Dyslipidemia associated with body constitution in Traditional Chinese Medicine

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Objective: This study aimed at investigating the association between dyslipidemia and body constitution of traditional Chinese medicine (BCTCM) may be clinically meaningful for the early diagnosis and treatment of dyslipidemia.

Methods: More than 4,000 participants were invited to a screening visit between 2011 and 2014, and 3,748 participants were available for data analysis. All study subjects underwent complete clinical baseline characteristics evaluation. Differences were determined using one-way analysis and χ^2 analysis. Univariate regression analyses and multiple-variable logistic regressions (MLRs) determined the association between BCTCM variables and outcomes.

Results: In the dyslipidemia group, the Qi-deficient and Yang-deficient types accounted for more participants than others, and these two types were significantly associated with the outcome ($p < 0.05$). MLRs detected significant associations between the Qi-deficient and Yang-deficient types with dyslipidemia ($p < 0.05$ for the two), and their odds ratios (ORs) for dyslipidemia were 1.211 and 1.234, respectively.

Conclusion: Qi-deficient and Yang-deficient types are independently and significantly associated with dyslipidemia. Participants with Qi-deficient and Yang-deficient constitutions have a higher incidence of dyslipidemia.

Keywords: Dyslipidemia; body constitution; traditional Chinese medicine; association analysis.

Introduction

The body constitution of traditional Chinese medicine (BCTCM) is defined as a comprehensive, relatively stable peculiarity of morphological structure, physiological function, and psychological conditions in a person's lifetime based on genetic and environmental factors.¹ In 2009, the criteria for BCTCM published by the China Association of Chinese Medicine delineated BCTCM into nine types, including Neutral, Qi-deficient, Yang-deficient, Yin-deficient, Phlegm-dampness, Damp-heat, Blood-stasis, Qi-depression, and Special.^{2,3} BCTCM can influence not only an individual's

susceptibility to certain diseases and the progress of the disease, but also the efficiency of prevention and treatment efforts. Previous studies have presented evidence regarding the associations between BCTCM and the diseases, especially chronic conditions such as hypertension (HTN), diabetes mellitus (DM), metabolic syndrome (MetS), and anxiety/depression.^{4,5}

Dyslipidemia is a disorder of lipoprotein metabolism; it includes the elevation of the total serum cholesterol (TC), triglycerides (TG), low-density lipoprotein cholesterol (LDL-C), and/or a reduction of high-density lipoprotein cholesterol (HDL-C).⁶ Many researchers have proven it to be

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one of the leading risk factors for many cardiovascular diseases, such as atherosclerosis, coronary heart disease, and stroke.^{6,7} With this in mind, investigating the association between dyslipidemia and BCTCM may be clinically meaningful for its early diagnosis and treatment.

Recently, our group performed a series of studies to investigate the association among common diseases and BCTCM in a large-scale sample.^{8,9} However, there has been little reported on the relationships among BCTCM types and dyslipidemia. We hypothesize that BCTCM may be associated with dyslipidemia. The purpose of this study is to evaluate the extent to which BCTCM is associated with dyslipidemia in a large-scale Chinese sample.

Methods

Study population

As was detailed earlier,^{8,9} a risk factor study for BCTCM and chronic disease was conducted in Chinese population. We recruited participants aged 30–90 years from the communities in Shanghai. We invited more than 4,000 participants for this study between 2011 and 2014. Written consent was obtained from all the patients before the study. Briefly, the exclusion criteria were severe, abnormal renal and liver function and pregnancy. A total of 3,748 participants were available for next data analysis.

Data collection

As was mentioned in our previous studies,^{8,9} all study subjects underwent complete clinical baseline characteristics evaluation, including a physical examination and responses elicited from a nurse-assisted, structured, self-administrated questionnaire to collect information on general information, family history, lifestyle, and self-reported medical history. As mentioned in the previous osteoporosis studies,^{8–11} alcohol and smoking consumptions, education, regular exercise, and dietary habits were categorized. Additionally, the definitions of body-mass index (BMI), HTN, DM, and MetS detailed earlier were used.^{8–11} As mentioned in our early study,¹² the definition of dyslipidemia is based on the elevation of TC (≥ 6.19 mmol/L), LDL (≥ 4.14 mmol/L), TG (≥ 2.27 mmol/L), and/or decreased HDL (< 1.04 mmol/L) levels.

