NMR Metabolomics Risk Factors for Coronary Heart Disease in Postmenopausal Women Under Moderate Intensity Statins

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Research Article

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Abstract

Background The role of nuclear magnetic resonance (NMR) metabolomics in the prevention of coronary heart disease (CHD) in postmenopausal women is unclear.

Method 300 postmenopausal women, who were under moderate intensity statins, were enrolled in this study, of which, and 242 were assigned into CHD Group and the other 58 in non-CAHD Group. To seek the risk factors of CHD and the relationship among Gensini, PCSK9 and NMR results, Multivariate Logistic regression and Spearman correlation analysis were conducted, in all patients as well as the patients with CHD, diabetes mellitus (DM) and metabolic syndrome (MS).

Results As the result of this study showed, Age was the main risk factor of CHD. Other risk factors including the particle of low-density lipoprotein (LDL)-6, LDL- triglyceride (TG) and LDL-free cholesterol (FC), while, ethanol and glycerol were the protective factors. In the Spearman correlation analyses section, lipoprotein contents of very-low-density lipoprotein (VLDL)-2 ~ VLDL-5, intermediate-density lipoprotein (IDL), LDL-1 and LDL-2 were proved to be positively related to Gensini, while the lipoprotein contents of apolipoprotein A1 (ApoA1), ApoA2 and high-density lipoprotein (HDL)-1 ~ HDL-4 were negatively correlated with Gensini.

Conclusion In postmenopausal women, age was the main risk factor of CHD, besides, the NMR measured particle of LDL-6, LDL-TG and LDL-FC were also proved to be risk factors of CHD, while, ethanol and glycerol were the protective factors. The clinical significance of the NMR and the correlation among PCSK9, Gensini and NMR metabolomics need further studied.

Background

Dyslipidemia, especially high level of low-density lipoprotein cholesterol (LDL-C), is an important risk factor of coronary heart disease (CHD)[1, 2]. Postmenopausal women are a special group of females, featured with increased LDL-C and CHD risk[3, 4]. Patients with diabetes mellitus (DM) and metabolic syndrome (MS) are also more susceptible to CHD due to abnormal lipid metabolism[5, 6].

Proprotein convertase subtilisin/kexin type-9 (PCSK9) will bind to LDL receptor (LDL-R), resulting in the decrease of LDL-C metabolism, after synthesized and secreted from hepatocytes[7, 8]. PCSK9 has become a new target in lipid metabolism intervening in recent years. However, despite PCSK9 monoclonal antibodies, evolocumab and alirocumab, achieved approximate 50%-60% substantial reduction of LDL-C and 15% relative risk reduction of major adverse cardiac events (MACE)[9, 10], statins are still the most widely used first-line lipid-lowering therapy[11, 12].

Nuclear magnetic resonance (NMR) spectroscopy is an advanced measurement, can provide plenty of metabolomics data, including lipid indexes, metabolites and amino acids. In terms of lipids, NMR can not only group different lipoproteins according to the size of lipoprotein particles (very low-density lipoprotein (VLDL)-1 ~ VLDL-5, intermediate density lipoprotein (IDL), LDL-1 ~ LDL-6, high-density lipoprotein (HDL)-1

~ HDL-4), but also quantified the contents of lipoproteins (cholesteryl ester (CE), free cholesterol (FC), triglycerides (TG) and phospholipids (PL)) according to different reactions of the substances in magnetic field. Several studies have reported the correlation between advanced lipid indexes and CHD risk[13–17].

Dr. Sliz et al.[18] measured the effect of statins with numerous NMR results, in a large group of elderly individuals at risk of cardiovascular disease. While Dr. Guardiola et al.[19] reported the correlation between PCSK9 and NMR results in a group of DM and MS patients, who were not under statin therapy. In this study, we combined NMR spectroscopy and laboratory tests to explore the risk factors of CHD in 139 NMR results and try to find the relationship among NMR metabolomics, PCSK9 and coronary atherosclerosis in a group of postmenopausal women, under moderate intensity statins therapies.

Method

Study Populations

This study took patients who met the inclusion and exclusion criteria into experiment. The inclusion criteria including female, over 46 years old, natural menopause over 1 year, under continuous atorvastatin 10mg QD. or rosuvastatin 20mg QD. for at least 6 months, conducted coronary angiography (CAG) between June 2019 and June 2020, all necessary data were available, able to sign informed consent and willing to take blood measurements. The exclusion criteria including previous percutaneous coronary intervention (PCI) or coronary artery bypass graft (CABG), ovariectomy, under estrogen replacement medication or any PCSK9 inhibitors, cirrhosis or decompensated liver function (Child-Pugh Score > 6), abnormal renal function (glomerular filtration rate < 60mL/min/1.73m^2), unstable hemodynamics or left ventricular ejection fraction (LVEF) less than 30%, rheumatoid or systemic diseases such as sepsis, severe progressive diseases such as tumors. This study is approved by the ethics committee and conducted with signed consent of all participants.

