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Is there a difference between aortic and brachial vein blood lipoprotein and total cholesterol levels?

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SUMMARY

OBJECTIVE: Atherosclerosis is a disease of the arteries that is not practically observed in veins. There are a lot of proposed mechanisms underlying this phenomenon. We aimed to compare the lipoprotein and total cholesterol levels in aortic and venous blood samples.

METHODS: A total of 125 patients ≥18 years of age were included in the study. After overnight fasting, we drew blood from the proximal ascending aorta and brachial vein. Serum lipid profiles were compared between these samples.

RESULTS: Out of 125 patients, 45 (36%) were females, and 80 (64%) were males. The mean age of the patients was 62 years (24–85 years). Notably, 39 (31%) patients were using statin treatment. Coronary angiography showed that 103 (82%) patients had coronary artery disease. Mean arterial total cholesterol (low-density lipoprotein), high-density lipoprotein, and triglyceride levels were significantly lower than mean venous total cholesterol, low-density lipoprotein, high-density lipoprotein, and triglyceride levels (187.3±45.3 mg/dL vs. 204.5±52.6 mg/dL, p<0.001; 116.7±41.5 mg/dL vs. 128±45 mg/dL, p<0.001; 40.8±12.9 mg/dL vs. 45.3±13.3 mg/dL, p<0.001; and 142.8±81.5 vs. 161.5±100.3 mg/dL, p<0.001, respectively).

CONCLUSION: Aortic lipoprotein and total cholesterol levels are significantly lower than venous lipoprotein and total cholesterol levels in patients presenting to the hospital for coronary angiography.

KEYWORDS: Lipoproteins. Atherosclerosis. Coronary angiography. Cholesterol.

INTRODUCTION

Atherosclerosis is a disease of the arteries and is practically not observed in venous structures except for saphenous veins, which carry arterial blood when used for coronary artery bypass grafting. There is no unequivocal explanation for this phenomenon. However, some proposed mechanisms are as follows: the differences between the hemodynamic loads observed in arteries and veins, the structural differences between these vessels, the differences in the lipid composition of arteries and veins, the receptor differences in the walls of the vessels, and the shear stress differences in arteries and veins.

The hemodynamic load hypothesis is the most accepted one. A study on this issue observed that when arteries were interposed to veins, they did not develop atherosclerosis and underwent atrophic remodeling in cholesterol-fed rabbits[1]. Also, in patients with coronary bypass grafting, increased hemodynamic load on the grafted vein was one of the most important mechanisms underlying vein graft atherosclerosis, besides many other factors[2].

The literature is poor regarding the comparison of lipoproteins between the arteries and veins. Suppose there is a meaningful difference between the lipoprotein levels in these vessels. In that case, this can explain the basis of the difference in atherosclerotic processes in veins and arteries. So, we planned an investigation of patients undergoing coronary angiography and tried to compare the levels of lipoproteins in aortic and brachial venous blood. We also compared the frequency of lipid metabolism disorders in aortic and venous blood samples.

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METHODS

All procedures performed in this study were in accordance with the ethical standards of the institutional and national research committees and with the 1964 Helsinki Declaration and its later amendments or comparable ethical standards. The study was approved by the Ethics Committee of Near East University, Cyprus.

A total of 125 patients hospitalized for coronary angiography procedures who were ≥18 years of age were included in the study. The indication for coronary angiography was acute coronary syndrome in 95 (76%) patients. There were no exclusion criteria. We drew blood from all patients after overnight fasting from the brachial vein and proximal ascending aorta during the coronary angiography procedure just before contrast material ingestion. Venous blood sampling was mostly done before aortic blood sampling, except for one patient. The time interval between blood samplings was less than 24 h in 80 (64%) patients, and it was more than 24 h in 45 (36%) patients. The blood samples were sent to a central laboratory, and the serum specimens were centrifuged, aliquoted, and stored at -80°C until the analysis time. At the end of the study, the lipid profile tests were analyzed on the Architect c8000 clinical chemistry system (Abbott Laboratories, Abbott Park, IL, USA). The low-density lipoprotein (LDL) concentration of all serum samples was measured by the direct method. We compared the lipid profile test results between the arterial and venous samples.