Statistical analysis

In this study, univariate linear regression (ULR) analysis was conducted to evaluate the associations among the constitutions of traditional Chinese medicine (TCM) variables and outcomes. Additionally, multiple-variable logistic regression

(MLR) was employed to control potential confounders and to explore the independent contribution of variables to the outcomes. Results were analyzed using the Statistical Package for Social Sciences for Windows, version 16.0 (SPSS, Chicago, IL, USA). Tests were two-sided, and a p -value less than 0.05 was considered significant. Odds ratios (ORs) with 95% confidence intervals (CIs) were calculated for the relative risk of BCTCM with the outcome of dyslipidemia.

Results

Subjects' clinical characteristics

The clinical baseline characteristics of the 3,748 Chinese subjects are mentioned earlier^{8,9} and listed in Table 1. Briefly, in the total sample, the prevalence percentages of HTN, CI, DM, and overweight were 42.58%, 3.31%, 16.84%, and 35.73%, respectively. The mean levels of TC, TG, HDL, and LDL were 5.40 mmol/L, 1.85 mmol/L, 1.22 mmol/L, and 3.49 mmol/L for the total sample, respectively. The prevalence of dyslipidemia was 37.83% in this sample. We found significant differences for age, gender, height, smoking, and alcohol between the dyslipidemia and free of dyslipidemia groups ($p < 0.05$ for all). Additionally, we observed a significantly higher prevalence of HTN, overweight, and DM between the two groups ($p < 0.05$ for all).

Univariate and multiple-variable analyses for dyslipidemia

ULR analyses were developed to include the constitution of TCM to estimate the association for DM. The variables of Qi-deficient and Yang-deficient were significantly associated with the outcome ($p < 0.05$; see Table 2). There were significantly higher levels of TC, TG, HDL, and LDL in the Qi-deficient group, compared with the Neutral group [$p < 0.05$ for all; see Figs. 1(a), 2(a), 3(a), and 4(a)]. Similar results were found between the Yang-deficient and Neutral groups [$p < 0.05$ for all; see Figs. 1(b), 2(b), 3(b), and 4(b)]. The comparison of the prevalence of dyslipidemia among groups according to the constitutions of TCM revealed that the prevalence values of dyslipidemia were 36.37% and 40.76% in Neutral and Qi-deficient groups [$p = 0.017$; see Fig. 5(a)], respectively. In addition, the prevalence of dyslipidemia was 40.48% in Yang-deficient participants [$p = 0.030$; see Fig. 5(b)]. Univariate analysis demonstrated a positive correlation between the constitution of TCM and DM.

MLR analyses were employed to evaluate the association between the constitution of TCM and the dyslipidemia outcome. After adjusting for relevant potential confounding factors, the MLR detected significant associations in the Qi-deficient and Yang-deficient groups with dyslipidemia

Table 1. Baseline characteristics of the participants.

