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Intima–media complex thickness and carotid atherosclerotic plaque formation in Lublin's population in the context of selected comorbidities

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carotid intima–media thickness, atherosclerotic plaque, Doppler ultrasound, carotid artery, common

Abstract

Introduction: Atherosclerosis (arteriosclerosis) is a chronic arterial disease of the arteries with chronic inflammatory. The pathology of atherosclerosis is complex, and the atherosclerotic process is multi-factorial, not fully understood. Risk factors of atherosclerotic lesions may include: lipid disorders, hypertension or diabetes. One of the diagnostic methods of discovering atherosclerosis covers the assessment of the intima–media complex thickness by Doppler ultrasonography. **Aim:** The aim of this report was an evaluation of the relationships between intima–media complex thickness in the right and left carotid arteries and the occurrence of atheromatous plaque in the Lublin population with respect to three possible concomitant medical conditions, mentioned above. **Material and methods:** A group of 121 subjects was included into the study, all of the participants being residential inhabitants of the Lublin Voivodship. All the participating patients were requested to fill in a questionnaire. After that, the patients were submitted to Doppler sonography concentrated on intima–media complex thickness evaluation. The occurrence of atheromatous plaque was also assessed in obtained sonographic images. **Results:** There were statistically significant differences for the intima–media complex thickness and for the atheromatous plaque according to all of the reported diseases: hypocholesterolaemia, hypertension and diabetes. Conclusions: The present study confirms that there is a relationship between the thickness of the intima–media complex in the right and left carotid arteries as well as the occurrence of the atherosclerotic plaque regarding the coexistence of specific disease entities in the subjects of the Lublin population.

Introduction

Atherosclerosis (arteriosclerosis) is a chronic degenerative inflammatory disease of the arteries. Progressive atherosclerotic process leads to the formation of plaque inside the vessel, which results in the narrowing of the vessel lumen, limited blood flow and ischemia. Currently, the disease is increasingly linked with the lifestyle in highly-developed countries[1]. Risk factors for atherosclerotic lesions may include lipid disorders (hyperlipidemia, e.g. hypercholesterolemia), hypertension and diabetes.

Hyperlipidemia is the major modifiable factor responsible for atherosclerosis and its cardiovascular complications. Lipid profile shows elevated total cholesterol levels, which are accompanied by an increase in low-density lipoprotein (LDL) cholesterol (the "bad" cholesterol), and a decrease in high density lipoprotein cholesterol (HDL) (the "good" cholesterol). Studies assessing angiographic changes in cardiovascular patients have shown that LDL cholesterol plays a crucial and negative role in the pathogenesis of atherosclerosis[2]. There is also a close reverse relationship between HDL cholesterol levels and the risk of cardiovascular events – the lower the HDL cholesterol, the higher the cardiovascular risk[3].

Hypertension is defined as an increase in systolic and diastolic blood pressure above normal values. Systolic blood pressure is as strong a coronary risk factor as diastolic blood pressure. Similarly, isolated systolic blood pressure is currently considered as a primary risk factor for coronary heart disease and stroke[2].

Diabetes is a common chronic disease affecting the human population. Serious metabolic disorders of carbohydrates, fats and proteins develop in the course of diabetes due to dysfunction of insulin, a pancreatic hormone responsible for lowering blood glucose levels. The consequences of long-term persistence of high blood glucose levels include severe disorders in the form of diabetic micro- and macroangiopathies. Diabetic microangiopathies are pathologies in small blood vessels, whereas macroangiopathies are adverse changes in large vessels (arteries and veins), which can lead to accelerated development of arteriosclerosis[4–6].