Statistical analysis

Statistical Package for the Social Sciences (SPSS), version 17.0, was used for the study's statistical evaluation. For the comparison of venous and arterial blood test results, paired samples t-test was used. The subgroup analyses (for sex, statin usage, and coronary artery disease status) of the venous and arterial blood sample results were again performed with paired samples t-test. The relationship between blood sample type and lipid metabolism disorders (hyperlipidemia, hypertriglyceridemia, and hipohigh-density lipoproteinemia) was analyzed with the Pearson chi-square test. A p-value <0.05 was considered significant.

RESULTS

Out of 125 patients, 45 (36%) were females, and 80 (64%) of them were males. The mean age of the patients was 62 years (24–85 years). Notably, 71 (57%) patients had a history of hypertension, whereas 36 (29%) were diabetic, and 39 (31%) patients were using statin treatment before enrollment in the study. As a result of the coronary angiography procedure, 103 (82%) patients were found to have coronary artery disease. Also, 30 (24%) patients had elective coronary angiography, whereas 95 (76%) patients had coronary angiography for acute coronary syndrome.

Mean arterial total cholesterol levels were significantly lower than mean venous total cholesterol levels (187.3±45.3 mg/dL vs. 204.5±52.6 mg/dL, p<0.001). The mean arterial LDL levels were also significantly lower than the mean venous LDL levels (116.7±41.5 mg/dL vs. 128±45 mg/dL, p<0.001). Mean arterial high-density lipoprotein (HDL) levels were also significantly lower than mean venous HDL levels (40.8±12.9 mg/dL vs. 45.3±13.3 mg/dL, p<0.001). Finally, mean arterial triglyceride levels were also found to be significantly lower than mean venous triglyceride levels (142.8±81.5 vs. 161.5±100.3 mg/dL, p<0.001) (Table 1). When the data was put into a subgroup analysis for the sex status of the patients, this subgroup analysis showed that the results did not change according to sex (Table 2). Another subgroup analysis was done for the statin usage status of the patients. This showed that statin users and non-users had reduced total cholesterol, LDL, and HDL levels in aortic blood compared with venous blood. Aortic triglyceride levels were significantly reduced compared to venous triglyceride levels in the statin non-user group, but in statin-users, aortic and venous triglyceride levels were not significantly different (Table 3). Moreover, we analyzed the data for coronary artery disease status according to coronary angiography, and this subgroup analysis showed that the results did not change according to the coronary artery disease status of the patients. Aortic lipoprotein and total cholesterol levels were lower than venous blood lipoprotein and total cholesterol levels, both in patients with coronary artery disease and in patients free of coronary artery disease.

When hyperlipidemia was defined as a serum total cholesterol level ≥200 mg/dL, according to aortic blood sample test results, 47 (38%) patients had hyperlipidemia. According to venous blood sample results, 64 (51%) patients had hyperlipidemia. Hypertriglyceridemia (defined as a serum triglyceride

Table 1. Lipoprotein and total cholesterol levels in aortic and venous blood.

Lipoprotein type	Blood type		p-value*
	Aortic	Venous	
Total cholesterol (mg/dL)	187.3±45.3	204.5±52.6	**<0.001**
LDL (mg/dL)	116.7±41.5	128.0±45.0	**<0.001**
HDL (mg/dL)	40.8±12.9	45.3±13.3	**<0.001**
Triglyceride (mg/dL)	142.8±81.5	161.5±100.3	**<0.001**

*Aortic lipoprotein and total cholesterol levels were significantly lower than venous lipoprotein and total cholesterol levels. HDL: high-density lipoprotein; LDL: low-density lipoprotein. Bold indicates statistically significant p-values.

level ≥150 mg/dL) was observed in 41 (33%) patients based on arterial blood sample results and in 58 (46%) patients based on venous sample results. Low HDL levels were defined as values <40 mg/dL for men and <50 mg/dL for women. Low HDL levels were detected in 76 (61%) patients according to arterial blood sample results and in 56 (45%) patients according to venous blood sample results. According to the Pearson chi-square test, all of the differences in lipid metabolism disorders (hyperlipidemia, hypertriglyceridemia, and hypohigh-density lipoproteinemia) were related to the blood sample type (p-values: 0.030, 0.028, and 0.011, respectively).

