Open Access Full Text Article

ORIGINAL RESEARCH

## Distribution of Arteriosclerotic Vessels in Patients with Arteriosclerosis and the Differences of Serum Lipid Levels Classified by Different Sites

Weiyong Xu<sup>1,2</sup>, Zhenchang Wang<sup>3</sup>, Huaqing Yao<sup>1,2</sup>, Zifeng Zeng<sup>1,2</sup>, Xinping Lan<sup>1,2</sup>

<sup>1</sup>Center for Cardiovascular Diseases, Meizhou People's Hospital, Meizhou, People's Republic of China; <sup>2</sup>Guangdong Provincial Engineering and Technology Research Center for Molecular Diagnostics of Cardiovascular Diseases, Meizhou People's Hospital, Meizhou, People's Republic of China; <sup>3</sup>Department of Emergency Medicine, Meizhou People's Hospital, Meizhou, People's Republic of China

Correspondence: Xinping Lan, Center for Cardiovascular Diseases, Meizhou People's Hospital, Meizhou Academy of Medical Sciences, Meizhou, People's Republic of China, Email lan-xinping@163.com

**Objective:** To investigate the distribution of arteriosclerotic vessels of arteriosclerosis, differential serum lipid profiles, and differences in the proportion of dyslipidaemia between patients with single-site arteriosclerosis and multi-site arteriosclerosis (significant hardening of  $\geq 2$  arteries).

**Methods:** The data of 6581 single-site arteriosclerosis patients and 5940 multi-site arteriosclerosis patients were extracted from the hospital medical record system. Serum total cholesterol (TC), triglycerides (TGs), high-density lipoprotein cholesterol (HDL-C), low-density lipoprotein cholesterol (LDL-C), apolipoprotein (Apo) A1, ApoB concentrations and C-reactive protein (CRP) between patients with single-site arteriosclerosis and multi-site arteriosclerosis were collected and analyzed.

**Results:** The most diseased arteries were coronary arteries (n=7099, 33.7%), limb arteries (n=6546, 31.1%), and carotid arteries (n=5279, 25.1%). TC, LDL-C, TC/HDL-C, and LDL-C/HDL-C levels were higher and CRP level was lower in multi-site arterio-sclerosis patients than those in single-site arteriosclerosis patients. The TC, LDL-C levels in non-elderly (<65 years old) female patients were higher and TG/HDL-C, TC/HDL-C, LDL-C/HDL-C levels were lower than those in non-elderly male patients, while the TG, TC, LDL-C, and TG/HDL-C levels in elderly ( $\geq$ 65 years old) female patients were higher and TG/HDL-C levels in elderly ( $\geq$ 65 years old) female patients were higher and LDL-C/HDL-C levels in elderly ( $\geq$ 65 years old) female patients were higher and LDL-C/HDL-C levels was lower than those in elderly male patients. The proportion of dyslipidemia in descending order was as follows: low HDL-C (31.9%), elevated TG (16.9%), elevated TC (9.0%), and elevated LDL-C (4.2%). The levels of TC, LDL-C, TC/HDL-C, and LDL-C/HDL-C in patients with peripheral arteriosclerosis were higher than those in patients with cardio-cerebrovascular arteriosclerosis.

**Conclusion:** There were differences in serum lipid levels in patients with arteriosclerosis with different age, gender and distribution of arteriosclerotic vessels.

Keywords: arteriosclerosis, arteriosclerotic vessels, dyslipidemia, serum lipid, CRP

#### Introduction

In recent years, the incidence of vascular diseases is increasing year by year.<sup>1,2</sup> Arteriosclerosis is the intermediate pathological state of some vascular events, and the prevention of arteriosclerosis can prevent and delay the occurrence of vascular events.<sup>3</sup> Arteriosclerosis is the aging of the arterial system accompanied by structural changes, and is the risk factor for cardiovascular and cerebrovascular diseases.<sup>4,5</sup> It is a kind of arterial disease caused by the thickening and hardening of the intima of blood vessels, which leads to the narrowing and obstruction of the lumen, and eventually leads to the ischemia or even necrosis of tissues and organs.<sup>6</sup>

Arteriosclerosis is a systemic disease that can involve multiple arteries, and the risk factors for arteriosclerosis may have different effects on different parts of the arterial system.<sup>7,8</sup> Intima thickening is the early manifestation of arteriosclerosis, and further development leads to the formation of arteriosclerosis plaques and even hemodynamic changes. Currently, most scholars believe that the occurrence of arteriosclerosis is related to inflammation and lipid

metabolism.<sup>9–11</sup> Serum lipids include serum cholesterol, triglycerides, and other lipids. Dyslipidemia due to the disorder of lipid metabolism is a risk factor for arteriosclerotic disease.<sup>12</sup> Chinese adults have high rates of high total cholesterol (TC), high low-density lipoprotein cholesterol (LDL-C), low high-density lipoprotein cholesterol (HDL-C), and high triglycerides (TG).<sup>13</sup> The proportion of dyslipidemia in Chinese adults is relatively high, while the identification rate, treatment rate and control rate of dyslipidemia are relatively low, which requires extensive attention.<sup>14</sup> In addition, inflammation has been linked to arteriosclerosis.<sup>15</sup> C-reactive protein (CRP) is a marker of cardiovascular disease, and it has been associated with adverse outcome of acute coronary syndrome (ACS), but the role in initiation and development of the arteriosclerosis has controversy.<sup>16</sup>

Clinically, the degree of arterial lesions in different parts of the same patient is different, suggesting that some factors (age, sex, lipid level) have different effects on arterial lesions in different parts.<sup>17,18</sup> Serum lipid profiles in patients with arteriosclerotic cardiovascular disease<sup>19</sup> and the differences in lipid levels in coronary and peripheral artery disease<sup>20,21</sup> have been studied in some studies, however, few systematic, large sample studies have focused on the distribution of different sites of arteriosclerotic vessels and the differences among them in serum lipid and CRP levels. In this study, the distribution of different sites of arteriosclerotic vessels and the differences among them in serum lipid and CRP protein levels were analyzed.