Study Design

This was a single-center cross-sectional clinical study. All enrolled patients were grouped according to three criteria. Patients with any coronary stenosis ≥ 50% were divided into CHD Group, with all coronary stenosis < 50% were divided into non-CHD Group, according to CAG results. In the same measure, patients were assigned to DM Group and non-DM Group, MS Group and non-MS Group, according to the diagnoses of DM and MS. The diagnoses of DM and MS were collected from the medical record system according to the standard diagnostic criteria[20, 21]. (Fig. 1) Gensini scores were calculated based on CAG. The clinical characters were collected from medical record system, blood samples were collected for NMR spectroscopy, lipoprotein a (Lp(a)), PCSK9 and C-reactive protein (C-RP) test, once the patients were enrolled in this study. This study is approved by the ethics committee and conducted with signed consent of all participants in accordance with the Helsinki Declaration.

Laboratory Testing and NMR Spectroscopy Lipid Measurement

Fasting venues blood samples were collected the day before CAG, and stored at -70° C after centrifugation. PCSK9 and C-RP were measured with ELISA. Lp(a) were measured in nmol/L by particle-enhanced turbidimetric immunoassay with Tina-quant Lipoprotein (a) Gen.2 (Latex) (LPA2) Roche® on Cobas system. Advanced lipid measurement of NMR spectroscopy (AvanceIII IVDr, ProteinT®, Bruker®) was conducted according to the standard process.

CAG and Gensini Score

The CAGs were performed for patients who had typical or untypical unstable angina pectoris along with myocardial ischemic changes in electrocardiogram. Coronary plaque burden was evaluated by Gensini Score[22], which could qualify the severity of the coronary lesions by 3 main parameters: severity score, region multiplying factor and collateral adjustment factor.

Statistical Analysis

Categorical variables were presented as n (%), and the differences between groups were assessed with chi-square test. The continuous variables were tested with Kolmogorov-Smirnov for the normality of distributions and presented as mean ± standard deviations when normally distributed, medians (25th, 75th percentile) when non-normally distributed. Student's *t*-test was used to assess the differences of continuous variables between groups, among which, the non-normally distributed ones were converted into natural logarithm before assessment. Variables that were considered clinically relevant and that showed a univariate relationship with the diagnose of CHD were entered into multivariate Logistic regression model. Variables for inclusion were carefully chosen after eliminating those with collinearity, given the number of patients with CHD, to ensure parsimony of the final model. Heatmaps based on the Spearman correlation analysis of variables and Gensini or PCSK9 were charted. All statistical analysis was performed with Stata version 15. Data were considered statistically significant when *P* value was less than 0.05.

Result

Clinical Demography Characteristics, Routine and Advanced Lipid Indexes

300 patients were enrolled in this study, among which, 242 patients were diagnosed with CHD and assigned to CHD Group, 123 patients were diagnosed with DM and 75 patients were diagnosed with MS, assigned to DM Group and MS Group (Table 1). As the Supplement Table 1 ~ 3 showed, 9 clinical information and 139 NMR results were listed and compared between CHD Group and non-CHD Group,

DM Group and non-DM Group, MS Group and non-MS Group. Among the variables, age, fasting plasma glucose (FPG), LDL particle/concentration (P/C) discordance, apolipoprotein A2 (ApoA2), apolipoprotein B (ApoB), total particles, LDL-6 particle, HDL-PL, LDL-6-TG, LDL-6-CE, LDL-6-FC, LDL-6-PL, LDL-6-ApoB, HDL-3-PL, HDL-2-apolipoprotein A1 (ApoA1) and HDL-3-ApoA1 were the items with difference in all the three comparisons, among which, ApoA2, HDL-PL, HDL-3-PL, HDL-2-ApoA1 and HDL-3-ApoA1 were significantly lower in CHD, DM and MS groups.

Table 1
Clinical Demography Characteristics, Routine and Advanced Lipids

	non-CHD Group (n = 58)	CHD Group(n = 242)	T / χ^2	*P*
Age, y	58.86 ± 8.03	65.76 ± 8.46	5.628	< 0.001
Smoking, No.	7 (12.07%)	18 (7.44%)	1.708	0.252
Overweight [a], No.	19 (32.76%)	65 (26.86%)	1.327	0.369
Diabetes, No.	19 (32.76%)	104 (42.98%)	2.022	0.155
Hypertension, No.	34 (58.62%)	143 (59.09%)	0.981	0.948
Family history [b], No.	11 (18.97%)	37 (15.29%)	1.297	0.493
TG(mg/dL)*	133.92 (106.85, 200.46)	148.82 (100.94, 209.08)	0.394	0.694
ApoA1(mg/dL)	134.31 ± 15.94	130.41 ± 15.74	1.693	0.092
ApoB(mg/dL)*	77.91 (58.51,89.86)	82.10 (68.75,98.49)	2.839	0.005
TC-p(nmol/L)*	1416.58 (1063.81, 1633.81)	1492.63 (1250.06, 1790.84)	2.839	0.005
TC(mg/dL)	168.16 ± 38.43	177.74 ± 38.68	1.696	0.091
Lp(a)-p(nmol/L)*	42.80 (16.35, 93.88)	36.40 (13.40, 80.00)	0.801	0.424
Lp(a)(mg/dL)*	17.83 (6.81, 39.12)	14.96 (5.42, 33.12)	0.801	0.424
LDL-p(nmol/L)	1042.17 ± 360.58	1168.91 ± 366.35	2.374	0.018
LDL-C(mg/dL)	81.15 ± 32.77	87.30 ± 30.60	1.354	0.177
LDL-size(nm)*	20.44 (20.23, 20.68)	20.37 (20.17, 20.61)	1.634	0.103
LDL-p-corr(nmol/L)	977.50 ± 357.33	1108.44 ± 366.46	2.456	0.015
LDL-C-corr(mg/dL)	73.10 ± 32.30	79.76 ± 30.41	1.481	0.140
HDL-p(nmol/L)*	73.35 (45.78, 121.62)	78.87 (51.55, 114.60)	0.747	0.455
HDL-C(mg/dL)*	45.81 (38.86, 55.28)	45.23 (40.46, 50.51)	0.877	0.381
non-HDL-p(nmol/L)	1300.29 ± 381.68	1463.23 ± 424.55	2.675	0.008
non-HDL-p-corr(nmol/L)	1235.62 ± 377.88	1402.76 ± 426.11	2.740	0.007
non-HDL-C(mg/dL)	120.62 ± 34.74	131.50 ± 37.68	2.004	0.046