DISCUSSION

The present study's main finding is that all lipoproteins are found in lower amounts in aortic blood when compared with peripheral venous blood. The results do not change when stratified by sex or the coronary artery disease status of the patients. However, when we stratified the patient group for statin usage status, we observed that, in statin users, venous and aortic triglyceride levels were similar. In contrast, total cholesterol, HDL, and LDL levels were significantly lower in aortic blood than in venous blood. In statin non-users, total cholesterol levels and lipoproteins were lower in aortic samples than in venous samples.

Very few studies in the literature compare the lipoproteins of arteries and veins. In one of these studies, LDL was higher in aortic blood versus femoral venous blood; all other lipoproteins were similar[3]. This study also showed that when incubated with mouse peritoneal macrophages, arterial LDL, and very-low-density lipoprotein (VLDL) increased cholesterol accumulation and enhanced cholesterol esterification within these macrophages, whereas venous lipoproteins had less effect. They concluded that this difference in the function of venous and arterial lipoproteins might explain the atherosclerosis seen in arteries. Another historical study found that arterial HDL and triglyceride levels were lower when compared with venous blood. Also, arterial platelet activity was higher than venous platelet activity, which might serve as a mechanism for the atherosclerotic process in the arteries[4]. Another study compared the uptake and degradation of labeled LDL between arteries and veins. It showed that the uptake of LDL was similar between these vessels, but degradation was two times higher in the arteries compared to the veins[5]. They argued that this difference might be due

Table 2. Lipoprotein and total cholesterol levels in aortic and venous blood stratified for sex.

Sex	Blood type	Lipoprotein level (mg/dL)	p-value*
Female	Aortic total cholesterol	196.1	**<0.001**
	Venous total cholesterol	214.2	
	Aortic LDL	120.1	**<0.001**
	Venous LDL	135	
	Aortic HDL	46	**<0.001**
	Venous HDL	51.6	
	Aortic triglyceride	130.9	**0.016**
	Venous triglyceride	143.2	
Male	Aortic total cholesterol	182.3	**<0.001**
	Venous total cholesterol	199	
	Aortic LDL	114.7	**<0.001**
	Venous LDL	124.1	
	Aortic HDL	37.9	**<0.001**
	Venous HDL	41.8	
	Aortic triglyceride	149.5	**0.002**
	Venous triglyceride	171.8	

*Aortic lipoprotein and total cholesterol levels are lower than venous blood lipoprotein and total cholesterol levels both in female and male patients. HDL: high-density lipoprotein; LDL: low-density lipoprotein. Bold indicates statistically significant p-values.

Table 3. Lipoprotein and total cholesterol levels in aortic and venous blood stratified for statin usage.

Statin usage	Blood type	Lipoprotein level (mg/dL)	p-value*
Yes	Aortic total cholesterol	165.6	**<0.001**
	Venous total cholesterol	177.2	
	Aortic LDL	93.8	**0.002**
	Venous LDL	103.2	
	Aortic HDL	42.5	**<0.001**
	Venous HDL	46.7	
	Aortic triglyceride	133.1	0.204
	Venous triglyceride	140.1	
No	Aortic total cholesterol	198.2	**<0.001**
	Venous total cholesterol	218.3	
	Aortic LDL	128.5	**<0.001**
	Venous LDL	140.4	
	Aortic HDL	39.8	**<0.001**
	Venous HDL	44.4	
	Aortic triglyceride	149.4	**<0.001**
	Venous triglyceride	174.3	

*Aortic lipoprotein and total cholesterol levels are lower than venous blood lipoprotein and total cholesterol levels both in statin users and non-users, except for triglyceride levels in statin users. In statin users, aortic and venous triglyceride levels are not significantly different. HDL: high-density lipoprotein; LDL: low-density lipoprotein. Bold indicates statistically significant p-values.

to increased plasmalemmal vesicles, which work in the endocytosis of LDL through the vessel wall in the endothelium of large arteries compared to large veins[6].

These studies were ancient and also enrolled very few patients. The results were inconclusive. So, we tried to compare the lipoprotein levels in aortic and venous blood samples in a broader patient population presenting to the hospital for coronary angiography. The levels of arterial lipoproteins and total cholesterol levels were significantly lower than their venous counterparts. Mainly, the patients were not using statins at the time of enrollment in the study. However, in 31% of the patients who were using statins, total cholesterol, LDL, and HDL levels were reduced in the arterial blood. In contrast, triglyceride levels were not significantly different between arterial and venous samples.