Over the last dozen or so years, there has been tremendous progress in diagnostics and, consequently, effective treatment of cardiovascular diseases. Doppler ultrasonography (US) is becoming an increasingly used non-invasive vascular imaging technique as well as one of the most useful and effective methods for detecting and monitoring of the first pathological structural changes in arteries before the onset of symptoms. An assessment of the thickness of the middle and inner layers of the arteries, especially the jugular veins, and the assessment of intima-media complex (IMC) thickness are the essence of Doppler US. Most often, accessible segments of the common carotid artery (CCA) are assessed. It is believed that the thickness of the IMC is an important indicator of the risk of cardiovascular events, as the thickening of the carotid intima may suggest an early stage of atherosclerosis in the absence of specific disease symptoms[7–9].

The primary aim of the study was to evaluate the relationships between IMC thickness in right and left CCA and the presence of atheromatous plaque in Lublin's population in the context of three potential comorbidities (hypercholesterolemia, hypertension, diabetes).

Materials and methodology

A total of 121 randomly selected subjects (males n = 54; 44.63%; females n = 67; 55.37%) from Lublin Voivodeship were included in the study.

The mean age of patients was under 53 years. The mean age was 54 years for women, and 51 years for men. The youngest patients were 18 years old. The oldest woman was

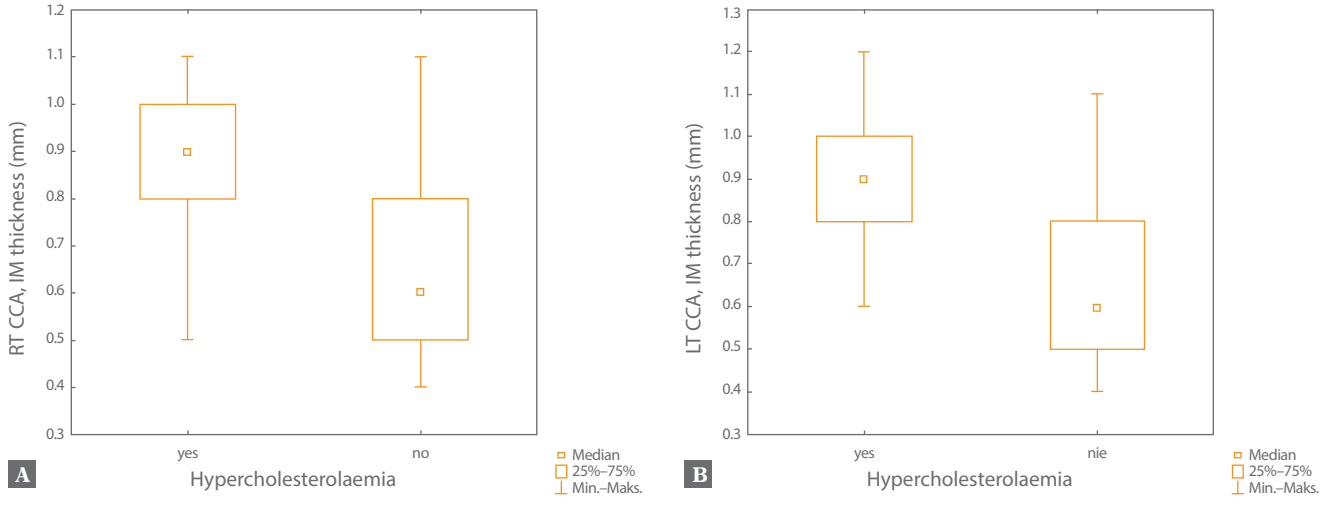

Fig. 1. *The thickness of IMC in RT CCA (***A***) and LT CCA (***B***) in elevated cholesterol levels*