#### **Materials and Methods**

#### **Subjects**

This study is a hospital-based, retrospective, descriptive study of the distribution of arteriosclerotic vessels and the serum lipid and CRP levels in patients with arteriosclerosis. Data of 12,521 patients with arteriosclerosis (7363 men and 5158 women) admitted to Meizhou People's Hospital from November 2017 to June 2022 was collected. The extent of vascular lumen stenosis or calcification was examined by imaging methods. Arteriosclerosis is determined by examining arterial plaque using techniques such as angiography, magnetic resonance imaging (MRI), computed tomography, or color doppler ultrasonography, assessed by two senior radiologists in a double-blind evaluation. Pulse Wave Velocity (PWV) and Ankle-Brachial Index (ABI) were measured using an arterioscleroscope to assess arterial stiffness. The diagnostic criteria for arteriosclerosis were in accordance with the relevant diagnostic criteria formulated by the Cardiovascular Branch and the Neurology Branch of the Chinese Medical Association. In this study, arteriosclerosis was observed in coronary artery, aorta, carotid artery, cerebral artery, vertebral artery, subclavian artery, internal mammary artery, mesenteric artery, renal artery, femoral artery, and limb artery. Single-site arteriosclerosis refers to the clinically obvious hardening of up to one artery. Multi-site arteriosclerosis refers to clinically significant hardening of two or more arteries ( $\geq 2$  arteries).

The inclusion criteria were as follows: (1) patients diagnosed with arteriosclerosis; (2) complete clinical medical record data; and (3) Adults. The exclusion criteria were as follows: (1) incomplete clinical medical record data; and (2) arteriosclerosis patients with severe infectious diseases, autoimmune diseases, and organ insufficiency. This study was performed in accordance with the ethical standards of the Declaration of Helsinki and approved by the Human Ethics Committee of Meizhou People's Hospital.

#### Serum Lipid Measurements

Approximately 3mL of blood was taken from each subject, and serum was immediately separated. The serum lipid levels of the samples were evaluated by an Olympus AU5400 system (Olympus Corporation, Tokyo, Japan). TC, TG, LDL-C, HDL-C, apolipoprotein A1 (Apo-A1) and apolipoprotein B (Apo-B) analyses were carried out using the cholesterol esterase/peroxidase (CHOD/PAP) enzymatic method,<sup>22</sup> glycerophosphate oxidase/peroxidase (GPO-PAP) enzymatic method,<sup>24</sup> direct immunoinhibition method,<sup>25</sup> and immunoturbidimetry method,<sup>26</sup> respectively, according to the manufacturers' instructions. Patients with a clear past history of hyperlipidemia and/or a current serum lipid test that met criteria according to the 2016 Chinese Guidelines were diagnosed with dyslipidaemia.<sup>27</sup> CRP was detected by immunoturbidimetric method on HITACHI automatic biochemical analyzer.<sup>28</sup>

#### Statistical Analysis

Statistical analysis was performed using SPSS statistical software version 26.0 (IBM Inc., USA) and GraphPad software version 8.0 (GraphPad Software, Inc, USA). For the analysis of continuous variables, when the data follows normal distribution, the Student's *t*-test was used. When the data did not follow the normal distribution, the Mann–Whitney *U*-test was used to compare and analyze the non-normal distribution quantitative variables. Chi-square test was used to analyze the difference in the proportion of dyslipidemia among the groups. P<0.05 was used as the level of statistical significance for all statistical analyses in this study.

#### Results

#### The Distribution of Arteriosclerotic Vessels in Patients with Arteriosclerosis

12,521 patients with arteriosclerosis were enrolled, including 7363 (58.8%) male patients and 5158 (41.2%) female patients. In this study, there were 6581 (52.6%) single-site arteriosclerosis patients and 5940 (47.4%) multi-site arteriosclerosis patients (Figure 1A). In single-site arteriosclerosis patients, there were 3979 (3979/6581, 60.5%) cases of coronary arteriosclerosis, 1690 (1690/6581, 25.7%) cases of limb arteriosclerosis, 751 (751/6581, 11.4%) cases of carotid arteriosclerosis, 134 (134/6581, 2.0%) cases of cerebral arteriosclerosis and 27 (27/6581, 0.4%) cases of aortic sclerosis, respectively (Figure 1B).

In this study, 67 different combinations of arteriosclerosis were detected in multi-site arteriosclerosis patients. Among these patients, the top 5 types with a most number of patients were as follows: carotid and limb arteriosclerosis (1929 cases, 32.5%), coronary, carotid and limb arteriosclerosis (1276 cases, 21.5%), coronary and limb arteriosclerosis (573 cases, 9.6%), coronary and carotid arteriosclerosis (372 cases, 6.3%), and coronary and aortic arteriosclerosis (334 cases, 5.6%) (Figure 1C and Supplemental Table 1).

In this study, 7099 (33.7%) patients (4154 (33.5%) men and 2945 (34.0%) women) had coronary arteriosclerosis, followed by 6546 (31.1%) cases of limb arteriosclerosis (3896 (31.4%) cases of males and 2650 (30.6%) cases of females), and 5279 (25.1%) cases of carotid arteriosclerosis (3190 (25.7%) cases of males and 2089 (24.2%) cases of females) (Figure 1D). In non-elderly patients, 2899 (37.1%) patients had coronary arteriosclerosis; followed by 2162 (27.7%) cases of limb arteriosclerosis, and 1967 (25.2%) cases of carotid arteriosclerosis; in elderly patients, 4384 (33.1%) cases of limb arteriosclerosis. Compared with non-elderly patients, limb arteries had the most lesions in elderly patients (Figure 1E).