Variable	Free of dyslipidemia	Dyslipidemia	Total	p-Value
<i>Demographical Information</i>				
N	2,330	1,418	3,748	
Age (years)	70.08 ± 7.71	68.09 ± 7.06	69.33 ± 7.53	< 0.001
Gender	1,139 (48.88%)	900 (63.47%)	2,039 (54.4%)	< 0.001
Height (cm)	161.99 ± 18.11	160.06 ± 8.27	161.26 ± 15.19	< 0.001
Weight (kg)	62.43 ± 11.24	62.25 ± 10.1	62.37 ± 10.82	0.627
SBP (mmHg)	133.92 ± 21.66	135.31 ± 17.15	134.44 ± 19.98	0.744
DBP (mmHg)	67.94 ± 24.05	65.83 ± 24.34	67.12 ± 24.07	0.666
HR (beats per min)	73.98 ± 14.53	74.52 ± 12.3	74.19 ± 13.73	0.238
<i>Lifestyle</i>				
Exercise	1,451 (62.27%)	850 (59.94%)	2,301 (61.39%)	0.155
Dietary	2,005 (86.95%)	1,246 (88.56%)	3,251 (87.56%)	0.108
Smoking	477 (20.47%)	233 (16.43%)	710 (18.94%)	0.002
Alcohol	423 (18.15%)	206 (14.53%)	629 (16.78%)	0.004
<i>Lipid Profile</i>				
TC (mmol/L)	4.79 ± 1.67	6.39 ± 1.73	5.40 ± 1.71	< 0.001
TG (mmol/L)	1.45 ± 1.18	2.51 ± 1.24	1.85 ± 1.22	< 0.001
HDL (mmol/L)	1.31 ± 0.41	1.08 ± 0.48	1.22 ± 0.45	< 0.001
LDL (mmol/L)	3.01 ± 0.95	4.29 ± 1.05	3.49 ± 0.99	< 0.001
<i>Medical History</i>				
HTN	1,023 (43.91%)	573 (40.41%)	1,596 (42.58%)	0.036
DM	574 (24.64%)	57 (4.02%)	631 (16.84%)	< 0.001
CI	84 (3.61%)	40 (2.82%)	124 (3.31%)	0.193
Overweight	806 (34.62%)	532 (37.54%)	1,338 (35.73%)	0.070

Note: SBP: Systolic blood pressure, DBP: diastolic blood pressure, HR: heart rate, DM: diabetes mellitus, CI: cerebral infarction, and TCM: traditional Chinese medicine.

Table 2. Comparison of prevalence of dyslipidemia among groups according to the constitutions of traditional Chinese medicine.

Variable	Free of dyslipidemia	Dyslipidemia	Total	p-Value
Neutral	1,279	731	2,010	—
Qi-deficient	683	470	1,153	0.014
Yang-deficient	536	366	902	0.030
Yin-deficient	194	136	330	0.091
Phlegm-dampness	193	109	302	0.926
Damp-heat	81	43	124	0.704
Blood-stasis	43	31	74	0.333
Qi-stagnation	31	22	53	0.443
Special	46	39	85	0.075

Note: The difference analysis of rate between neutral group and the other group by using χ^2 test, respectively.

($p < 0.05$ for the two; see Table 3), respectively. In Qi-deficient and Yang-deficient participants, the ORs for MetS were 1.211 and 1.234, respectively. No significant associations were found in the other constitutions of TCM (data not shown).

Discussion

With the improvement of living conditions and the transformation of typical Chinese dietary structures, the morbidity of dyslipidemia is increasing; statins, the main intervention, have many side effects.¹³ In recent years, the association

between BCTCM and dyslipidemia has attracted increasing attention among researchers who are looking for another safer intervention. However, most of the concerned studies to date are small-sample studies. To the best of our knowledge, little is known about the association between lipid profile and body constitution of traditional Chinese medicine in large-scale sample. Our study is a large-sample analysis containing 3,748 participants, which makes it more representative and reliable. Of our 3,748 participants, 1,418 participants were found to have dyslipidemia, and 2,330 were free of it.

Our findings showed that Qi-deficient and Yang-deficient types were significantly associated with the outcome. MLR also detected significant and independent associations between dyslipidemia and the Qi-deficient and Yang-deficient types, and their ORs for dyslipidemia were 1.211 and 1.234, respectively. All results reveal that Qi-deficient and Yang-deficient people have a higher susceptibility to dyslipidemia. Lei *et al.* showed that blood rheology and TG were significantly associated with the TCM syndrome of dyslipidemia.¹⁴ However, Gu's study of 394 participants showed that Qi-deficient and Yin-deficient types account for most of the patients with dyslipidemia.¹⁵ These differences may come from the variation in samples' age composition, capacity, and region. Even though differences have been found, almost all studies have revealed that the Qi-deficient type is the most important constitution in dyslipidemia

Figure 1. Difference analysis for the level of serum total cholesterol among groups according to the body constitutions of traditional Chinese medicine. (a) The comparison for mean level of TC between Neutral group and Qi-deficient group (5.37 ± 1.61 mmol/L versus 5.45 ± 1.72 mmol/L, $p = 0.010$). (b) Comparison analysis between Neutral group and Yang-deficient group (5.37 ± 1.61 mmol/L versus 5.44 ± 1.89 mmol/L, $p = 0.015$).