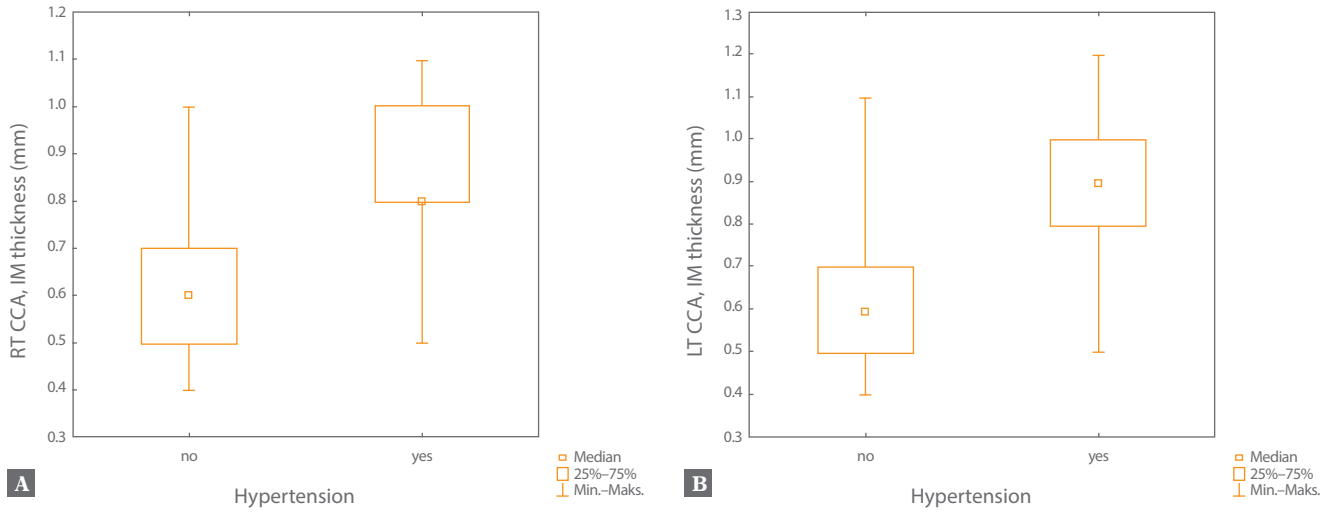

Fig. 2. *The thickness of IMC in RT CCA (***A***) and LT CCA (***B***) in hypertension*

76 years old, while the oldest man was 82 years old. Half of the women surveyed were up to 56 years old and half of the men were up to 53 years old (Tab. **1**). All participants were asked to complete a questionnaire. The questionnaire included, among other things, questions concerning comorbidities (hypercholesterolemia, hypertension, diabetes).

Sonographic scanning of carotid arteries was performed in the Department of Interventional Radiology and Neuroradiology of the Medical University of Lublin with the Logiq 7 scanner, using a linear, HD, 6–12 MHz transducer. Each ultrasound examination was performed by the same experienced person.

	n	*x* ± SD	Me ($Q_1 - Q_3$)	Min.	Max.
Female	67	54.03 ± 14.40	56 (45 – 65)	18	76
Male	54	51.06 ± 16.18	53 (39 – 64)	18	82
Total	121	52.70 ± 15.23	54 (42 – 65)	18	82

Tab. 1. *Age of the subjects*

CCA IMC thickness was assessed 1 to 2 cm below the bifurcation for both: left (LT) and right (RT) carotid arteries. All IMC measurements were performed on the posterior wall under optimal imaging conditions, i.e. with zoom options and the focus placed at the depth of exactly posterior wall.

The StatSoft, Inc. (2014). STATISTICA (data analysis software system), version 12 (www.statsoft.com.program) was used for statistical analysis. A p-value < 0.05 was considered statistically significant.

The normality of the distribution for a quantitative variable was tested with the Shapiro-Wilk W test. Since the normality of the distribution was rejected, the comparisons of the results between two groups were performed with the Mann-Whitney U test. The Pearson's Chi^2 test was used to determine the independence of two nominal variables.

