Better Health Related Quality of Life Reduced Elevated Lp(a) Levels in Man

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Research

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Abstract

Background: Elevated Lipoprotein(a) (Lp(a)) is an independent risk factor for premature coronary heart disease (PCHD), but drug therapy rarely changes. Recently, health related quality of life (HRQOL) has been used to measure the prognosis of PCHD, but it is unclear whether HRQOL can improve Lp(a) levels.

Aim: To explore whether HRQOL score in PCHD patients is closely related to increased Lp(a) level.

Methods: The retrospective study included 448 male patients, 218 male patients with PCHD (49.63 ± 3.72 years) and 230 male healthy controls, the two groups were matched in age. According to Lp(a) levels, they were divided into normal Lp(a) group (Lp(a) < 30 mg/dL) and elevated Lp(a) group (Lp(a) ≥ 30 mg/dL). All participants received HRQOL scores. HRQOL scores were assessed using the health Survey of 36 items (SF-36).

Results: Elevated Lp(a) subgroup had more PCHD patients 150(65.5%) than normal Lp(a) subgroup 68(31.1%), $P < 0.001$. In elevated Lp(a) subgroup and normal Lp(a) subgroup, the Lp(a) level of PCHD patients were significantly higher than healthy controls, and HRQOL scores were significantly lower than healthy controls ($P < 0.001$). HRQOL scores significantly reduced the risk of PCHD ($P < 0.001$), while Lp(a) levels significantly increased the risk of PCHD ($P < 0.001$). HRQOL scores in the whole Lp(a) group were negatively correlated with Lp(a) levels ($r = -0.131$, $P = 0.006$), but not with the elevated Lp(a) and normal Lp(a) subgroups.

Conclusion: Better HRQOL may be an important indicator to reduce the risk of high Lp(a) and PCHD in man.

1. Introduction

Lipoprotein(a) (Lp(a)) is an independent risk factor for premature coronary heart disease (PCHD)¹⁻⁵. Strong evidence from epidemiological and genome-wide association studies shown that elevated Lp(a) concentration has an important impact in the coronary heart disease progression⁶. Specially, Lp(a) ≥ 30 mg/dL was recommended to be considered as a risk factor for CHD in the 2016 Canadian cardiovascular meeting^{7,8}. When the Lp(a) concentration lower by 10 mg/dL, the risk of CHD will reduce 5.8% with the significant level⁹. Similarly, when the Lp(a) concentration lower by 101.5 mg/dL or the LDL-C will reduce 38.67 mg/dL, the risk of CHD is also significantly reduced^{5,9}. However, few drugs are currently effective in reducing Lp(a) levels^{4,9}. JUPITER (Justification for the Use of Statins in Prevention: an Intervention Trial Evaluating Rosuvastatin) study reported that statin regulating Lp(a) levels as similar as placebo¹⁰ and highly elevated Lp(a) are residual coronary heart disease risk in LDL-C controlled populations^{10,11}. A meta-analysis reported that statin can reduce the LDL-C levels by 39% without changing Lp(a) level¹². Furthermore, a recent study measured Lp(a) levels in 3,896 patients at pre- and post-statin therapy, founding that the mean Lp(a) levels was increased 11% by atorvastatin, pravastatin, rosuvastatin, pitavastatin, and simvastatin/ezetimibe treatment¹¹. Currently, neither treatment can effectively reduce the Lp(a) level in a PCSK9 Phase II conducted trial¹³.

Health related quality of life (HRQOL) is used progressively as a measure of the outcome of CHD in the previous studies¹⁴, while HRQOL can effectively improve the Lp(a) levels remain poorly understood. Coronary heart disease has worse HRQOL than healthy controls, and well treated patients have better HRQOL than that of untreated patients^{15,16}. EUROASPIRE III survey reported that poor HRQOL can predict morbidity and mortality of CHD patients when standard risk factors remained unchanged¹⁷. HRQOL was considered as an individual's subjective evaluation of his own health and well-being¹⁸, which assesses the risk factors of disease and the effectiveness of intervention and therapy¹⁵. HRQOL has great advantage in measuring special disease¹⁴, including mental components and physical components, which are measured by using the 36-Item Short Form Health Survey (SF-36)^{15,18,19}. Moreover, depression, anxiety, and psychotic disorders are independent risk factors for cardiovascular morbidity and mortality^{20,21}. In addition, mental disorders are found to increase PCHD risk^{5,21}.

