

Table 3 The linear correlation between Lp(a) levels and HRQoL

Variable	Unstandardized coefficients		Standardized coefficients	t	P
	B	Std. error	Beta		
PCHD group, N=226					
Mental component summary (MCS)	−2.342	0.511	−0.295	−4.582	<0.001
Vitality	−5.884	1.614	−0.242	−3.647	<0.001
Social functioning	−4.862	1.616	−0.201	−3.009	0.003
Role emotional	−1.943	0.957	−0.138	−2.031	0.043
Mental health	−5.866	1.595	−0.243	−3.670	<0.001
Physical component summary (PCS)	0.620	0.614	0.069	1.010	0.314
Physical functioning	−1.284	2.294	−0.038	−0.560	0.576
Role physical	1.574	0.945	0.112	1.665	0.097
Body pain	−0.002	1.939	0	−0.001	0.999
General health	0.456	1.787	0.017	0.255	0.799
HRQoL	−0.907	0.368	−0.166	−2.469	0.014
Healthy control group, N=230					
Mental component summary (MCS)	−0.517	0.346	−0.097	−1.495	0.136
Vitality	−1.243	14.29	−0.063	−0.961	0.338
Social functioning	−1.238	1.210	−0.067	−1.023	0.308
Role emotional	−0.536	0.542	−0.066	−0.989	0.324
Mental health	−1.606	1.345	−0.079	−1.194	0.234
Physical component summary (PCS)	−0.090	0.447	−0.013	−0.202	0.840
Physical functioning	0.051	1.460	0.002	0.035	0.972
Role physical	0.262	0.803	0.022	0.326	0.745
Body pain	−0.529	1.271	−0.027	−0.417	0.677
General health	−0.930	1.295	−0.047	−0.718	0.474
HRQoL	−0.253	0.230	−0.071	−1.096	0.274

Beta as linear correlation coefficient. Lp(a), lipoprotein(a); HRQol, health related quality of life; PCHD, premature coronary heart disease; MCS, mental component summary; PCS; physical component summary.

At present, the relationship between BMI and Lp(a) is unclear. Some studies found an association in 20–29 years adults (50) and obese South Indian men (51), while no correlation was detected in women (52). This current meta-analysis showed that BMI was significantly higher in patients with PCHD compared to healthy volunteers. However, after adjusting for risk factors, BMI did not increase the risk of PCHD. This may be due to the small sample size and different ethnicities in our study cohort. Furthermore, PCS was not associated with Lp(a) levels in neither PCHD patients nor healthy controls, suggesting that exercise alone cannot decrease Lp(a) levels. Some studies have shown that Lp(a) is composed of apoA and apoB-100 (10,13). Interestingly, in our study cohort, levels of ApoA1 in patients with PCHD were significantly higher than that observed in healthy subjects.

Poor lipid control is a risk for premature coronary artery disease (53). Our previous study confirmed that low plasma HDL-C level was positively correlated with PCHD (54). Notably, there are many traditional risk factors for PCHD,

Table 4 The relationship between Lp(a) levels, HRQoL, and PCHD risk

Variable	OR, 95% CI	P
TC (mmol/L)	0.847 (0.284–2.563)	0.769
LDL-C (mmol/L)	3.204 (0.592–17.350)	0.177
ApoA1 (g/L)	1.386 (0.362–5.311)	0.634
ApoB (g/L)	0.185 (0.011–2.997)	0.235
FPG (mmol/L)	1.279 (1.030–1.588)	0.026
Diabetes	0.768 (0.348–1.697)	0.515
Smoking	2.178 (1.298–3.652)	0.003
BMI (kg/m2)	1.074 (0.912–1.265)	0.390
Lp(a) (mg/dL)	1.033 (1.024–1.043)	<0.001
HRQoL	0.873 (0.838–0.910)	<0.001

Lp(a), lipoprotein(a); HRQol, health related quality of life; PCHD, premature coronary heart disease; TC, total cholesterol; LDL-C, low density lipoprotein cholesterol; apoA1, apoplipoprotein A1; apoB, apolipoprotein B; FPG, fasting plasma glucose; BMI, body mass index; OR, odds ratio; CI, confidence interval.

Table 5 The relationship between MCS, PCS, and PCHD risk

Variable	OR, 95% CI	P
MCS	0.811 (0.760–0.860)	<0.001
Vitality	0.759 (0.628–0.918)	0.004
Social functioning	0.941 (0.791–1.120)	0.494
Role emotional	0.774 (0.705–0.849)	<0.001
Mental health	0.452 (0.362–0.565)	<0.001
PCS	0.874 (0.820–0.932)	<0.001
Physical functioning	0.745 (0.594–0.935)	0.011
Role physical	0.847 (0.761–0.943)	0.002
Body pain	0.844 (0.697–1.024)	0.085
General health	0.740 (0.615–0.890)	0.001

MCS, mental component summary; PCS; physical component summary; PCHD, premature coronary heart disease; OR, odds ratio; CI, confidence interval.

including smoking, hyperlipidemia, hypertension, and diabetes (1,2,4,5). A German study found that 61% of people with PCHD were current smokers (55). In this current study, approximately 34.07% and 21.3% of PCHD patients and healthy controls were smokers, respectively. While hypertriglyceridemia is an important hazard factor for myocardial infarction in young patients (56), there was no significant difference in triglyceride levels between the PCHD group and the healthy controls in this study. The difference between our study and previous reports may be due to variations in diet across different countries and regions.