	non-CHD Group (n = 58)	CHD Group(n = 242)	T / χ^2	P
non-HDL-C-corr(mg/dL)*	112.53 (84.79, 136.45)	116.96 (96.00, 147.17)	2.148	0.033
a, Overweight was defined as body mass index (BMI) > 28 (BMI = weight (Kg) / height (m)). b, Family history was defined as the age of onset of coronary heart disease less than 55 for men and less than 65 for women, in the immediate family members of patients.				
TG, triglyceride; ApoA1, apolipoprotein A1; ApoB, apolipoprotein B; TC-p, total particles of cholesterol; TC, total cholesterol; Lp(a), lipoprotein a; Lp(a)-p, particles of Lp(a); LDL-C, low-density lipoprotein cholesterol; LDL-p, particles of LDL; LDL-size, average diameter of LDL-p; LDL-p-corr and LDL-C-corr, corrected LDL-p and LDL-C; HDL-C, high-density lipoprotein cholesterol; HDL-p, particles of HDL; non-HDL-C, none high-density lipoprotein cholesterol; non-HDL-p, particles of non-HDL; non-HDL-p-corr and non-HDL-C-corr, corrected non-HDL-p and non-HDL-C.				
Lp(a) = Lp(a)-p*0.4167; LDL-p-corr = LDL-p – Lp(a)-p; LDL-C-corr = LDL-C – 0.3*Lp(a); non-HDL-p = TC-p – HDL-p; non-HDL-p-corr = non-HDL-p – Lp(a)-p; Non-HDL-C = TC – HDL-C; non-HDL-C-corr = non-HDL-C – 0.3*Lp(a)				
TG, ApoB, TC-p, Lp(a)-p, Lp(a), LDL-C-size, HDL-C-p, HDL-C and non-HDL-C-corr were skew distribution and shown as median (25th percentile, 75th percentile). Before the Student's t-test for the difference between groups, the nonnormal distribution variables were converted into natural logarithm form.				

As shown in Supplement Table 1, the particles of LDL, not the concentration, was significantly higher in CHD group. Further comparison showed that the difference was mainly caused by the particles of LDL-1 and LDL-6. In the comparison between DM and non-DM patients, shown in Supplement Table 2, IDL -PL and VLDL-PL were much higher in DM patients, HDL-FC were much lower in DM patients. Most of the NMR measured lipid indexes were different between MS patients and non-MS patients, as shown in Supplement Table 3. Despite the characteristics presented in the comparison between CHD patients and non-CHD patients, DM patients and non-DM patients, the comparison between MS patients and non-MS patients also showed that VLDL-PL, IDL-PL, LDL-PL and HDL-TG were much higher in MS patients, while HDL-CE and HDL-FC were much lower in MS patients. (Supplement Table 3) Compared with undiagnosed population, PCSK9 were lower in CHD patients and MS patients.

Risk Factors of CHD

As Fig. 2 showed the result of multiple Logistic regression, age (hazard ratio (HR) = 2.520, 95% confidence interval (CI): 1.081 ~ 5.086, $P = 0.032$), the particle of LDL-6 (HR = 1.006, 95% CI: 1.001 ~ 1.012, $P = 0.022$), LDL-TG (HR = 1.200, 95% CI: 1.034 ~ 1.393, $P = 0.016$) and LDL-FC (HR = 1.330, 95% CI: 1.142 ~ 1.549, $P < 0.001$) were risk factors of CHD. While, ethanol (HR = 0.862, 95% CI: 0.745 ~ 0.996, $P = 0.044$) and glycerol (HR = 0.114, 95% CI: 0.021 ~ 0.609, $P = 0.011$) were the protective factors of CHD. Even with no statistical significance, PCSK9 had a neutral effect on CHD.

The Relation between Gensini and NMR Results

Heatmaps, Figs. 3 and 4, showed the direction and intensity of the Spearman correlation between Gensini and NMR results as well as PCSK9 and NMR results, in all postmenopausal women and the patients diagnosed with CHD, DM, and MS.

In general, Fig. 3 showed that the positive correlation between Gensini and NMR results deposited in VLDL-2 ~ VLDL-5, IDL, LDL-1 and LDL-2, while the negative correlations concentrated on ApoA1, ApoA2 and HDL-1 ~ HDL-4.