# Comparison of Serum Lipid and CRP Levels in Different Sex and Age (Non-Elderly (<65 Years Old), Elderly (<65 Years Old)) Patients with Arteriosclerosis

TC ( $4.64\pm1.27 \text{ mmol/L}$  vs  $4.54\pm1.24 \text{ mmol/L}$ , P<0.001), LDL-C ( $2.58\pm0.88 \text{ mmol/L}$  vs  $2.50\pm0.86 \text{ mmol/L}$ , P<0.001), TC/HDL-C ratio ( $4.01\pm1.41 \text{ vs } 3.93\pm1.48$ , P=0.003), LDL-C/HDL-C ratio ( $2.24\pm0.90 \text{ vs } 2.17\pm0.90$ , P<0.001), Apo-A1 ( $1.11\pm0.29 \text{ g/L} \text{ vs } 1.10\pm0.29 \text{ g/L}$ , P=0.026), and Apo-B ( $0.83\pm0.27 \text{ g/L} \text{ vs } 0.81\pm0.26 \text{ g/L}$ , P<0.001) levels were higher and CRP level ( $17.77\pm35.86 \text{ mg/L} \text{ vs } 19.77\pm39.11 \text{ mg/L}$ , P=0.003) was lower in multi-site arteriosclerosis patients than those in single-site arteriosclerosis patients (Table 1).

Patients with arteriosclerosis were classified as non-elderly (<65 years old) male patients, non-elderly female patients, elderly (≥65 years old) male patients, and elderly female patients. Among the non-elderly patients, the TC, HDL-C, LDL-C levels in female patients were higher than those in male patients, while TG/HDL-C, TC/HDL-C, LDL-C/HDL-C, Apo-B/Apo-A1, and CRP levels were lower than those in male patients. In the elderly patients, the TG, TC, HDL-C, LDL-C, and TG/HDL-C levels in female patients were higher than those in male patients, while LDL-C/HDL-C, Apo-B/Apo-A1, and CRP levels were lower than those in male patients. Among the male patients, while LDL-C/HDL-C, TG/HDL-C, TC/HDL-C, TC/HDL-C, and Apo-B/Apo-A1 levels in elderly patients were lower than those in non-elderly patients. In the female patients, the TG, TC, LDL-C, TG/HDL-C, TG/HDL-C, TC/HDL-C, and LDL-C/HDL-C levels in elderly patients. In the female patients, the TG, TC, LDL-C, the there is non-elderly patients in elderly patients. In the female patients, the TG, TC, LDL-C, the there is non-elderly patients in elderly patients. In the female patients, the TG, TC, LDL-C, the there is non-elderly patients in elderly patients. In the female patients, the TG, TC, LDL-C, the there is non-elderly patients were lower than those in non-elderly patients, while the there is non-elderly patients in elderly patients were lower than those in non-elderly patients, while CRP level was higher than those in non-elderly patients (Figure 2).



Figure I The distribution of patients with arteriosclerosis in single artery, arteriosclerosis in multiple arteries, and in different gender and age (non-elderly (<65 years old), elderly ( $\geq$ 65 years old)). The number and composition ratio of patients with single-site arteriosclerosis and multi-site arteriosclerosis (**A**). The distribution of arteriosclerotic vessels in patients with single-site arteriosclerosis (**B**). The distribution of arteriosclerotic vessels in patients with multi-site arteriosclerosis (**C**). Distribution of arteriosclerotic arteries in non-elderly and elderly patients (**E**).

#### The Distribution of Dyslipidaemia in Arteriosclerosis Patients

Among all patients, the proportion of dyslipidemia in descending order was as follows: low HDL-C (31.9%), elevated TG (16.9%), elevated TC (9.0%), and elevated LDL-C (4.2%). According to the combination of normal or abnormal serum lipid indexes (LDL-C, HDL-C, and TG), the differences in the proportion of different combinations between multi-site arteriosclerosis patients and single-site arteriosclerosis patients, male and female were analyzed. The largest proportion of dyslipidemia types was independent low HDL-C (n=1498, 12.0%), followed by independent elevated TG (n=728, 5.8%), and low HDL-C combined with elevated TG (n=711, 5.7%). The female patients had lower the proportions of elevated LDL-C+ low HDL-C + elevated TG, elevated LDL-C+ low HDL-C + normal TG, and normal LDL-C+ normal HDL-C + normal HDL-C + normal TG, and normal LDL-C+ normal HDL-C + elevated TG than males.

	Total (n=12521)	Patients with Arteriosclerosis in Single Artery (n=6581)	Patients with Arteriosclerosis in Multiple Arteries (n=5940)	P values
Age, years				
<65, n(%)	4810 (38.4%)	2578 (39.2%)	2232 (37.6%)	0.069
≥65, n(%)	7711 (61.6%)	4003 (60.8%)	3708 (62.4%)	
Male/Female	7363/5158	3847/2734	3516/2424	0.413
TG, mmol/L	1.63±1.28	1.63±1.23	1.64±1.33	0.404
TC, mmol/L	4.59±1.26	4.54±1.24	4.64±1.27	<0.001
HDL-C, mmol/L	1.22±0.35	1.22±0.36	1.22±0.35	0.915
LDL-C, mmol/L	2.53±0.87	2.50±0.86	2.58±0.88	<0.001
TG/HDL-C	1.57±1.98	1.57±1.92	1.58±2.04	0.827
TC/HDL-C	3.97±1.44	3.93±1.48	4.01±1.41	0.003
LDL-C/HDL-C	2.21±0.90	2.17±0.90	2.24±0.90	<0.001
Apo-AI, g/L	1.11±0.29	1.10±0.29	1.11±0.29	0.026
Apo-B, g/L	0.82±0.27	0.81±0.26	0.83±0.27	<0.001
Аро-В/Аро-АІ	0.78±0.32	0.77±0.32	0.79±0.32	0.054
CRP, mg/L	18.82±37.62	19.77±39.11	17.77±35.86	0.003

 Table I Clinical Characteristics of Patients with Arteriosclerosis in Single Artery and Patients with

 Arteriosclerosis in Multiple Arteries

Abbreviations: TG, triglycerides; TC, total cholesterol; HDL-C, high-density lipoprotein cholesterol; LDL-C, low-density lipoprotein cholesterol; Apo-AI, apolipoprotein AI; Apo-B, apolipoprotein B; CRP, C reactive protein.