Figure 2. Difference analysis for the level of triglycerides among groups according to the body constitutions of traditional Chinese medicine. (a) The comparison for mean level of TG between Neutral group and Qi-deficient group (1.84 ± 1.18 mmol/L versus 1.89 ± 1.21 mmol/L, $p = 0.011$). (b) Comparison analysis between Neutral group and Yang-deficient group (1.84 ± 1.18 mmol/L versus 1.88 ± 1.27 mmol/L, $p = 0.030$).

Figure 3. Difference analysis for the level of high-density lipoprotein cholesterol among groups according to the body constitutions of traditional Chinese medicine. (a) The comparison for mean level of HDL between Neutral group and Qi-deficient group (1.23 ± 0.41 mmol/L versus 1.22 ± 0.46 mmol/L, $p = 0.152$). (b) Comparison analysis between Neutral group and Yang-deficient group (1.23 ± 0.41 mmol/L versus 1.22 ± 0.53 mmol/L, $p = 0.196$).

Figure 4. Difference analysis for the level of low-density lipoprotein cholesterol among groups according to the body constitutions of traditional Chinese medicine. (a) The comparison for mean level of LDL between Neutral group and Qi-deficient group (3.48 ± 0.95 mmol/L versus 3.53 ± 1.01 mmol/L, $p = 0.001$). (b) Comparison analysis between Neutral group and Yang-deficient group (3.48 ± 0.95 mmol/L versus 3.52 ± 1.08 mmol/L, $p = 0.002$).

Figure 5. The comparison of prevalence of dyslipidemia between Neutral participants and Qi-deficient participants. (a) The prevalence values of dyslipidemia were 36.37% and 40.76% in Neutral participants and Qi-deficient participants ($p = 0.017$), respectively. (b) The comparison of prevalence of dyslipidemia between Neutral participants and Yang-deficient participants. The prevalence values of dyslipidemia were 36.37% and 40.48% in Neutral participants and Yang-deficient participants ($p = 0.030$), respectively.

among the elderly, and that the Yang-deficient, Yin-deficient, and Phlegm-dampness types are also of importance, indicating that the physiological nature of dyslipidemia is asthenia in origin and in superficiality. Asthenic constitutions are the basic constitutions in the elderly with dyslipidemia.

Table 3. Multiple-variable analysis to include the constitutions of traditional Chinese medicine for dyslipidemia.

Variable	Beta	S.E.	p-Value	OR	95.0% CI
Qi-deficient	0.191	0.080	0.017	1.211	1.034–1.417
Yang-deficient	0.210	0.087	0.016	1.234	1.04–1.464

Note: Multiple-variable analysis adjusted for age, gender, BMI, exercise, smoking, alcohol, DM, and HTN.

Dyslipidemia is a metabolic disease involving many factors. Unhealthy lifestyle factors, such as smoking, drinking, and eating too much fatty food, can all disturb the balance of the lipid metabolism, and dyslipidemia will follow.^{16,17} Additionally, there is a significantly higher prevalence of HTN, overweight, and DM in the dyslipidemia group in our study, which demonstrates that patients with these diseases have a higher susceptibility to dyslipidemia. Overweight patients usually have higher levels of fat intake and more fat disposition in the body, in addition to disorders of the lipid metabolism, which make them more likely to develop dyslipidemia.¹⁵ Patients with HTN are usually accompanied by dyslipidemia, which significantly can increase the risk of cardiovascular events.¹⁸ Hyperlipidemia can not only increase the blood viscosity, leading to increased blood