In all postmenopausal women enrolled in this study, the indexes with positive correlation with Gensini including ApoB/A1, particles of VLDL and IDL, lipoprotein contents TG in VLDL-3 ~ VLDL-5, LDL-1 ~ LDL-2, LDL-5 ~ LDL-6, CE in VLDL-2 ~ VLDL4, IDL, FC in VLDL-2 ~ VLDL-4, IDL and LDL-1 and PH in VLDL-3 ~ VLDL-5, while the indexes with negative correlation were ApoA1, ApoA2, ApoA1, CE and PL in HDL-2 ~ HDL-4, FC in HDL-3 and ApoA2 in HDL-4. The NMR results of CHD and DM patients showed a similar but not identical trends with All patients. In the MS patients, the indexes positively related to Gensini were confined only to the TG, CE and PL in VLDL-3 ~ VLDL-5, while the negative correlated indexes were ApoA1, FC and PL in LDL-1, and ApoA1, CE, PL in HDL-1. The PCSK9 was negatively correlated with Gensini in all patients and DM patients.

The Relation between PCSK9 and NMR Results

Figure 4 showed correlations between plasma PCSK9 and NMR results. In all patients and CHD, DM subgroups, PCSK9 showed a similar trend that negatively correlated with total cholesterol (TC), ApoB/A1, the particles of VLDL, IDL and LDL, as well as nearly all the lipid contents in VLDL-3 ~ VLDL-5, IDL and LDL-1. In MS group, there was little correlation between PCSK9 and NMR results.

Discussion

Cardiovascular disease (CVD) is the leading cause of death in women[23]. We conducted this study in a group of postmenopausal women who received moderate intensity statins, which was proved with lower risk of MACE and re-ischemia events in Chinese population[24]. The result of this study indicated that age, the particle of LDL-6, LDL-TG and LDL-FC were risk factors of CHD, while ethanol and glycerol were the protective factors. The correlation analysis of Gensini and NMR results showed positive correlations with VLDL-2 ~ VLDL-5, IDL, LDL-1 and LDL-2, and negative correlations with ApoA1, ApoA2 and HDL-1 ~ HDL-4. PCSK9 was negatively related to TC, ApoB/A1, the particles of VLDL, IDL and LDL, as well as nearly all the lipid contents in VLDL-3 ~ VLDL-5, IDL and LDL-1.

Lipoproteins are the spherical containers of CE, FC, TG and PL. The traditional lipid measurements focused on the pathogenic effect of lipoprotein contents on CHD. But studies proved the amount and structure of lipoproteins were also risk factors of CVD[25, 26]. The TG in VLDL is exchanged for CE from

LDL and HDL by the cholesteryl ester transport protein, produced CE-depleted LDL and HDL. The TG in the core of VLDL, LDL and HDL are then hydrolyzed by hepatic lipases, producing IDL and smaller, denser LDL and HDL. NMR measured lipoprotein subfractions, VLDL-1 ~ VLDL-5, IDL, LDL-1 ~ LDL-6 and HDL-1 ~ HDL-4, arranged in a smaller, denser way with less TG and more PL. Dr. Sliz's study showed that the specific effect of pravastatin 40mg per day on the particle concentration and contents of lipoprotein, measured with NMR[18]. There is a "V" relationship between the lipid-lowering effect and the size of lipoprotein particles in the results of Dr. Sliz's study. In detail, to lipoprotein particles, the most reduced particle was extremely large VLDL (nearly 45% reduced), then the degree of reduction declined with the decrease of particle size to the lowest point of small VLDL (nearly 15%), then rose to medium LDL (over 30%). The downward trends of lipoprotein contents (CE, FC and TG) were similar, but the overall decreases of TG and FC in LDL were much lower (15–30%). In our study, the lipoprotein contents, TG and FC in LDL, remained the risk factor of CHD even under moderated intensity statin therapies. That may be related to the relatively lower reduction of these two items. In the correlation analysis session of this study, we noticed that the positive correlation between Gensini and NMR results focused on the lipoprotein contents of VLDL-2 ~ VLDL-5, IDL and LDL1. Those results also presented a trend associated with the lipoprotein size. And the NMR results, positively correlated with Gensini, were almost all proved with reductions of 15% ~ 30% in Dr. Sliz's study. There is a high correlation between the results of our's and Dr. Sliz's.

Conversely, the result of correlation analysis between PCSK9 and NMR results was the opposite of Dr. Guardiola's study[19]. Dr. Guardiola's study indicated that circulating PCSK9 level was positively correlated with large particles of VDLD, IDL, small and very small particles of LDL, small particles of HDL and VLDL particle size, and the negative correlation deposited on LDL size and HDL size. It has also been reported that serum PCSK9 level could be affected by latitude, gender, HDL-C, TG and physical activity[27–29]. But, In addition to the general heterogeneity of the patients participated in these two studies, the biggest difference was that the patients in our study received statins. It has been reported that statin can abolish the correlation between PCSK9 and the LDL-C[30]. Several studies had proved the PCSK9-elevate effect of statins[31, 32]. Our hypothesis is that statins reduced lipid levels while increasing circulating PCSK9, resulting in a negative correlation between them.

We also proved that ethanol and glycerol were protective factors of CHD in this study. Glycerol was mainly released from the hydrolysis of TG. It was reported that inflammation and homocysteine would inhibit the metabolic of TG[33, 34]. But we didn't find any evidence of the direct protective effect of glycerol on CHD. We tend to think that glycerol is just a marker of the decreased TG hydrolysis. Little studies had been conducted to confirm the clinical effect of ethanol on CHD in nondrinkers. The protective effect of self-synthesized ethanol needs further study.