In single-site arteriosclerosis patients, the female patients had lower the proportions of normal LDL-C+ low HDL-C+ elevated TG, normal LDL-C+ low HDL-C+ normal TG, while had higher proportions of elevated LDL-C+ normal HDL-C+ normal HDL-C+ elevated TG than male patients. And a similar result was found in multi-site arteriosclerosis patients. In addition, the female patients with arteriosclerosis in multiple arteries had higher proportions of elevated LDL-C, and elevated LDL-C+ normal HDL-C + elevated TG than the female patients with arteriosclerosis in single artery. The male multi-site arteriosclerosis patients had higher proportion of normal LDL-C+ low HDL-C+ low HDL-C+ normal TG than the male single-site arteriosclerosis patients (Table 2).

#### Comparison of Serum Lipid and CRP Levels in Patients with Cardio-Cerebrovascular Arteriosclerosis, Peripheral Arteriosclerosis, Cardio-Cerebrovascular Arteriosclerosis Combined with Peripheral Arteriosclerosis

The levels of TC, LDL-C, TC/HDL-C, LDL-C/HDL-C, Apo-B/Apo-A1 and CRP in patients with peripheral arteriosclerosis were higher than those in patients with cardio-cerebrovascular arteriosclerosis. The levels of TC, LDL-C, TC/ HDL-C, LDL-C/HDL-C, and Apo-B/Apo-A1 in patients with cardio-cerebrovascular arteriosclerosis combined with peripheral arteriosclerosis were higher than those in patients with cardio-cerebrovascular arteriosclerosis. While the patients with cardio-cerebrovascular arteriosclerosis combined with peripheral arteriosclerosis had higher LDL-C level and lower CRP level than those in patients with peripheral arteriosclerosis. There were no statistically significant differences in HDL-C and TG/HDL-C levels among the three groups (Figure 3).

#### Discussion

There are prone sites of arteriosclerotic plaque, that is, different arterial vessels and different parts of the same artery have different possibilities of forming arteriosclerosis.<sup>29,30</sup> Despite systemic exposure to hyperlipidemia, the progression of arteriosclerosis between the coronary and distal arteries is markedly different.<sup>31</sup> In mechanism, human genome-wide association studies have shown that arteriosclerosis at different vascular locations may involve different genetic pathways, and mouse experiments have shown that location specificity of arteriosclerosis susceptibility is controlled by genes.<sup>32</sup> In addition, Fenning et al reported that the role of lipoprotein-associated phospholipase A2 (Lp-PLA2) in the



Figure 2 Comparison of serum lipid and CRP levels in different sex and age (non-elderly (<65 years old), elderly (≥65 years old)) patients with arteriosclerosis. \*P<0.05; \*\*P<0.01; \*\*\*P<0.001.

inflammation and arteriosclerotic plaques development was fundamentally different among different vascular sites.<sup>33</sup> It is noteworthy that polyvascular disease, especially peripheral artery disease, may have a greater risk of adverse outcomes than coronary arteriosclerosis or stroke.<sup>7</sup>

	All subjects (n=12521)			Patients with Arteriosclerosis in Single Artery (n=6581)		Patients with Arteriosclerosis in Multiple Arteries (n=5940)	
	Total (n=12521)	Male (n=7363)	Female (n=5158)	Male (n=3847)	Female (n=2734)	Male (n=3516)	Female (n=2424)
Elevated TC	1128(9.0%)	498(6.8%)	630(12.2%)***	240(6.2%)	313(11.5%)***	258(7.3%)	317(13.1%)***
Elevated TG	2116(16.9%)	1200(16.3%)	916(17.8%)*	632(16.4%)	483(17.7%)	568(16.1%)	433(17.8%)
Low HDL-C	3989(31.9%)	2836(38.5%)	1153(22.4%)***	1491(38.8%)	623(22.8%)***	1345(38.2%)	530(21.8%)***
Elevated LDL-C	530(4.2%)	263(3.6%)	267(5.2%)***	122(3.2%)	123(4.5%)**	141(4.0%)	l 44(5.9%)**, <sup>#</sup>
Elevated LDL-C+ low HDL-C + elevated TG	37(0.3%)	29(0.4%)	8(0.2%)*	15(0.4%)	4(0.1%)	14(0.4%)	4(0.2%)
Elevated LDL-C+ low HDL-C+ normal TG	47(0.4%)	38(0.5%)	9(0.2%)*	14(0.4%)	5(0.2%)	24(0.7%)	4(0.2%)**
Elevated LDL-C+ normal HDL-C + elevated TG	124(1.0%)	54(0.7%)	70(1.4%)*	28(0.7%)	25(0.9%)	26(0.7%)	45(1.9%)***, <sup>##</sup>
Elevated LDL-C+ normal HDL-C+ normal TG	301(2.4%)	141(1.9%)	160(3.1%)***	64(1.7%)	78(2.9%)**	77(2.2%)	82(3.4%)**
Normal LDL-C+ low HDL-C+ elevated TG	711(5.7%)	479(6.5%)	232(4.5%)***	244(6.4%)	125(4.6%)**	235(6.7%)	107(4.4%)***
Normal LDL-C+ low HDL-C+ normal TG	1498(12.0%)	1086(14.7%)	412(8.0%)***	531(13.8%)	221(8.1%)***	555(15.8%) <sup>#</sup>	191(7.9%)***
Normal LDL-C+ normal HDL-C+ normal TG	4815(38.5%)	2546(34.6%)	2269(44.0%)***	1304(33.9%)	1193(43.6%)***	1242(35.3%)	1076(44.5%)***
Normal LDL-C+ normal HDL-C+ elevated TG	728(5.8%)	334(4.5%)	394(7.6%)***	181(4.7%)	213(7.8%)***	153(4.3%)	181(7.5%)***

Notes: Compared with males, \*P <0.05, \*\*P <0.01, and \*\*\*P <0.001 for all subjects, the patients with arteriosclerosis in single artery, and arteriosclerosis in multiple arteries. Compared with the patients with arteriosclerosis in single artery, \*P <0.05, \*\*P <0.01, and \*\*\*P <0.001 for both males and females.