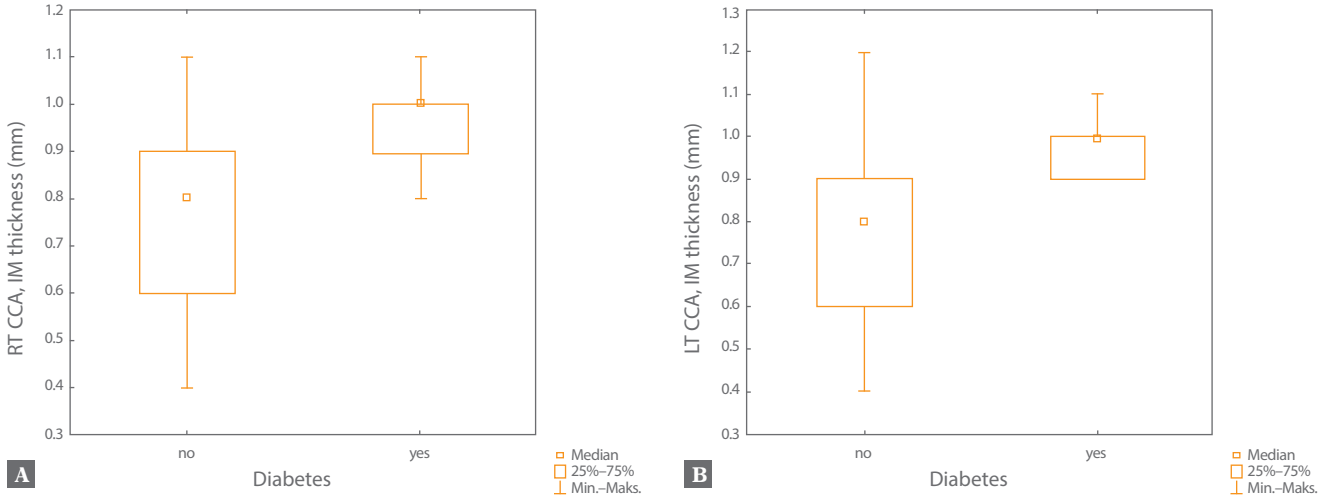

Fig. 3. *The thickness of IMC in RT CCA (***A***) and LT CCA (***B***) in diabetes*

Results

IMC thickness in RT/LT CCA

In the case of hypercholesterolemia (Fig. 1), hypertension (Fig. 2), and diabetes (Fig. 3), the difference in IMC thickness (RT/LT CCA) was statistically significant (patients without diagnosis vs. patients with a diagnosed disease). In all cases, the IMC thickness was higher in patients diagnosed with the discussed diseases (in each case $p < 0.001$ for RT/LT CCA) (Tab. 2).

Atheromatous plaque formation and diagnosed disease entities in the study population

Based on medical history, the possibility of a relationship between the diseases and the presence of carotid artery plaque was assessed in all subjects in the study group. Highly significant correlations were found between the atherosclerotic plaque and hypercholesterolemia, hypertension and diabetes (in each case $p < 0.001$).

Statistical analyses showed a highly significant relationship between the atherosclerotic plaque in ultrasonography and abnormal cholesterol levels. No atherosclerotic plaque was detected in almost 90% of patients ($n = 52$; 89.66%) without elevated cholesterol levels, as opposed to over half of those with elevated cholesterol ($n = 33$; 52.38%).

Likewise, the analysis showed a statistically significant correlation between atherosclerotic plaque and hypertension. No carotid artery atherosclerosis was diagnosed in patients without hypertension – up to 91.11% ($n = 41$).

A highly statistically significant correlation with plaque formation was also found among diabetic patients. While 86.67% ($n = 13$) of diabetic patients had ultrasonographically confirmed atherosclerotic plaque, three quarters ($n = 80$, 75.47%) of non-diabetic patients were free of atherosclerotic plaque (Tab. 3).

Discussion

CCA IMC thickness, atherosclerotic plaque and dyslipidemia

We also investigated the relationship between the thickness of IMC in RT/LT CCA, and the presence of atherosclerotic plaque and dyslipidemia in the study population.

In the group of patients with lipid metabolism impairment in the form of elevated total cholesterol, the IMC thickness of RT/LT CCA was statistically significantly higher compared to those with normal total cholesterol levels. Additionally, a relationship between plaque and cholesterol dysfunction was demonstrated. In the group of patients who did not declare cholesterol disorders, almost 90% were not diagnosed with atherosclerotic plaque.