This study aims to investigate the relationship between HRQOL and elevated Lp(a) levels in PCHD patients and to explore whether HRQOL is an important measure to significantly reduce Lp(a) levels in PCHD patients

2 Materials And Methods

2.1. Study population and data collection

This is a retrospective single center observation study, we consecutively enrolled 218 male patients at Department of Cardiology of Sun Yat-sen Memorial Hospital between January 2017 and January 2020. All patients were aged between 18–55 years and had been underwent coronary angiography, they were diagnosed with PCHD²², include 49 ST-segment elevation myocardial infarction (STEMI), 45 non-ST-segment elevation myocardial infarction (non-STEMI) and 124 unstable angina patients. There were 230 age matched male health controls. All participants undergo coronary angiography, who had at least one visible stenosis in any major vessel $\geq 50\%$ as PCHD patients, and major vessel without stenosis was considered as health controls. Meanwhile, rheumatic heart disease, valvular disease, cardiomyopathy, congenital heart disease and severe hepatic and renal insufficiency were excluded from this study.

Clinical characteristics, biochemical indicator, coronary angiography and HRQOL measurements by SF-36 were collected. The study complied with the Declaration of Helsinki and approved by the Ethics Committee of Sun Yat-sen Memorial Hospital of Sun Yat-sen University.

2.2 HRQOL and SF-36

HRQOL was measured self-rated health over the past 4 weeks by using the SF36-Item^{18, 23}. SF-36 contained the physical component summary (PCS) and the mental component summary (MCS). PCS contained four domains: physical functioning (10 items), role-physical limitation (4 items), bodily Pain (2 items), general Health (5 items). MCS contained four domains: vitality (4 items), social functioning (2 items), role-emotional limitation (3 items), and mental health (5 items). For each domain, score ranked from 0 (worst health) to 100 (best health). Total score was ranged from 0 to 100, the mental and physical health scores were combined from eight z-scores by using weights, standardized to mean 50 ± 10 ¹⁹ (supplement Table1).