Abbreviations: TG, triglycerides; TC, total cholesterol; HDL-C, high-density lipoprotein-cholesterol; LDL-C, low-density lipoprotein-cholesterol; Apo-AI, apolipoprotein AI; Apo-B, apolipoprotein B.

Table 2 The Number and Proportion of Dyslipidemia in Arteriosclerosis Patients



Figure 3 Comparison of serum lipid and CRP levels in patients with cardio-cerebrovascular arteriosclerosis, peripheral arteriosclerosis, cardio-cerebrovascular arterio-sclerosis combined with peripheral arteriosclerosis. \*P<0.01; \*\*\*P<0.001.

Different studies have had different results on the vascular distribution and regional distribution of arteriosclerosis. Most participants (greater than 93%) had arteriosclerosis in at least one vascular area, and arteriosclerosis is more common in aorta, iliac artery, subclavian artery, coronary artery, extracranial artery, renal artery, and intracranial artery in

a study of multiterritorial arteriosclerosis prevalence and vessel distribution in a population from southeast China.<sup>34</sup> Another study showed that arteriosclerosis was most common in the iliac arteries, followed by the carotid, aorta, and coronary arteries.<sup>35</sup> In addition, one study found that plaque was mainly distributed in some major arteries.<sup>36</sup> The arteriosclerotic location was significantly associated with age, but not with gender.<sup>37</sup> Peripheral arteriosclerosis is associated with long-term cardiovascular mortality.<sup>38</sup>

The mechanism by which arteriosclerosis occurs in the multi-arterial region is still poorly understood. There was a significant correlation between serum uric acid level and intracranial artery stenosis and arteriosclerosis in males.<sup>39</sup> Soluble CD40 ligand (sCD40L) levels were significantly elevated in polyvascular coronary arteriosclerosis and lower extremity arteriosclerosis.<sup>40</sup> Vascular endothelial function may change, triggering the initiation of arteriosclerosis under hyperlipidemia. Oxidized low density lipoprotein (ox-LDL) can cause vascular endothelial cell injury and dysfunction, which is the mechanism of hyperlipidemia to vascular endothelial injury.<sup>41</sup> Oxidized cholesterol increases in hyperlipidemia, and oxidized cholesterol has cytotoxic effects on vascular cells and induces apoptosis.<sup>42,43</sup> LDL-C and ox-LDL participate in the local oxidative stress process of vascular endothelium, and induce the local infiltration of mononuclear macrophages to form foam cells through inflammatory mediators, thus promoting the formation of arteriosclerosis.<sup>44</sup> Study has suggested that dyslipidemia is the strongest risk factor for the progression of multi-territorial subclinical arteriosclerosis.<sup>45</sup> In humans, dyslipidemia often manifests as low HDL-C and high triglyceride levels, which are also major risk factors for arteriosclerosis.<sup>46</sup> Level of LDL-C particles was most strongly associated with polyvascular disease.<sup>7</sup> Hypertriglyceridemia is an important risk factor for the progression of carotid artery stenosis.<sup>47</sup>

The TG, TC, LDL-C, TG/HDL-C, TC/HDL-C, and LDL-C/HDL-C levels were higher in the non-elderly patients that those in the elderly patients, in both males and females. A study showed that in both male and female patients with acute myocardial infarction (AMI), LDL-C and TC were higher in non-elderly patients than in elderly patients.<sup>48</sup> Another study showed that LDL-C, TC, and TG were higher in non-elderly AMI than in elderly for males.<sup>49</sup> Therefore, doctors should attach great importance to dyslipidemia in non-elderly patients, and the control of serum lipids in such patients may help to control and improve the progress of arteriosclerosis.

In non-elderly patients, the TC, LDL-C levels were higher and TG/HDL-C, TC/HDL-C, LDL-C/HDL-C, and CRP levels were lower in female patients than those in male patients. And in elderly patients, the TG, TC, LDL-C, and TG/HDL-C levels in female patients were higher and LDL-C/HDL-C, and CRP levels were lower than those in male patients. A study has shown that estrogen levels affect lipid metabolism.<sup>50</sup> A relationship between follicle-stimulating hormone (FSH) levels and serum cholesterol levels was also demonstrated.<sup>51</sup> Hormone levels may partly explain the difference in blood lipid levels between men and women, but the underlying mechanism of the difference in blood lipid metabolism needs further study.<sup>52,53</sup> It has also been suggested that sex differences in lipid levels may be caused by differences in rates of lipolysis and lipogenesis.<sup>54,55</sup> In addition, one study showed that women have the lowest incidence in the coronary area and a higher prevalence of carotid arteriosclerosis, while men have a higher prevalence of coronary and femoral arteriosclerosis.<sup>56</sup> In conclusion, dyslipidemia is more likely to lead to peripheral arteriosclerotic disease, and is more common in female patients.

Moreover, the serum lipid levels in patients with arteriosclerosis at different sites also vary. In this study, the levels of TC, LDL-C, TC/HDL-C, and LDL-C/HDL-C in patients with peripheral arteriosclerosis were higher than those in patients with cardio-cerebrovascular arteriosclerosis, and the same results were found in patients with cardio-cerebrovascular combined with peripheral arteriosclerosis. The most common cholesterol implicated in the formation of plaque in arterial walls is LDL-C. It has been noted that patients with coronary artery disease tend to have higher levels of LDL-C and a lower level of HDL-C. In contrast, patients with cerebrovascular disease or stroke are likely to have higher levels of TG and TC. Unfortunately, this study did not distinguish between patients with coronary arteriosclerosis and those with cerebrovascular sclerosis.

The distribution of arteriosclerotic vessels of arteriosclerosis, differential serum lipid profiles and differences in the proportion of dyslipidaemia between patients with single-site arteriosclerosis and multi-site arteriosclerosis were analyzed in this study. However, this study has several shortcomings. First, although the number of cases included in this study is considerable, these patients are from a single medical institution, which weakens the representativeness of

this study to a certain extent. Second, although we evaluated arteriosclerosis across a wide range of vessels in a large population, some marginal findings may have led to a lack of understanding of potential associations. Third, because lipid levels and CRP levels may be influenced by other factors, such as insidious diseases, the validity of the results may depend on the baseline background of the study population.