Limitations

There were several limitations to this study. Due to the cross-sectional design, it was not possible to make causal inferences regarding relationships between mental disorders and Lp(a) levels. Additionally, other undefined factors may account for both the psychological and metabolic outcomes.

Moreover, the sample size was small in this single center study and further research involving larger cohorts are warranted.

Conclusions

In summary, this study demonstrated a significant positive correlation between poor mental health and higher Lp(a) levels, and PCHD risk in men. The effect of poor mental health status on Lp(a) levels may contribute to the development of PCHD.

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Footnote

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Data Sharing Statement: Available at https://dx.doi.org/10.21037/apm-21-1024

Conflicts of Interest: All authors have completed the ICMJE uniform disclosure form (available at https://dx.doi.org/10.21037/apm-21-1024). The authors have no conflicts of interest to declare.

Ethical Statement: The authors are accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved. This research conformed with the Declaration of Helsinki (as revised in 2013) and was approved by the Ethics Committee of the Sun Yat-sen Memorial Hospital, Sun Yat-sen University. Because of the retrospective nature of the research, the requirement for informed consent was waived.

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Supplementary

Table S1 The 36-Item Short Form Health Survey (SF-36) (1)

HRQoL component	SF-36 questions	SF-36 scores
Physical function (PF)		
	Do you think your current health condition will limit you in the following activities? If so, to what extent? a. Engage in vigorous exercise, for instance running or/and lifting heavy objects; b. Engage in moderate activities, for example moving a table, pushing a vacuum cleaner , playing bowling or golf; c. Move groceries back and forth; d. Take many stairs; e. Take a few stairs; f. Bend your waist or knees; g. Walk more than a mile; h. Walk many blocks; i. Walk one block; j. Be able to bathe or dress yourself.	PF = (The actual score - 10)/20 ×100. a-j: Yes, very limited (1 point). Yes, a little bit limited (2 points) No, it's completely unlimited (3 points)
Physical Role (PR)		
	In the past four weeks, have you experienced any of the following problems at work or in your daily activities due to your physical health? a. Reduced time spent at work or other activities; b. Accomplished less than you anticipated; c. Restricted to certain work or activities ; d. Difficulty carrying out work or other activities (does it require extra effort?).	PR = (The actual score - 4)/4 ×100. a-d: Yes (1 point) No (2 points)
Body pain (BP)		
	a. How much physical pain have you had in the past four weeks? b. How much has the pain affected your normal work (including housework or other work) in the past four weeks?	BP = (The actual score - 2)/10 ×100. a, b: No pain/no effect on work (6 points); Occasionally (5 points); Slightly (4 points); Moderate (3 points); Relatively serious (2 points); Extremely severe (1 point).
General health (GH)		
	a. What is your general state of health? b. I get sick more easily than others. c. I am as healthy as anyone I know. d. I am afraid my health will deteriorate. e. I am in good health.	GH = (The actual score - 5)/20 ×100. a. Wonderful (5 points); Very well (4 points); Well (3 points); General (2 points); Bad (1 point). b and d: Always true (1 point); Mostly true (2 points); Unsure (3 points); Mostly not true (4 points); Not true (5 points). c and e: Always true (5 points); mostly true (4 points); Unsure (3 points); Mostly not true (2 points); Not true (1 points).
Vitality (V)		
	How much time in the last four weeks have you felt the following? a. Energetic; b. Good about your energy; c. Exhausted; d. A little tired;	V = (The actual score - 4)/20 ×100. a and b: Always (6 points); Frequently (5 points); Occasionally (4 points); Sometimes (3 points); Seldom (2 points); Never (1 point). c and d: Always (1 point); Frequently (2 points); Occasionally (3 points); Sometimes (4 points); Seldom (5 points); Never (6 points).
Social function (SF)		
	a. To what extent has your physical health or emotional problems affected your normal social interactions with family members, friends, neighbors, or teammates in the past four weeks? b. How often do physical or emotional problems affect your social activities (for example, visiting relatives and friends)?	SF = (The actual score - 2)/8 ×100 a: Never (5 points); Slightly (4 points); Moderate (3 points); Often (2 points); Always (1 point). b: Always (1 point); Often (2 points); Sometimes (3 points); Seldom (4 points); Never (5 points).
Emotional role (ER)		
	In the past four weeks, have you experienced any of the following problems at work or in your daily life due to emotional problems (such as depression or anxiety)? a. Reduced time spent at work or other activities; b. Accomplished less than anticipated; c. Not working as hard or performing usual activities.	ER = (The actual score - 3)/3 ×100 a-c: Yes (1 point); No (2 points)
Mental health (MH)		
	a. Are you a nervous person? b. Do you feel so depressed that nothing can cheer you up? c. Do you feel calm and at peace? d. Are you feeling depressed and anxious? e. Are you a happy person?	MH = (The actual score - 5)/25 ×100. a-c: Always (1 point); Often (2 points); Frequently (3 points); Sometimes (4 points); Occasionally (5 points); Never (6 points). d-e: Always (6 points); Often (5 points); Frequently (4 points); Sometimes (3 points); Occasionally (2 points); Never (1 point).

HRQoL, health related quality of life.

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