Table 1
Clinical characteristics for Elevated Lp(a) and normal Lp(a) subgroup

	Total Lp(a) group			Normal Lp(a) subgroup			Elevated Lp(a) subgroup		
	PCHD patients N = 218	Health controls N = 230	P	PCHD patients N = 68	Health controls N = 151	P	PCHD patients N = 150	Health controls N = 79	P
Age, years	49.63 ± 3.72	49.48 ± 4.24	0.682	49.64 ± 3.35	49.05 ± 4.78	0.405	49.43 ± 3.83	49.84 ± 3.52	0.434
BMI(KG/m2)	23.59 ± 1.29	23.31 ± 1.65	0.045	23.49 ± 1.18	23.36 ± 1.73	0.574	23.63 ± 1.34	23.21 ± 1.48	0.029
Hypertension, n(%)	74(33.9%)	65(28.3%)	0.220	23(33.8%)	46(30.7%)	0.641	51(34%)	19(23.8%)	0.133
Diabetes, n(%)	51(23.4%)	35(15.2%)	0.031	13(19.1%)	26(17.3%)	0.849	38(25.3%)	9(11.3%)	0.016
Hyperlipidemia, n(%)	21(9.6%)	23(10%)	1	9(13.2%)	15(10%)	0.490	12(8.0%)	8(10%)	0.628
Hyperuricemia, n(%)	21(9.6%)	20(8.7%)	0.746	8(11.8%)	11(7.3%)	0.305	13(8.7%)	9(11.3%)	0.638
Smoking, n(%)	70(32.1%)	49(21.3%)	0.010	27(39.7%)	34(22.7%)	0.014	43(28.7%)	15(18.8%)	0.112
Drinking, n(%)	14(6.4%)	16(7.0%)	0.852	3(4.4%)	11(7.3%)	0.557	11(7.3%)	5(6.3%)	1
PCHD family history, n(%)	17(7.8%)	15(6.5%)	0.714	5(7.4%)	11(7.3%)	1	12(8.0%)	4(5%)	0.587
Cholesterol therapy, n(%)	22(10.1%)	21(9.1%)	0.751	5(7.4%)	14(9.3%)	0.797	17(11.3%)	7(8.8%)	0.654
TC(mmol/L)	5.64 ± 1.30	4.95 ± 1.19	< 0.001	5.55 ± 1.37	4.88 ± 1.20	< 0.001	5.68 ± 1.27	5.08 ± 1.19	0.001
TG(mmol/L)	1.67 ± 0.83	1.59 ± 0.99	0.395	1.66 ± 0.75	1.67 ± 1.12	0.942	1.67 ± 0.86	1.44 ± 0.65	0.043
HDL-C(mmol/L)	1.33 ± 0.36	1.27 ± 0.31	0.069	1.29 ± 0.31	1.24 ± 0.30	0.237	1.34 ± 0.38	1.33 ± 0.33	0.753
LDL-C(mmol/L)	3.58 ± 0.92	3.08 ± 0.90	< 0.001	3.54 ± 0.98	3.06 ± 0.90	< 0.001	3.60 ± 0.90	3.14 ± 0.91	< 0.001
apoA1(g/L)	1.36 ± 0.30	1.28 ± 0.25	0.002	1.33 ± 0.28	1.24 ± 0.23	0.009	1.37 ± 0.31	1.35 ± 0.28	0.682
apoB (g/L)	1.03 ± 0.26	0.90 ± 0.25	< 0.001	1.01 ± 0.28	0.90 ± 0.25	0.004	1.04 ± 0.25	0.91 ± 0.26	0.001
apoE (mg/L)	37.48 ± 11.59	37.44 ± 13.72	0.974	37.08 ± 13.35	37.74 ± 14.88	0.755	37.67 ± 10.74	36.89 ± 11.30	0.609
Lp(a)(mg/dL)	50.31 ± 32.81	26.42 ± 21.93	< 0.001	17.97 ± 5.91	13.08 ± 6.82	< 0.001	64.97 ± 29.29	51.43 ± 18.32	< 0.001
Creatinine(umol/L)	83.11 ± 24.25	83.45 ± 26.92	0.886	84.81 ± 22.09	83.24 ± 27.16	0.678	82.33 ± 25.20	83.85 ± 26.61	0.671
Uric Acid(umol/L)	369.16 ± 100.43	379.72 ± 114	0.300	371.62 ± 106.51	372.65 ± 102.08	0.945	368.04 ± 97.90	392.96 ± 133.21	0.108

BMI: body mass index: total cholesterol(TC), triglycerides(TG), low density lipoprotein cholesterol (LDL-C), high density lipoprotein cholesterol(HDL-C);Fasting blood glucose(FBG); apolipoprotein A1 (ApoA1);apolipoprotein B(ApoB); apolipoprotein E(ApoE); p-value < 0.05 was considered statistically significant.

	Total Lp(a) group			Normal Lp(a) subgroup			Elevated Lp(a) subgroup		
FPG(mmol/L)	6.01 ± 1.59	5.57 ± 1.34	0.001	5.96 ± 1.59	5.65 ± 1.45	0.161	6.03 ± 1.59	5.40 ± 1.09	0.002
BMI: body mass index: total cholesterol(TC), triglycerides(TG), low density lipoprotein cholesterol (LDL-C), high density lipoprotein cholesterol(HDL-C);Fasting blood glucose(FBG); apolipoprotein A1 (ApoA1);apolipoprotein B(ApoB); apolipoprotein E(ApoE); p-value < 0.05 was considered statistically significant.									

2.3 Measurements of LP(a) levels and Coronary angiography

Blood samples were collected fast for 8 hours. Measurements of lipoprotein(a) were used particle enhanced quantitative turbidimetric immunoassay (PETIA) (Tina-quant® Lipoprotein (a) Gen.2, Roche Diagnostics International Ltd.), on a COBAS automated chemistry analyzer. In this study, Lp(a) ≥ 30 mg/dL was considered as elevated^{7,8} and Lp(a) < 30 mg/dL was considered as normal. Lp(a) was divided into two subgroups according to its level: normal Lp(a) subgroup and elevated Lp(a) subgroup.