#### Conclusions

In patients with arteriosclerosis, differences in serum lipid levels are correlated with differences in age and sex. (1) The most diseased arteries were coronary arteries, limb arteries, and carotid arteries. (2) Dyslipidemia is more common in nonelderly arteriosclerosis patients than elderly. (3) In non-elderly patients, the levels of TC and LDL-C were higher and the levels of TG/HDL-C, TC/HDL-C, LDL-C/HDL-C and CRP were lower in female patients than those in male patients, while the TG, TC, LDL-C, and TG/HDL-C levels in elderly female patients were higher and LDL-C/HDL-C, and CRP levels were lower than those in elderly male patients. (4) The levels of TC, LDL-C, TC/HDL-C, and LDL-C/HDL-C in patients with peripheral arteriosclerosis were higher than those in patients with cardio-cerebrovascular arteriosclerosis, and the same results were found in patients with cardio-cerebrovascular combined with peripheral arteriosclerosis. Therefore, serum lipid levels in hypertensive patients should receive more attention, especially in non-elderly female patients. And patients with dyslipidemia and cardiovascular and cerebrovascular arteriosclerosis should be examined for peripheral artery lesions to achieve early detection and treatment of peripheral arteriosclerosis.

## **Data Sharing Statement**

The data that support the findings of this study are available from the corresponding author upon reasonable request.

## **Ethics Approval and Consent to Participate**

The study was approved by the Ethics Committee of Medicine, Meizhou People's Hospital. All participants signed informed consent in accordance with the Declaration of Helsinki.

#### **Acknowledgments**

The author would like to thank other colleagues whom were not listed in the authorship of Center for Cardiovascular Diseases, Meizhou People's Hospital, for their helpful comments on the manuscript.

## **Author Contributions**

All authors made a significant contribution to the work reported, whether that is in the conception, study design, execution, acquisition of data, analysis and interpretation, or in all these areas; took part in drafting, revising or critically reviewing the article; gave final approval of the version to be published; have agreed on the journal to which the article has been submitted; and agree to be accountable for all aspects of the work.

## Funding

This study was supported by the Science and Technology Program of Meizhou (Grant No.: 2019B0202001).

#### Disclosure

The authors declare that they have no competing interests.

## References

- 1. Turana Y, Tengkawan J, Chia YC. Hypertension and stroke in Asia: a comprehensive review from HOPE Asia. J Clin Hypertens. 2021;23 (3):513-521. doi:10.1111/jch.14099
- 2. Ji E, Lee S. Antibody-based therapeutics for atherosclerosis and cardiovascular diseases. Int J Mol Sci. 2021;22(11):5770. doi:10.3390/ijms22115770
- 3. Chen Q, Lv J, Yang W, et al. Targeted inhibition of STAT3 as a potential treatment strategy for atherosclerosis. *Theranostics*. 2019;9(22):6424–6442. doi:10.7150/thno.35528
- 4. Jing L, Shu-Xu D, Yong-Xin R. A review: pathological and molecular biological study on atherosclerosis. *Clin Chim Acta*. 2022;531:217–222. doi:10.1016/j.cca.2022.04.012