There are several limitations of this study. First, due to the lack of the patients without statins treatment as the control group, it is difficult to draw a solid conclusion in the correlation analysis between PCSK9 and NMR results. However, if compared with other studies, the heterogeneity of research population and methods will also affect the credibility of the results. Second, The number of people in this study was too

small for further multivariate Logistic regression in each subgroup. Third, limited by the cross-sectional design, reversal causality is possible. Finally, further research is needed to confirm the stability of lipid indexes in frozen samples and repeatability of the advanced lipid measurement.

Conclusion

In this study, we explored the risk factors of CHD in NMR results, in a group of postmenopausal women who received statins. The results indicated that age, the particle of LDL6, LDL-TG and LDL-FC were risk factors of CHD, while ethanol and glycerol were the protective factors. NMR results, lipoprotein contents of VLDL-2 ~ VLDL-5, IDL, LDL-1 and LDL-2 were positively related to Gensini, while the lipoprotein contents of ApoA1, ApoA2 and HDL-1 ~ HDL-4 showed negative correlations with Gensini. Between PCSK9 and NMR results, the negative relation deposited in the particles of VLDL, IDL and LDL, TC, ApoB/A1, as well as nearly all the lipid contents in VLDL-3 ~ VLDL-5, IDL and LDL-1. The clinical significance and value of these findings need to be further studied.

Abbreviations

CHD, coronary heart disease; CVD, cardiovascular disease; DM, diabetes mellitus; MS, metabolic syndrome; MACE, major adverse cardiac events; PCSK9, proprotein convertase subtilisin/kexin type-9; NMR, nuclear magnetic resonance; CAG, coronary angiography; PCI, percutaneous coronary intervention; CABG, coronary artery bypass graft; LVEF, left ventricular ejection fraction; TC, total cholesterol; LDL-C, low-density lipoprotein cholesterol; LDL-R, LDL receptor; IDL, intermediate-density lipoprotein; VLDL, very-low-density lipoprotein; HDL, high-density lipoprotein; CE, cholesteryl ester; FC, free cholesterol; TG, triglycerides; PL, phospholipids; Lp(a), lipoprotein a; C-RP, c-reactive protein; FPG, fasting plasma glucose; ApoA2, apolipoprotein A2; ApoB, apolipoprotein B.

Declarations

Ethics approval and consent to participate: All methods were carried out in accordance with the Helsinki Declaration. This study has been approved by the Ethics Committee of Special Medical Center of Chinese Armed Police Force. All the patients had been informed about the rights and obligations in this study and signed in informed consent before took part in.

Consent for publication: Not applicable.

Availability of data and material: All data generated or analyzed during this study are included in this published article.

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Authors' contributions: Dr. MZ put forward research ideas and was responsible for the organization of research. Dr. YS C, J T, XN and WC provided parts of patients and data sources. CL was responsible for data collection and article writing. Dr. JX C, FP M, JY W, J L, and Dr. Y Y helped to collect patients' information and provided comments on article revision. Miss. SY W helped with the statistical analysis.