resistance, but also lead to the development of atheromatous plaque, resulting in luminal stenosis and decreased vascular elasticity. What is more, it can reduce the sensibility of vessels to hypotensors.¹⁹ In short, dyslipidemia is a risk factor of HTN, while HTN is an omen of dyslipidemia, as it is easier to detect. Patients with DM also are more likely to develop dyslipidemia. On one hand, these patients usually have symptoms of polyphagia, so they consume more food, while on the other hand, they also develop metabolic disturbances of lipids, proteins, and water-electrolytes, except the glucose metabolic disorder.¹⁸ In addition, when there is an insulin deficiency in the body, lipase activity decreases, which leads to the elevation of blood lipids.²⁰

In TCM, dyslipidemia is thought to be associated with the transporting and transforming functions of the spleen and closely related to the transpiration and gasification functions of the kidneys. The stagnation of Phlegm-dampness is thought to be the basic pathogenesis of dyslipidemia.^{21–23} Any factors that may inhibit such functions or produce Phlegm-dampness will result in dyslipidemia. Our study is focused on the elderly; the mean age was 69.33 years. As age increases, the function of our internal organs declines gradually, especially among Qi-deficient and Yang-deficient individuals, as Yang–Qi is essential for maintaining the function of the internal organs.²⁴ Thus, the hypofunction of the spleen will lead to abnormal transportation and the transformation of water and grain into Phlegm-dampness, rather than the essence. The stagnation of Phlegm-dampness in the body will eventually lead to dyslipidemia.¹⁷ Further, the essence of water and grain that the spleen transforms is the vital resource of Qi and blood. Therefore, the hypofunction of the spleen will lead to a decreased generation of Qi, due to a lack of resources. However, the deficiency of Qi will also conversely restrain the function of the spleen, and a vicious circle develops. However, the Yang–Qi of the kidneys is usually manifest as asthenia in the elderly. The deficiency of kidney-Yang will lead to the failure in the transpiration and gasification of water-dampness, so the abnormal retention of water-dampness in the body, for some, will develop Phlegm-dampness, and the stagnation of phlegm will eventually result in dyslipidemia.^{14,16,17,24} In summary, Qi-deficient and Yang-deficient constitutions are more vulnerable to dyslipidemia.

There are some limitations to this study. The association between dyslipidemia and TCM constitution (TCMC) is obviously affected by age, but patients with dyslipidemia at different ages present various TCMC distributions.^{14,22} The participants in our study were between the ages of 30 years and 90 years, but we did not identify the most common BCTCM of dyslipidemia according to ages. Additionally, many patients with dyslipidemia present more than one TCMC, a state known as “concurrent constitution”.^{16,17} Even though the Qi-deficient and Yang-deficient types are the most common constitutions in

our study, they are usually accompanied by other constitutions, such as Phlegm-dampness, Yin-deficient, and Blood-stasis. Thus, when employing clinical interventions, concurrent constitutions should be taken into consideration.

Our findings provided evidence that Qi-deficient and Yang-deficient types were independently and significantly associated with dyslipidemia, respectively. A higher prevalence of dyslipidemia was found in participants with Qi-deficient and Yang-deficient types, compared with participants of the Neutral type. These findings may provide insight for clinical practices to prevent and diagnose dyslipidemia.

Ethical Approval and Consent to Participate

All procedures performed in the studies involving human participants were in accordance with the ethical standards of the institutional and/or national research committee and with the 1964 Helsinki Declaration and its later amendments or comparable ethical standards.

Availability of Data and Materials

Data may be obtained from the authors of this study, who may be contacted at the Department of Integrative Medicine, Huashan Hospital of Fudan University, Shanghai, China. The authors can be contacted for all data requests.

Conflict of Interest

The authors have no conflicts of interest to declare.

Author Contributions

Qiuping Li drafted the manuscript. Qing Kong participated in the design of the study and performed the statistical analysis. Zihui Tang conceived of the study, participated in its design and coordination, and helped to draft the manuscript. All authors read and approved the final manuscript.

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