The results are new and may be similar to the historical study in 1989[4]. There is no proven mechanism that may explain the difference in lipoprotein levels between arteries and veins. The most plausible mechanism underlying this phenomenon may be the differences in receptors in the aortic and venous walls. We know that LDL enters the arterial wall through endocytosis (to the arterial endothelium) and transcytosis (directly to the arterial wall beneath the endothelium). Some receptors and ligands are found in the arterial endothelium that work for this process, like the LDL receptor, scavenger receptor B1 (SR-B1), CD36, activin-like kinase 1 (ALK1), and so on, which transfer LDL from the lumen to the arterial wall through endocytosis and transcytosis[7-11]. The SR-B1 receptor was found much more abundantly in atherosclerotic regions of arteries relative to normal arterial regions[7]. These receptors may be found much less frequently in the venous wall. Nevertheless, this is just a hypothesis that needs to be proved. A historical study in rats has shown that the endothelium of large arteries contains about twice as many plasmalemmal vesicles as that of large veins[12]. More lipoproteins entering the vessel wall may explain the lower levels in the arterial lumen. There are also studies comparing the structures of arterial and venous grafts to understand the difference in atherosclerosis development in these conduits. One of these studies showed that arterial grafts undergo less lipid synthesis, slower lipid uptake, and more lipid lipolysis[13]. This is not a direct comparison between normal arteries and veins because venous grafts are prone to atherosclerosis due to increased hemodynamic load after the grafting procedure, and they carry arterial blood. However, it may give an opinion about the differences in lipid metabolism in arteries and veins, which need further studies to be elucidated. If the receptor hypothesis underlying low levels of aortic lipoproteins is true, more lipoproteins enter the aortic wall, which supports the atherosclerotic process seen in arteries.

As a result of the lower total cholesterol, LDL, HDL, and triglyceride levels in aortic blood, the frequency of lipid metabolism disorders was also significantly different in aortic blood and venous blood. Of course, the abnormal values used to define lipid metabolism disorders were traditionally derived from venous blood samples. So, this may not mean that these levels are also abnormal in aortic blood because we do not know the average lipoprotein values in aortic blood. This brings up the question: which one is more predictive for future cardiovascular events, venous or arterial lipoprotein levels? We do not know the answer because this has never been tested before. However, when we think of atherosclerosis as an arterial process, one can guess that arterial lipoprotein levels may matter more than their venous counterparts. We hope that this question can be answered in the future.

On the contrary, taking venous blood samples from patients or healthy people to check their cholesterol levels is much easier and more feasible than taking arterial blood samples. Moreover, using drugs for patients with lipid metabolism disorders will probably also lower arterial lipoprotein levels, as was the case in our study. However, arterial blood sampling may be used primarily for high-risk patients if arterial lipoprotein levels foresee future cardiovascular events better than venous lipoprotein levels. We think these are the future implications of the present study.

Limitations of the study

The main limitation of the present study is the time interval between aortic and venous blood sampling. Venous blood sampling was mostly done before aortic blood sampling due to angiography laboratory conditions. Another limitation may be the place where the venous blood was taken. The brachial vein is a peripheral vein, whereas the aorta is a central arterial site. So, we compared blood samples between central blood and a peripheric blood sample site. Moreover, the patient population may be seen as a small sample for this kind of study. Finally, statin usage may have affected the results, but the results were mostly similar between statin users and non-users.

CONCLUSION

Aortic lipoprotein and total cholesterol levels are significantly lower than venous lipoprotein and total cholesterol levels in a patient population presenting to the hospital for coronary angiography.

AUTHORS' CONTRIBUTIONS

UY: Conceptualization, Data curation, Investigation, Methodology, Resources, Writing – original draft. **LC:** Data curation, Project administration, Supervision, Validation, Writing – review & editing. **BY:** Data curation, Formal Analysis, Resources, Validation. **SU:** Conceptualization, Data curation, Formal Analysis, Resources. **EC:** Conceptualization, Data curation, Investigation, Methodology, Project administration, Resources. **OHE:** Data curation, Formal Analysis, Methodology, Resources. **OA:** Conceptualization, Formal Analysis, Supervision, Project administration, Writing – review & editing. **HD:** Conceptualization, Project administration, Supervision, Writing – review & editing.

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