The available literature data also indicates that there is a close relationship not only between serum levels of total cholesterol, but also between individual lipid fractions and IMC thickness[10–14]. Kunicka *et al*.[12] showed a statistically significant correlation between IMC thickness and HDL fraction only. A similar relationship between HDL values and IMC thickness was described in the Rotterdam study[15]. Moreover, this correlation was

	A disease		No disease		Statistical analysis
	$x \pm SD$	Me ($Q_1 - Q_3$)	$x \pm SD$	Me ($Q_1 - Q_3$)	
Hypercholesterolaemia					
	$n = 63$; 52.07%		$n = 58$; 47.93%		
RT CCA	0.87 ± 0.13	0.9 (0.8 – 1.0)	0.66 ± 0.16	0.6 (0.5 – 0.8)	$Z = 6.48$; $p < 0.001$
LT CCA	0.89 ± 0.13	0.9 (0.8 – 1.0)	0.65 ± 0.17	0.6 (0.5 – 0.8)	$Z = 6.86$; $p < 0.001$
Hypertension					
	$n = 76$; 62.81%		$n = 45$; 37.19%		
RT CCA	0.86 ± 0.13	0.8 (0.8 – 1.0)	0.61 ± 0.14	0.6 (0.5 – 0.7)	$Z = -7.03$; $p < 0.001$
LT CCA	0.86 ± 0.14	0.9 (0.8 – 1.0)	0.62 ± 0.17	0.6 (0.5 – 0.7)	$Z = -6.56$; $p < 0.001$
Diabetes					
	$n = 15$; 12.40%		$n = 106$; 87.60%		
RT CCA	0.95 ± 0.08	1.0 (0.9 – 1.0)	0.74 ± 0.17	0.8 (0.6 – 0.9)	$Z = -4.31$; $p < 0.001$
LT CCA	0.98 ± 0.08	1.0 (0.9 – 1.0)	0.74 ± 0.18	0.8 (0.6 – 0.9)	$Z = -4.75$; $p < 0.001$

Tab. 2. *IMC thickness (mm) in RT CCA and LT CCA for the diagnosed disease. Mann Whitney* U *test*

	No atheromatous plaque *n* = 82; 67.77%	Present atheromatous plaque *n* = 39; 32.23%	Statistical analysis
Hypercholesterolaemia			
No *n* = 58	*n* = 52; 89.66%	*n* = 6; 10.34%	$\chi^2 = 24.43$ $p < 0.001$
Yes *n* = 63	*n* = 30; 47.62%	*n* = 33; 52.38%	
Hypertension			
No *n* = 45	*n* = 41; 91.11%	*n* = 4; 8.89%	$\chi^2 = 17.87$ $p < 0.001$
Yes *n* = 76	*n* = 41; 53.95%	*n* = 35; 46.05%	
Diabetes			
No *n* = 106	*n* = 80; 75.47%	*n* = 26; 24.53%	$\chi^2 = 20.47$ $p < 0.001$
Yes *n* = 15	*n* = 2; 13.33%	*n* = 13; 86.67%	

Tab. 3. *Atheromatous plaque vs. hypercholesterolemia, hypertension and diabetes. Pearson's χ^2 test*

also significant after including the factor of patient's age. In patients over 40 years of age, a relatively low level of HDL fraction was associated with higher IMC thickness. However, such a correlation was not found in those under the age of 40 years. Interestingly, regardless of age, the lowest IMC thickness oscillated within the optimal HDL range, which could be attributed to the protective effects of the "good" cholesterol on the cardiovascular system. Furthermore, the authors suggest that low HDL levels are a risk factor for cardiovascular disease in the context of organ damage (IMC thickening), and become significant only after a certain age limit has been exceeded[12].