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Figures

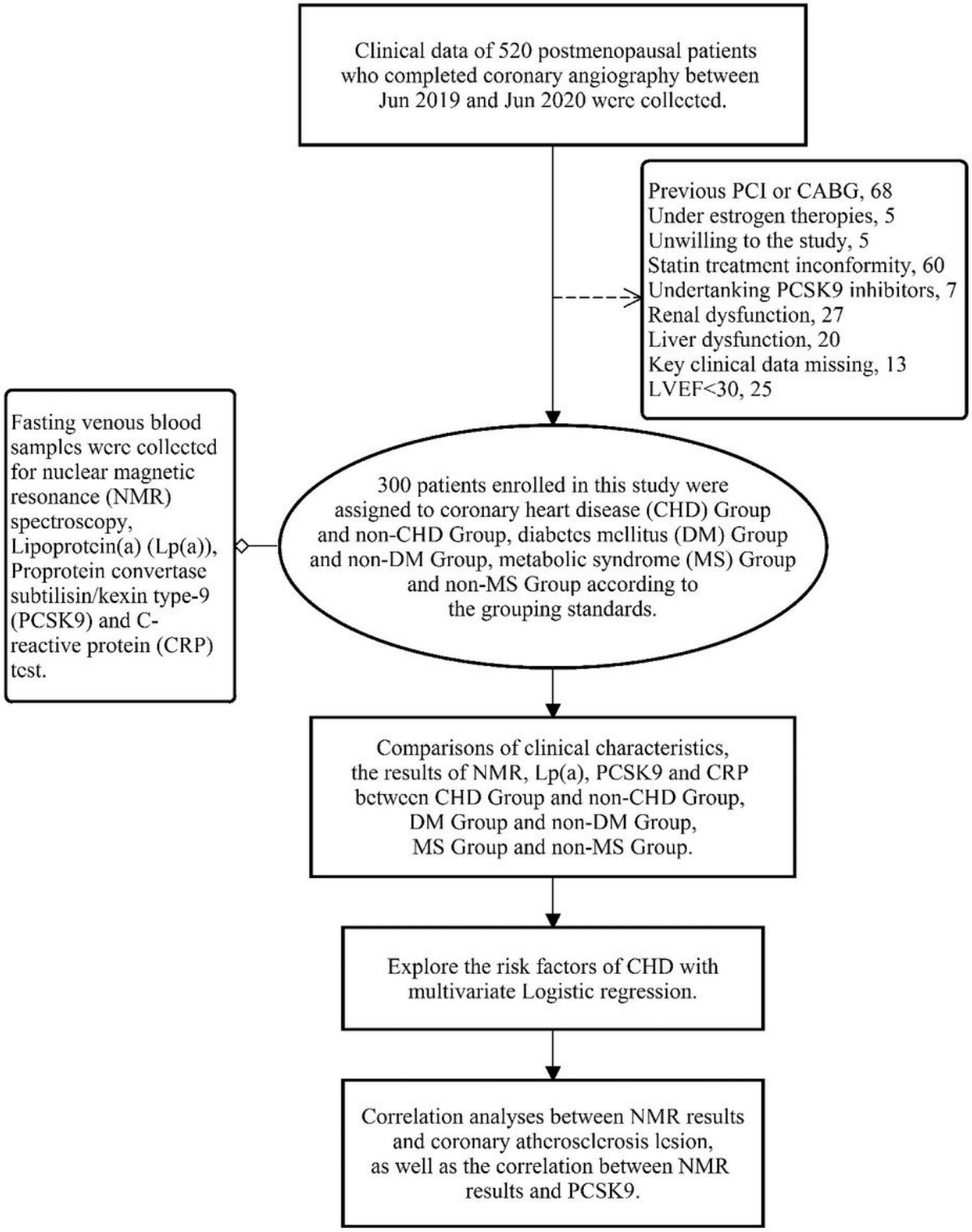
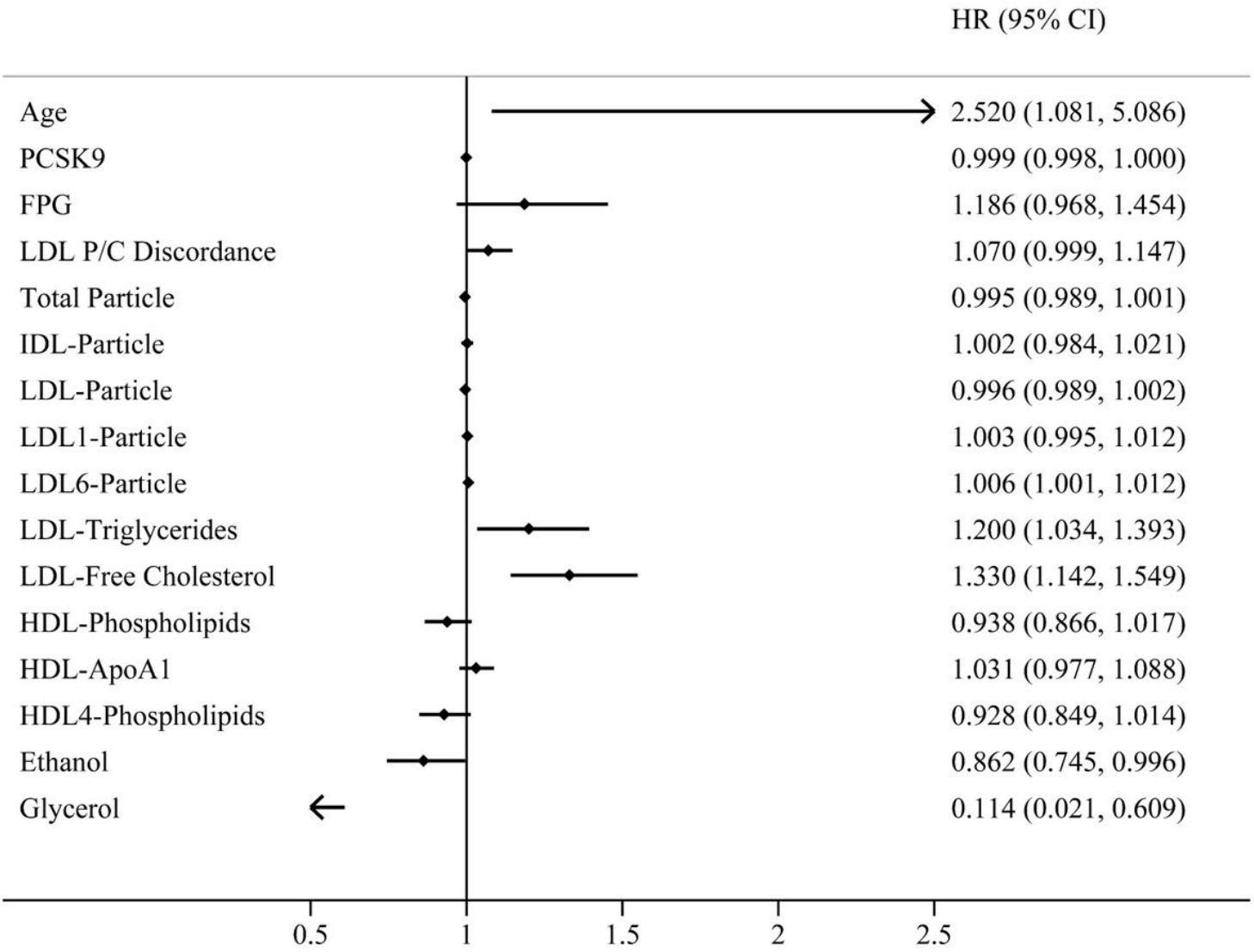