2.4 Diagnosis of hypertension, hyperlipidemia and other factors

Hypertension was defined as blood pressure ≥ 140/90 mmHg and/or took antihypertensive drug therapy previously. Hyperlipidemia was defined as total cholesterol (TC) ≥ 5.18 mmol/L; low-density lipoprotein cholesterol (LDL-C) > 3.37 mmol/L and/or lipid lowering therapy; Diabetes mellitus (DM) were defined as FPG ≥ 7.0 mmol/L and 2-hour post-meal plasma glucose ≥ 11.1 mmol/L, and/or glucose lowering treatment. Body mass index (BMI) was defined as the body weight(kg) divided by the square of the height(m²) and BMI > 28.0 kg/m² was defined as obesity. Smokers were defined by at least one cigarette per day. Drinking was defined as at least 50 g wine per day.

2.5 Statistical analysis

Continuous variables are presented as mean ± standard deviation or median and interquartile range (IQR), the independent-samples T-test or Mann-Whitney test was used to compare two continuous variable groups. One-way analysis of variance was used for comparison among multiple groups. Categorical variables are presented as numbers and percentages n(%), using Pearson chi-square test. Multiple linear regression model was used to investigate the relationship between Lp(a) and HRQOL score. Multivariate logistic regression model was used to determine association between Lp(a) levels and PCHD, adjusted for diabetes, smoking, TC, LDL-C, ApoA1, ApoB, FBG and BMI. p-value < 0.05 was considered statistically significant. SPSS 23.0 statistical software version was used to all statistical analyses.

3. Results

3.1 Clinical and biochemical characteristics

Elevated Lp(a) subgroup had more PCHD patients than normal Lp(a) subgroup 150(65.5%) VS 68(31.1%), P < 0.001. In normal Lp(a) subgroup, PCHD patients had higher smokers than health controls 27(39.7%) VS 34(22.7%), p = 0.014, but no difference in elevated Lp(a) subgroup. In elevated Lp(a) subgroups and normal Lp(a) subgroups, PCHD patients showed higher Lp(a), TC, LDL-C, ApoB levels than health controls (Table 1).

3.2 HRQOL and SF-36

In elevated Lp(a) and normal Lp(a) subgroup, PCHD patients significantly lower HRQOL, mental health, vitality, role-emotional limitation and role-physical limitation than health controls (Table 2). Health controls were significantly higher HRQOL than STEMI, non-STEMI and unstable angina patients, no difference in three groups (Fig. 1).

Table 2
HRQOL and SF-36

	Total Lp(a) group			Normal Lp(a) subgroup			Elevated Lp(a) subgroup		
	PCHD patients N = 218	Health controls N = 230	P	PCHD patients N = 68	Health controls N = 151	P	PCHD patients N = 150	Health controls N = 79	P
Vitality	9.61 ± 1.27	10.15 ± 1.12	< 0.001	9.59 ± 1.19	10.21 ± 1.11	< 0.001	9.62 ± 1.31	10.04 ± 1.12	0.016
Social functioning	9.95 ± 1.32	10.22 ± 1.19	0.024	9.98 ± 1.32	10.26 ± 1.23	0.121	9.94 ± 1.32	10.14 ± 1.11	0.251
Role-emotional limitation	7.70 ± 2.23	9.17 ± 2.68	< 0.001	7.66 ± 1.98	9.36 ± 2.55	< 0.001	7.72 ± 2.33	8.80 ± 2.89	0.002
Mental health	9.16 ± 1.26	10.32 ± 1.07	< 0.001	9.14 ± 1.17	10.40 ± 1.16	< 0.001	9.17 ± 1.30	10.16 ± 0.86	< 0.001
Physical functioning	10.07 ± 0.96	10.31 ± 0.97	0.009	10.14 ± 0.97	10.35 ± 1.00	0.154	10.04 ± 0.95	10.25 ± 0.90	0.109
Role-physical limitation	8.39 ± 2.37	9.0 ± 1.81	0.002	8.32 ± 2.33	8.96 ± 1.90	0.033	8.42 ± 2.40	9.07 ± 1.62	0.032
Body pain	9.89 ± 1.16	10.01 ± 1.12	0.266	9.80 ± 1.03	10 ± 1.17	0.221	9.93 ± 1.21	10.02 ± 1.04	0.572
General health	9.87 ± 1.27	10.32 ± 1.12	< 0.001	9.77 ± 1.22	10.36 ± 1.15	0.001	9.91 ± 1.29	10.23 ± 1.05	0.053
HRQOL	74.64 ± 5.68	79.49 ± 6.18	< 0.001	74.40 ± 4.61	79.90 ± 6.19	< 0.001	74.74 ± 6.12	78.71 ± 6.13	< 0.001
HRQOL by using the SF-36, For each domain, a score ranking from 0 (worst health) to 100 (best health). Total score ranking from 0 to 100, so mental and physical health scores were combined from eight z-scores by using weights, standardized to have mean of 50 and standard deviation of 10. p-value < 0.05 was considered statistically significant.									