CCA IMC thickness, atherosclerotic plaque and diabetes

The present study also investigated the relationship between the thickness of RT/LT CCA, IMC and the presence of atherosclerotic plaque and diabetes in the study population. In diabetic patients, the values of CCA IMC thickness were statistically significantly higher in both arteries compared to non-diabetic patients.

There was also a statistically significant relationship between atherosclerotic plaque and diabetes. In the diabetic group, over 86.67% of patients (n = 13) were diagnosed with atherosclerotic plaque based on the ultrasound image. In contrast, no atherosclerotic plaque was found in 75.47% (n = 80) of individuals without diabetes.

The relationship between carbohydrate disorders and IMC thickness has already been described by many authors[12,16–19]. Most of available data concerns patients with already diagnosed diabetes, but less is mentioned about the relationship between IMC thickness and impaired glucose tolerance. Taniwaki *et al*.[16] demonstrated that the thickness of IMC was statistically significantly higher in diabetic subjects than those with proper glucose metabolism. The authors also highlighted the relationship between the duration of diabetes and the thickness of the IMC. Wagenknecht *et al*.[18] demonstrated not only the correlation between IMC thickening and the incidence of diabetes, but also the relationship between the prevalence of impaired pre-diabetes glucose tolerance and the IMC thickness.

There is little data available that would describe the possible correlation between IMC thickness and glycemia. Kunicka *et al*.[12] did not show a statistically significant relationship between these parameters, but such significance appears when the relationships between IMC thickness and the age and glycemia are assessed. Therefore, it can be suggested that, in addition to glucose intolerance or diabetes, abnormal glycemic levels indicating carbohydrate disorders may affect the thickness of the IMC.

The thickness of CCA IMC, atherosclerotic plaque and hypertension

The present study further investigated the correlation between the thickness of IMC in RT/LT CCA and the diagnosis of atherothrombotic plaque and hypertension in patients. In hypertensive patients, the IMC thickness in RT/LT CCA was significantly higher compared to those with normal blood pressure.

Also, a statistically significant correlation was found between the presence of atherosclerotic plaque and hypertension. No carotid artery plaque was found in almost all individuals in the group without diagnosed hypertension.

The relationship between IMC thickness and the prevalence of hypertension has been confirmed previously[20–22]. Both higher systolic blood pressure and the duration of hypertension closely correlate with higher IMC thickness. In the group of hypertensive patients, age and systolic blood pressure were the strongest determinants of IMC thickness[23,24]. In the above context, the findings presented by Gariepa *et al*.[25], who compared the thickness of the IMC between the group of untreated hypertensive men and a healthy male group, appear to be relevant. The relationship between IMC thickness and age was observed only for normotensive subjects (with normal blood pressure), which again confirms that age is the only determinant of IMC thickness values in healthy individuals. Similar results were reported by Kunicka *et al*.[12], who assessed a group of subjectively healthy men and found no statistically significant relationships between blood pressure value and IMC thickness.

Considering the above cited literature data as well as the results obtained in this work, the IMC thickness assessment plays an important role in hypertensive individuals. Recommendations of the Polish Society of Hypertension emphasize, among other things, the need to perform this type of assessment when evaluating the risk of cardiovascular events in patients with hypertension. The European Societies of Hypertension and Cardiology recommend measuring the IMC thickness in hypertensive patients, with IMC thickness of > 0.9 mm as an indication of organ damage[26].

Conclusion

The present study investigated the relationship between RT/LT CCA IMC thickness and the diagnosis of atherosclerotic plaque and the coexistence of certain diseases in patients from Lublin's population. We found:

- statistically significant differences in RT/LT CCA IMC thickness for lipid metabolism disorders (increased total cholesterol levels), carbohydrate metabolism disorders (diabetes), hypertension;
- a statistically significant relationship between atheromatous plaque formation and the discussed diseases.

This work confirms the importance of measuring the IMC thickness.

Conflict of interest

The authors declare that there is no conflict of interest regarding the publication of this paper.

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