Figure 1

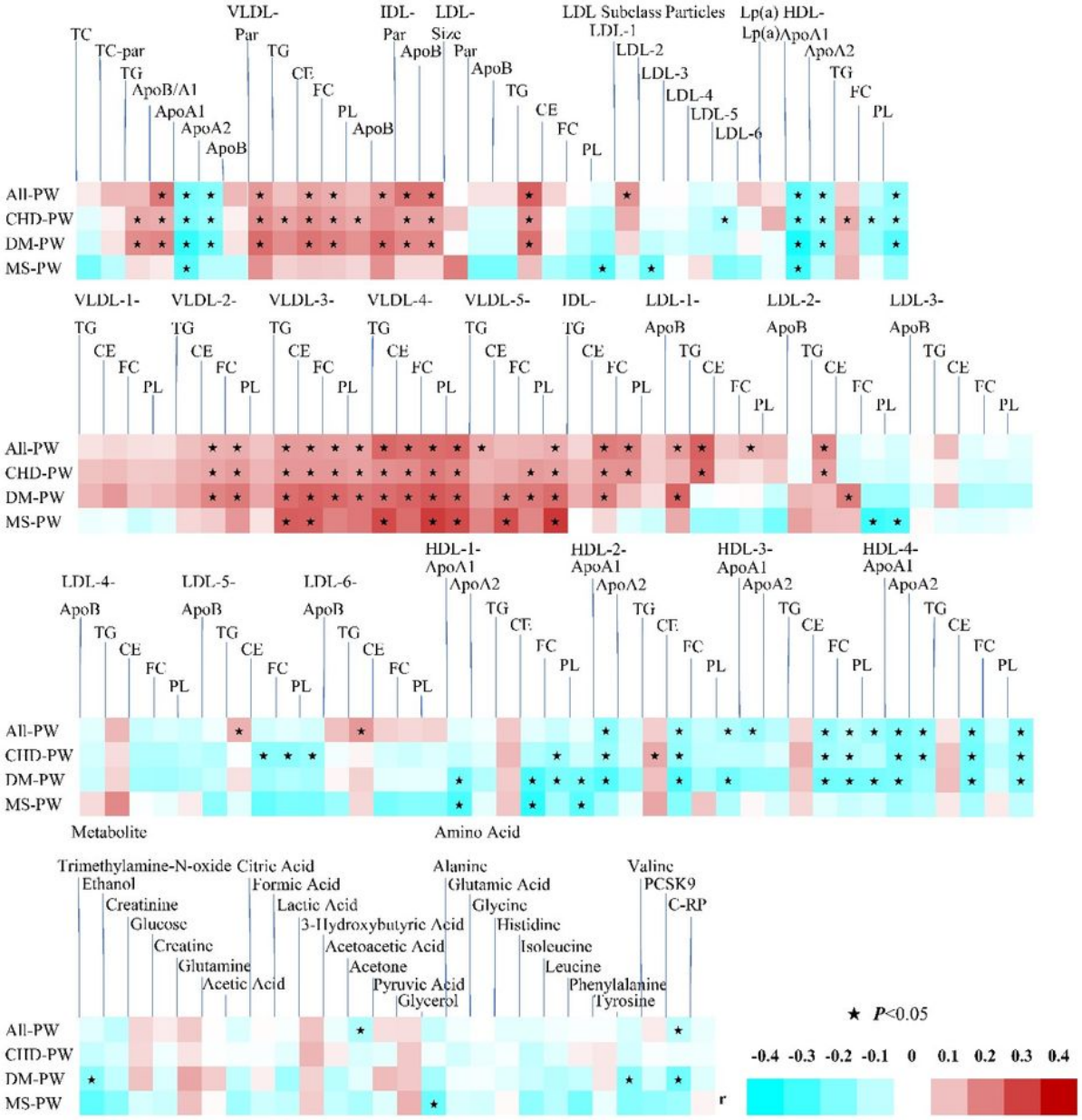
Flow Chart



PCSK9, proprotein convertase subtilisin/kexin type-9; FPG, fasting plasma glucose; IDL, intermediate-density lipoprotein; LDL, low-density lipoprotein; HDL, high-density lipoprotein; ApoA1, apolipoprotein A1; LDL P/C Discordance was calculated with the particle and concentration of LDL.