- 5. Gutierrez J, Turan TN, Hoh BL, Chimowitz MI. Intracranial atherosclerotic stenosis: risk factors, diagnosis, and treatment. *Lancet Neurol*. 2022;21 (4):355–368. doi:10.1016/S1474-4422(21)00376-8
- Shamaki GR, Markson F, Soji-Ayoade D, Agwuegbo CC, Bamgbose MO, Tamunoinemi BM. Peripheral artery disease: a comprehensive updated review. Curr Probl Cardiol. 2022;47(11):101082. doi:10.1016/j.cpcardiol.2021.101082
- 7. Aday AW, Matsushita K. Epidemiology of peripheral artery disease and polyvascular disease. *Circ Res.* 2021;128(12):1818–1832. doi:10.1161/ CIRCRESAHA.121.318535
- Gutierrez JA, Aday AW, Patel MR, Jones WS. Polyvascular disease: reappraisal of the current clinical landscape. *Circ Cardiovasc Interv*. 2019;12 (12):e007385. doi:10.1161/CIRCINTERVENTIONS.119.007385
- 9. Oliveira HCF, Raposo HF. Cholesteryl ester transfer protein and lipid metabolism and cardiovascular diseases. *Adv Exp Med Biol.* 2020;1276:15–25. doi:10.1007/978-981-15-6082-8\_2
- 10. Libby P. Inflammation during the life cycle of the atherosclerotic plaque. Cardiovasc Res. 2021;117(13):2525-2536. doi:10.1093/cvr/cvab303
- 11. Anto L, Blesso CN. Interplay between diet, the gut microbiome, and atherosclerosis: role of dysbiosis and microbial metabolites on inflammation and disordered lipid metabolism. *J Nutr Biochem.* 2022;105:108991. doi:10.1016/j.jnutbio.2022.108991
- 12. Hussain I, Patni N, Garg A. Lipodystrophies, dyslipidaemias and atherosclerotic cardiovascular disease. *Pathology*. 2019;51(2):202-212. doi:10.1016/j.pathol.2018.11.004
- 13. Zhang M, Deng Q, Wang L, et al. Prevalence of dyslipidemia and achievement of low-density lipoprotein cholesterol targets in Chinese adults: a nationally representative survey of 163,641 adults. *Int J Cardiol*. 2018;260:196–203. doi:10.1016/j.ijcard.2017.12.069
- 14. Yang W, Xiao J, Yang Z, et al. Serum lipids and lipoproteins in Chinese men and women. *Circulation*. 2012;125(18):2212–2221. doi:10.1161/ CIRCULATIONAHA.111.065904
- 15. Libby P. Inflammation in atherosclerosis-no longer a theory. Clin Chem. 2021;67(1):131-142. doi:10.1093/clinchem/hvaa275
- 16. Denegri A, Boriani G. High sensitivity c-reactive protein (hsCRP) and its implications in cardiovascular outcomes. *Curr Pharm Des.* 2021;27 (2):263–275. doi:10.2174/1381612826666200717090334
- 17. Dabagh M, Vasava P, Jalali P. Effects of severity and location of stenosis on the hemodynamics in human aorta and its branches. *Med Biol Eng Comput.* 2015;53(5):463–476. doi:10.1007/s11517-015-1253-3
- Chen X, Chu Y, Hou X, et al. Application of model-building based on arterial ultrasound imaging evaluation to predict CHD risk. Comput Math Methods Med. 2022;2022:4615802. doi:10.1155/2022/4615802
- 19. Farnier M, Zeller M, Masson D, Cottin Y. Triglycerides and risk of atherosclerotic cardiovascular disease: an update. Arch Cardiovasc Dis. 2021;114(2):132–139. doi:10.1016/j.acvd.2020.11.006
- Khan N, Khan J, Lyytikäinen L-P, Lehtimäki T, Laurikka J, Oksala N. Serum apolipoprotein A-I concentration differs in coronary and peripheral artery disease. Scand J Clin Lab Invest. 2020;80(5):370–374. doi:10.1080/00365513.2020.1746974
- Hsiao CH, Chen YC, Wang JH, Hsu BG. Serum angiopoietin-like protein 3 level is associated with peripheral arterial stiffness in patients with coronary artery disease. *Medicina*. 2021;57(10):1011. doi:10.3390/medicina57101011
- 22. Kusumastuti K, Jaeri S. The effect of long-term valproic acid treatment in the level of total cholesterol among adult. *Indian J Pharmacol*. 2020;52 (2):134–137. doi:10.4103/ijp.IJP\_655\_18
- 23. Li Z, Lan D, Zhang H, Zhang H, Chen X, Sun J. Electroacupuncture mitigates skeletal muscular lipid metabolism disorder related to high-fat-diet induced insulin resistance through the AMPK/ACC signaling pathway. *Evid Based Complement Alternat Med.* 2018;2018(1):7925842. doi:10.1155/ 2018/7925842
- Carr SS, Hooper AJ, Sullivan DR, Burnett JR. Non-HDL-cholesterol and apolipoprotein B compared with LDL-cholesterol in atherosclerotic cardiovascular disease risk assessment. *Pathology*. 2019;51(2):148–154. doi:10.1016/j.pathol.2018.11.006
- 25. Contois JH, Warnick GR, Sniderman AD. Reliability of low-density lipoprotein cholesterol, non-high-density lipoprotein cholesterol, and apolipoprotein B measurement. J Clin Lipidol. 2011;5(4):264–272. doi:10.1016/j.jacl.2011.05.004
- 26. Dong H, Zhang Y, Hu P, Wang J, Lu N. Serum apolipoprotein A1 rather than apolipoprotein B is associated with hypertension prevalence in Chinese people with coronary artery disease. *Blood Press Monit.* 2021;27(2):121–127. doi:10.1097/MBP.00000000000576
- Han SN, Yang WH, Yin JJ, Tao HL, Zhang LR. Drug treatment of hyperlipidemia in Chinese patients: focus on the use of simvastatin and ezetimibe alone and in combination. Am J Cardiovasc Drugs. 2019;19(3):237–247. doi:10.1007/s40256-018-00317-1
- Liu J, Qi Y, Zheng L, et al. Xinfeng capsule improves pulmonary function in ankylosing spondylitis patients via NF-KB-iNOS-NO signaling pathway. J Tradit Chin Med. 2014;34(6):657–665. doi:10.1016/s0254-6272(15)30079-0
- 29. Yang SS, Woo SY, Kim DI. Analysis of atherosclerotic plaque distribution in the carotid artery. *Clin Cardiol*. 2022;45(12):1272–1276. doi:10.1002/ clc.23903
- 30. van der Toorn JE, Rueda-Ochoa OL, van der Schaft N, et al. Arterial calcification at multiple sites: sex-specific cardiovascular risk profiles and mortality risk-the Rotterdam study. *BMC Med.* 2020;18(1):263. doi:10.1186/s12916-020-01722-7
- 31. Mohler ER 3rd, Sarov-Blat L, Shi Y, et al. Site-specific atherogenic gene expression correlates with subsequent variable lesion development in coronary and peripheral vasculature. *Arterioscler Thromb Vasc Biol.* 2008;28(5):850–855. doi:10.1161/ATVBAHA.107.154534
- 32. Kayashima Y, Maeda-Smithies N. Atherosclerosis in different vascular locations unbiasedly approached with mouse genetics. *Genes.* 2020;11 (12):1427. doi:10.3390/genes11121427
- 33. Fenning RS, Burgert ME, Hamamdzic D, et al. Atherosclerotic plaque inflammation varies between vascular sites and correlates with response to inhibition of lipoprotein-associated phospholipase A2. J Am Heart Assoc. 2015;4(2):e001477. doi:10.1161/JAHA.114.001477
- 34. Pan Y, Jing J, Cai X, et al. Prevalence and vascular distribution of multiterritorial atherosclerosis among community-dwelling adults in Southeast China. *JAMA Network Open*. 2022;5(6):e2218307. doi:10.1001/jamanetworkopen.2022.18307
- 35. Fernández-Friera L, Peñalvo JL, Fernández-Ortiz A, et al. Prevalence, vascular distribution, and multiterritorial extent of subclinical atherosclerosis in a middle-aged cohort: the PESA (progression of early subclinical atherosclerosis) study. *Circulation*. 2015;131(24):2104–2113. doi:10.1161/ CIRCULATIONAHA.114.014310
- 36. Denswil NP, van der Wal AC, Ritz K, et al. Atherosclerosis in the circle of Willis: spatial differences in composition and in distribution of plaques. *Atherosclerosis*. 2016;251:78–84. doi:10.1016/j.atherosclerosis.2016.05.047
- 37. Llopis G, Quinones S, Konschake M, et al. Atheromatosis of the brain-supplying arteries: circle of Willis, basilar, vertebral and their branches. Ann Anat. 2022;243:151941. doi:10.1016/j.aanat.2022.151941