3.3 Relationship between Lp(a) levels and PCHD risk

In elevated Lp(a) and normal Lp(a) subgroup, Lp(a) levels was significantly increase PCHD risk, but HRQOL significantly decrease PCHD risk. Smoking was significantly increase PCHD risk in elevated Lp(a) subgroup, but no correlation with normal Lp(a) subgroup (Table 3).

Table 3
Multiple logistic analysis of relationship between Lp(a) level, HRQOL and PCHD risk

	Total Lp(a) group		Normal Lp(a) subgroup		Elevated Lp(a) subgroup	
	OR,95%CI	p	OR,95%CI	p	OR,95%CI	p
TC (mmol/L)	0.830(0.274,2.508)	0.741	0.550(0.062,4.853)	0.591	1.122(0.222,5.669)	0.889
LDL-C (mmol/L)	3.224(0.598,17.382)	0.173	5.427(0.220,133.731)	0.301	2.263(0.187,27.326)	0.521
ApoA1 (g/L)	1.457(0.377,5.628)	0.585	3.710(0.305,45.162)	0.304	0.677(0.098,4.696)	0.693
ApoB (g/L)	0.195(0.012, 3.163)	0.250	0.137(0.004,5.165)	0.283	0.256(0.002,31.400)	0.579
FPG (mmol/L)	1.297(1.042,1.614)	0.020	1.285(0.937,1.762)	0.120	1.411(0.994,2.004)	0.054
Diabetes	0.745(0.335,1.660)	0.472	0.465(0.124,1.740)	0.256	1.066(0.347,3.276)	0.912
Smoking	2.150(1.280,3.611)	0.004	1.953(0.928,4.113)	0.078	2.214(1.034,4.742)	0.041
BMI (KG/m2)	1.076(0.913,1.267)	0.377	1.095(0.858,1.398)	0.464	1.116(0.879,1.416)	0.367
Lp(a) (mg/dL	1.034(1.024,1.044)	< 0.001	1.114(1.056,1.175)	< 0.001	1.025(1.010,1.041)	0.001
HRQOL	0.875(0.840,0.913)	< 0.001	0.853(0.799,0.912)	< 0.001	0.898(0.849,0.950)	< 0.001
Fully adjusted for: TC, LDL-C, apoA1, apoB, FPG, BMI levels, diabetes and smoking history; OR: Odds Ratio:95%CI:95% Confidence Interval.						

3.4 Relationship between Lp(a) level and HRQOL

HRQOL was negatively correlation with Lp(a) levels in total Lp(a) group ($r=-0.131$, $P = 0.006$), no correlation with elevated Lp(a) levels and normal Lp(a) levels. However, mental health was negatively correlated with Lp(a) levels ($r=-0.153$, $p = 0.023$) and role-physical limitation was positively correlated with Lp(a) levels ($r = 0.171$, $p = 0.011$) in elevated Lp(a) levels (Table 4).