Figure 2

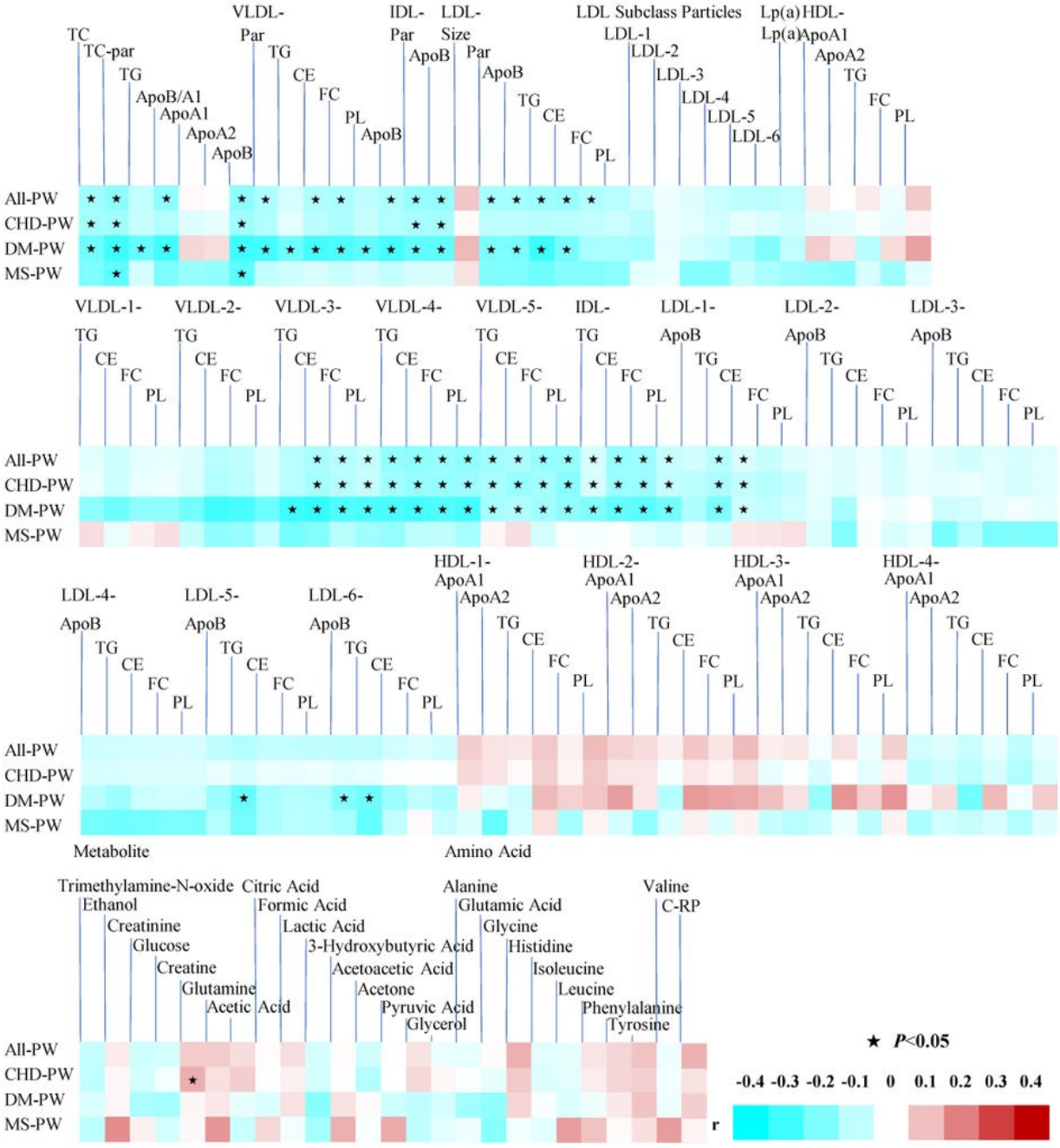
Forest Plot Based on Multivariate Logistic Regression Analysis of Coronary Heart Disease Risk Factors



- This Heatmap was based on Spearman correlation analysis between the results of NMR, PCSK9, C-RP and Gensini score. Correlation efficiency rs were assigned with different colors according to the values. Pentagrams were marked at the items with statistical significance in the analysis.
- PW, postmenopausal women; CHD, coronary heart disease; DM, diabetes mellitus; MS, metabolic syndrome; TC, total cholesterol; TC-par, total cholesterol particles; TG, triglycerides; Apo A1, A2, B, apolipoprotein A1, A2, B; VLDL, very-low-density lipoprotein; IDL, intermediate-density lipoprotein; LDL, low-density lipoprotein; HDL, high-density lipoprotein; Lp(a), lipoprotein a; Size, average diameter of the particles; Par, particles; CE, cholesteryl ester; FC, free cholesterol; PL, phospholipids; PCSK9, proprotein convertase subtilisin/kexin type-9; C-RP, c-reactive protein
- Lipoproteins are the spherical containers of CE, FC, TG and PL. NMR measured lipoprotein and subfractions, VLDL-1~VLDL-5, IDL, LDL-1~LDL-6 and HDL-1~HDL-4, arranged in a smaller, denser way with less TG and more PL.

Figure 3

Heatmap based on Spearmen Correlation Analysis between Gensini and NMR results



- This Heatmap was based on Spearman correlation analysis between the results of NMR and PCSK9. Correlation efficiency rs were assigned with different colors according to the values. Pentagrams were marked at the items with statistical significance in the analysis.
- PW, postmenopausal women; CHD, coronary heart disease; DM, diabetes mellitus; MS, metabolic syndrome; TC, total cholesterol; TC-par, total cholesterol particles; TG, triglycerides; Apo A1, A2, B, apolipoprotein A1, A2, B; VLDL, very-low-density lipoprotein; IDL, intermediate-density lipoprotein; LDL, low-density lipoprotein; HDL, high-density lipoprotein; Lp(a), lipoprotein a; Size, average diameter of the particles; Par, particles; CE, cholesteryl ester; FC, free cholesterol; PL, phospholipids; PCSK9, proprotein convertase subtilisin/kexin type-9
- Lipoproteins are the spherical containers of CE, FC, TG and PL. NMR measured lipoprotein and subfractions, VLDL-1~VLDL-5, IDL, LDL-1~LDL-6 and HDL-1~HDL-4, arranged in a smaller, denser way with less TG and more PL.

Figure 4

Heatmap based on Spearmen Correlation Analysis between PCSK9 and NMR results

Supplementary Files

This is a list of supplementary files associated with this preprint. Click to download.

- STable1.docx
- STable2.docx
- STable3.docx