- Wickström JE, Jalkanen JM, Venermo M, Hakovirta HH. Crural Index and extensive atherosclerosis of crural vessels are associated with long-term cardiovascular mortality in patients with symptomatic peripheral artery disease. *Atherosclerosis*. 2017;264:44–50. doi:10.1016/j. atherosclerosis.2017.07.023
- 39. Song M, Li N, Yao Y, Wang K, Yang J. Longitudinal association between serum uric acid levels and multiterritorial atherosclerosis. J Cell Mol Med. 2019;23(8):4970–4979. doi:10.1111/jcmm.14337
- 40. Pereira-da-Silva T, Napoleão P, Pinheiro T. The proinflammatory soluble cd40 ligand is associated with the systemic extent of stable atherosclerosis. *Medicina*. 2021;57(1):39. doi:10.3390/medicina57010039
- 41. Zhang YZ, Wang L, Zhang JJ, et al. Vascular peroxide 1 promotes ox-LDL-induced programmed necrosis in endothelial cells through a mechanism involving β-catenin signaling. *Atherosclerosis*. 2018;274:128–138. doi:10.1016/j.atherosclerosis.2018.04.031
- 42. Levy D, de Melo TC, Ruiz JLM, Bydlowski SP. Oxysterols and mesenchymal stem cell biology. *Chem Phys Lipids*. 2017;207(Pt B):223-230. doi:10.1016/j.chemphyslip.2017.06.009
- 43. Lemaire-Ewing S, Berthier A, Royer MC, et al. 7β-hydroxycholesterol and 25-hydroxycholesterol-induced interleukin-8 secretion involves a calcium-dependent activation of c-fos via the ERK1/2 signaling pathway in THP-1 cells: oxysterols-induced IL-8 secretion is calciumdependent. *Cell Biol Toxicol*. 2009;25(2):127–139. doi:10.1007/s10565-008-9063-0
- Maliukova NG. Effect of hyperlipidemia on the activity of renin-angiotensin-aldosterone system in patients with chronic cardiac insufficiency. Lik Sprava. 2004;2004(5–6):29–32. PMID: 15605816.
- 45. López-Melgar B, Fernández-Friera L, Oliva B, et al. Short-term progression of multiterritorial subclinical atherosclerosis. J Am Coll Cardiol. 2020;75(14):1617–1627. doi:10.1016/j.jacc.2020.02.026
- 46. Azarpazhooh MR, Najafi F, Darbandi M, Kiarasi S, Oduyemi T, Spence JD. Triglyceride/high-density lipoprotein cholesterol ratio: a clue to metabolic syndrome, insulin resistance, and severe atherosclerosis. *Lipids*. 2021;56(4):405–412. doi:10.1002/lipd.12302
- 47. Kitagami M, Yasuda R, Toma N, et al. Impact of hypertriglyceridemia on carotid stenosis progression under normal low-density lipoprotein cholesterol levels. J Stroke Cerebrovasc Dis. 2017;26(8):1793–1800. doi:10.1016/j.jstrokecerebrovasdis.2017.04.010
- 48. Wei Y, Qi B, Xu J, et al. Age- and sex-related difference in lipid profiles of patients hospitalized with acute myocardial infarction in East China. *J Clin Lipidol*. 2014;8(6):562–567. doi:10.1016/j.jacl.2014.09.006
- 49. Zhong Z, Liu J, Li B, et al. Serum lipid profiles in patients with acute myocardial infarction in Hakka population in southern China. *Lipids Health Dis.* 2017;16(1):246. doi:10.1186/s12944-017-0636-x
- 50. Patel S, Homaei A, Raju AB, Meher BR. Estrogen: the necessary evil for human health, and ways to tame it. *Biomed Pharmacother*. 2018;102:403–411. doi:10.1016/j.biopha.2018.03.078
- Guo Y, Zhao M, Bo T, et al. Blocking FSH inhibits hepatic cholesterol biosynthesis and reduces serum cholesterol. *Cell Res.* 2019;29(2):151–166. doi:10.1038/s41422-018-0123-6
- 52. Wang X, Magkos F, Mittendorfer B. Sex differences in lipid and lipoprotein metabolism: it's not just about sex hormones. *J Clin Endocrinol Metab*. 2011;96(4):885–893. doi:10.1210/jc.2010-2061
- Defreyne J, Van de Bruaene LDL, Rietzschel E, Van Schuylenbergh J, T'Sjoen GGR. Effects of gender-affirming hormones on lipid, metabolic, and cardiac surrogate blood markers in transgender persons. *Clin Chem.* 2019;65(1):119–134. doi:10.1373/clinchem.2018.288241
- 54. Fappi A, Mittendorfer B. Different physiological mechanisms underlie an adverse cardiovascular disease risk profile in men and women. Proc Nutr Soc. 2020;79(2):210–218. doi:10.1017/S0029665119001022
- 55. Wat LW, Chowdhury ZS, Millington JW, Biswas P, Rideout EJ. Sex determination gene transformer regulates the male-female difference in drosophila fat storage via the adipokinetic hormone pathway. *Elife*. 2021;10:e72350. doi:10.7554/eLife.72350
- 56. Mattina A, Giammanco A, Giral P, et al. Polyvascular subclinical atherosclerosis in familial hypercholesterolemia: the role of cholesterol burden and gender. Nutr, Metab Cardiovasc Dis. 2019;29(10):1068–1076. doi:10.1016/j.numecd.2019.06.015

International Journal of General Medicine

#### **Dove**press

Publish your work in this journal

The International Journal of General Medicine is an international, peer-reviewed open-access journal that focuses on general and internal medicine, pathogenesis, epidemiology, diagnosis, monitoring and treatment protocols. The journal is characterized by the rapid reporting of reviews, original research and clinical studies across all disease areas. The manuscript management system is completely online and includes a very quick and fair peer-review system, which is all easy to use. Visit http://www.dovepress.com/testimonials.php to read real quotes from published authors.

Submit your manuscript here: https://www.dovepress.com/international-journal-of-general-medicine-journal