Table 4
Multiple linear regression model for relationship between Lp(a) levels and HRQOL

	Total Lp(a) group			Normal Lp(a) subgroup			Elevated Lp(a) subgroup		
	r	t	p	r	t	p	r	t	p
Vitality	-0.109	-2.283	0.023	-0.054	-0.764	0.446	-0.093	-1.372	0.171
Social functioning	-0.095	-2.028	0.043	0.069	0.990	0.323	-0.121	-1.814	0.071
Role-emotional limitation	-0.119	-2.552	0.011	-0.043	-0.625	0.533	-0.043	-0.638	0.524
Mental health	-0.206	-4.405	< 0.001	-0.077	-1.066	0.288	-0.153	-2.287	0.023
Physical functioning	-0.052	-1.127	0.260	-0.009	-0.134	0.893	0.018	0.262	0.794
Role-physical limitation	0.056	1.179	0.239	-0.118	-1.701	0.090	0.171	2.562	0.011
Body pain	-0.011	-0.245	0.807	-0.085	-1.229	0.221	0.002	0.029	0.977
General health	-0.045	-0.951	0.342	-0.009	-0.129	0.897	-0.013	-0.197	0.844
HRQOL	-0.131	-2.762	0.006	-0.088	-1.246	0.214	-0.031	-0.459	0.647
Fully adjusted for: TC, LDL-C, apoA1, apoB, FPG, BMI levels, diabetes and smoking history.									

4. Discussion

Previous epidemiological studies have reported that elevated Lp(a) levels were the remarkable independent risk factor for premature coronary heart disease (PCHD)^{1–5}. The PROCAM Study reported that Lp(a) as a risk factor for premature myocardial infarction, and the age of premature events was less than 45 years^{3,4}. The GRIP Study reported that elevated Lp(a) levels substantially increases cardiovascular risks in men aged 40–59 years⁴. However, rare available measures were used to reduced Lp(a) levels effectively. In this retrospective study, we indicated that PCHD patients showed higher Lp(a) levels than health controls, and the Lp(a) levels increased PCHD risk remarkably, the results was similar with previously study^{1–5}.

Nevertheless, there was no standardized Lp(a) measurement in terms of heterogeneity of Lp(a) particle sizes^{9,24,25}. Several epidemiological, Mendelian randomization and genome-wide association studies reported that elevated Lp(a) (≥ 50 mg/dl) is an independent and significant risk factor for CHD^{26–28}. However, this recommendation neglects patients with Lp(a) level 25–50 mg/dl². The risk of Calcific aortic valve stenosis (CAVS) was defined as high Lp(a) > 40 to 60 mg/dl². The German and U.K. apheresis guidelines recommended Lp(a) > 60 mg/dl to specially treat who has elevated Lp(a) level and recurrent CVD events, or uncontrollable elevated LDL-C¹¹. A large meta-analysis collected 126,634 participants and 1.3 million person-years of follow-up, showing that Lp(a) > 30 mg/dl increased myocardial infarction risk¹. The 2016 Canadian Cardiovascular Society Guidelines for the Management of Dyslipidemia recommended Lp(a) ≥ 30 mg/dl as a risk factor for CHD^{7,8}. In our study, we defined Lp(a) ≥ 30 mg/dl as elevated Lp(a). Elevated Lp(a) subgroup had more PCHD patients than normal Lp(a) subgroup, which was consistent with the results of previous research.

Diet, exercise and the majority of lipid lowering drugs rarely change Lp(a) levels⁴. Of note, a meta-analysis reported that statin reduced LDL-C levels by 39% without changing Lp(a) levels¹². In a PCSK9 Phase II conducted trial, the Lp(a) did not substantially reduced in any dosing groups¹³. 10 mg Ezetimibe remarkably reduced plasma Lp(a) levels when compared with placebo²⁹. In amipomersen Phase III trials, the mean percent Lp(a) levels decreased at 28 weeks was substantially more than placebo group, but it had more side effects, such as injection site reactions, hepatic steatosis and hepatic enzyme elevation⁹. Research reported that CETP inhibitors reduced the mean Lp(a) levels by 25–40% in a larger Phase II or Phase III clinical trial^{9,30,31}. Other studies showed Lp(a) levels association with daily intake of vitamin D or monounsaturated fatty acids, but no correlation with lifestyle⁹. Smoking cessation was shown to reduce or increase Lp(a) concentrations³². Recent genome-wide association studies showed that LPA SNP rs10455872 was significantly associated with elevated Lp(a) levels¹¹. However, some individuals have alleles that not express elevated Lp(a)^{11,32}. Therefore, several therapies have been shown to reduce Lp(a) levels, but none of them was widely used clinically⁹.

Currently, HRQOL can effectively improve the elevated Lp(a) levels was hardly known. Coronary heart disease has poorer HRQOL than that of healthy controls^{15,16}. It was also found that mental disorders increased PCHD risk^{5,21}. Psychological interventions had effect on mortality and cardiovascular morbidity^{33,34}, while HRQOL can notably decrease Lp(a) levels is still unknown. Our study discovered that mental health can significantly decrease Lp(a) levels and PCHD risk in elevated Lp(a) subgroup, while was not correlated with normal elevated Lp(a) subgroup. Therefore, we suggested that better mental health is a promising protective factor for elevated Lp(a) levels. Previously, the association between BMI and Lp(a) levels is controversial³⁵. BMI was not correlated with Lp(a) levels in the Women's Health Study³⁶, while it was correlated with 20–29 years young adults in the Cherokee Diabetes Study³⁷ and obese South Indian men^{35,38}. Our finding suggested that PCHD patients significantly high BMI than health controls in elevated Lp(a) group. Moreover, Exercise does not significantly reduce Lp(a) levels^{4,9}. Our study indicated that physical functioning and role-physical limitation did not effectively decrease Lp(a). Herein, we suggested that Lp(a) levels was not able to be lower by only doing exercise. In our study, PCHD patients high ApoA1 levels than health controls in total Lp(a) group. Some studies reported that Lp(a) is made up of apoA covalently bound to ApoB-100^{9,11}. IONIS-Apo(a)Rx antisense oligonucleotide selectively reduced the synthesis of apoA in the liver and consequently the plasma concentration of Lp(a) in Phase I study⁹. We suggested that decreased apoA levels were another novel therapy for elevated Lp(a) levels.

Other risk factors, such as smoking, hypertension, diabetes and dyslipidemia were the independent risk factors for PCHD^{1,2,4,5}, our finding was consistent with previous studies. A German's study reported that 61% current smokers, approximately 40% active

smokers in young and mid-aged German adults, increases premature MI significantly. In the DEGS1 survey, 40% of young and 16% mid-aged German population have hypertension, while other studies showed that the proportion of arterial hypertension was 70% in German⁴. Hypertriglyceridemia was the most important risk factor for young myocardial infarction³⁹. However, triglycerides did not increase PCHD risk in our study, the result was consistent with previous research⁴, and uric acid had no difference between PCHD group and health control group, which is consistent with before⁴⁰, we considered different regions and eating habits.

5. Limitations

This data was a selection from China in a single center. First, this study was conducted in a single with limited data, the results of this study was not able to represent general population and other ethnicities. Second, as it was a retrospective study, it would not have follow-up and prospective studies, which had a preselection bias.

6. Conclusion

In this study, we considered that HRQOL maybe decrease the PCHD risk by reducing elevated Lp(a) levels in man. Therefore, we recommend that better HRQOL is a promising protective factor for elevated Lp(a) levels in man. Furthermore, more evidences need to be found through multicenter, large- sample, prospective studies to investigate whether better HRQOL can effectively reduce elevated Lp(a) levels and PCHD risk.

Abbreviations

Lipoprotein(a)	Lp(a)
Coronary heart disease	CHD
Premature coronary heart disease	PCHD
Total Cholesterol	TC
Triglyceride	TG
Low density lipoprotein cholesterol	LDL-C
High density lipoprotein cholesterol	HDL-C
Apolipoprotein A1	ApoA1
Apolipoprotein B	ApoB
Apolipoprotein E	ApoE
Fasting blood glucose	FBG
Health related quality of life	HRQOL
36-Item Short Form Health Survey	SF-36
Body mass index	BMI
Physical functioning	PF
Role-physical	RP
Bodily pain	BP
General health	GH
Vitality	VT
Social functioning	SF
Role-emotional	RE
Mental health	MH

Declarations

Conflicts of interest

The authors declare they have no conflicts of interest relevant to this observational retrospective study.

Conflicts of Interest Statement

The authors declare they have no conflicts of interest relevant to this observational retrospective study.

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Figures

Figure 1

Correlation with health controls, STEMI, Non-STEMI and Unstable angina patients were significantly lower HRQOL, but no different in three groups.* Compared with the health controls.

Supplementary Files

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