ORIGINAL ARTICLE

Carotid artery stenosis and ultrasound vascular indices predict coronary revascularization in patients with high cardiovascular risk scheduled for coronary angiography

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KEY WORDS
carotid artery stenosis, coronary revascularization, extra-media thickness, intima-media thickness, PATIMA index

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ABSTRACT

BACKGROUND Carotid artery atherosclerosis is a complex and multifactorial chronic disease.

AIMS We aimed to assess the predictive value of cardiovascular (CV) risk factors, carotid artery stenosis (CAS), and ultrasound vascular indices for coronary revascularization in patients referred for coronary angiography.

METHODS Patients scheduled for elective coronary angiography were enrolled. The following ultrasound indices were obtained: CAS, carotid intima-media thickness (IMT), extra-media thickness (EMT), intra-abdominal thickness (IAT), and the combined PATIMA index.

RESULTS The study included 322 patients (118 women, 204 men) with CV risk factors (mean [SD] number, 5.4 [1.5]) and coronary artery disease (n = 228; 71%) with equal rates of 1-, 2-, and 3-vessel disease (35%, 33%, and 32%, respectively). Indications for percutaneous or surgical coronary revascularization were reported for 158 patients (49%). Patients with and without revascularization had a similar total number of CV risk factors (mean [SD], 5.4 [1.3] vs 5.3 [1.1]; $P = 0.9$) and IAT (mean [SD], 74 [24] mm vs 77 [28] mm; $P = 0.4$). The receiver operating characteristic (ROC) curve analysis showed that baseline CAS, carotid IMT, EMT adjusted for body mass index, and PATIMA index have a similar significant predictive value for coronary revascularization (mean [SD] area under the ROC curve, 610 [31] u, 590 [31] u, 610 [32] u, and 630 [30] u, respectively).

CONCLUSIONS The severity of CAS and carotid vascular indices (IMT, EMT, and PATIMA index) may predict coronary revascularization in patients with high or very high CV risk. Clinical assessment and the presence of CV risk factors do not add predictive value in these patients.

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INTRODUCTION Coronary artery disease (CAD) is a complex multifactorial disease, which involves genetic predisposition and numerous cardiovascular (CV) risk factors.[1] Despite a large body of evidence from several studies, all the diagnostic pathways recommended in the current guidelines[2] are suboptimal, which constitutes a disadvantage in everyday clinical practice. Clinical assessment based only on CV risk factors has a moderate prognostic value, and there is a need for improving outcome prediction.

Carotid artery ultrasound is a relatively simple method used worldwide for diagnostic screening for atherosclerosis. Carotid arteries are so close to the probe that we can obtain a precise view of the lumen and carotid wall, which enables the assessment of carotid artery stenosis (CAS) and wall indices.[3] Carotid intima-media thickness (IMT) is the main vascular index, with a large body of evidence showing its association with atherosclerosis and CV diseases.[4-7] It is currently used as a noninvasive

WHAT'S NEW?

A total number of clinical risk factors is the basis for cardiovascular (CV) risk estimation, but it does not predict the need for coronary revascularization in patients with at least high CV risk. Carotid artery stenosis, carotid wall parameters (intima-media thickness and extra-media thickness indexed for body mass index), and the combined PATIMA index provide similar significant predictive values for coronary revascularization. To the best of our knowledge, this is the first study showing a predictive value of the main vascular indices for coronary revascularization and not only for the presence or severity of coronary artery disease.

screening tool for early atherosclerosis and CV risk in patients with a few risk factors.[8] Given that atherosclerosis is a multifactorial disease, recently new indices, related mainly to perivascular fat, have been developed: carotid extra-media thickness (EMT)[9-11] and the combined vascular index PATIMA (Periarterial Adipose Tissue Intima Media Adventitia).[12] Previous studies showed that CAS,[13,14] carotid IMT,[4-7] carotid EMT,[12,15] and PATIMA index[12] are associated with the presence or severity of CAD.

All the ultrasound indices used in our research are more or less related to vascular risk. However, given that they correspond to different anatomical structures and tissues, they may also provide independent and additional predictive value. Major imaging indices, including carotid IMT and carotid plaques, are considered in the current European guidelines on CV disease prevention as CV risk modifiers.[16] However, the authors emphasized some limitations and the lack of studies showing a link between the imaging indices and treatment outcomes or clinical prognosis.[16] It was suggested that associations only with the anatomical features of CAD or increased CV risk reported in previous studies are not strong enough to recommend ultrasound indices in clinical practice.[16] Therefore, there is a need for evidence showing that some of the indices can predict the outcomes of treatment (pharmacologic or interventional) or help modify the treatment strategy (eg, modification of pharmacotherapy based on an ultrasound index).

Given the current data[16] and ethical considerations, there is a low probability for conducting a prospective randomized study with a long-term follow-up and different CV pharmacotherapies based on baseline ultrasound measures. Thus, we aimed to assess a predictive value of CV risk factors, CAS, and ultrasound vascular indices for coronary revascularization in patients with high and very-high CV risk who are referred for coronary angiography.

METHODS All consecutive patients (age range, 45–80 years) scheduled for coronary angiography in the years 2016 and 2017 at the Department of Cardiology (Medical University of Silesia, Katowice, Poland) were screened for the presence of the exclusion criteria listed below. A total of 322 patients were enrolled in this prospective study. The study protocol included the assessment of clinical characteristics, examination of ultrasound indices, and complete coronary angiography performed during the index hospitalization. All the clinical data, ultrasound indices, and coronary angiograms were obtained and analyzed by different investigators, blinded to patient names and other results. The indication for coronary revascularization was established according to the European Society of Cardiology (ESC) guidelines,[17] and the decision was at the discretion of interventional cardiologists. For the purpose of this study, coronary revascularization was defined as percutaneous or surgical coronary revascularization regardless of the type of the procedure.

The main exclusion criteria were as follows: acute coronary syndrome, heart failure or left ventricular systolic dysfunction, severe heart valve disease (with referral for cardiac surgery), severe chronic inflammatory diseases, active malignancy, significant liver failure, severe chronic kidney disease (estimated glomerular filtration rate <15 ml/min/1.73 m^2 or dialysis), surgery or radiotherapy within the region of interest (neck or abdomen), and known diagnosis of genetic predisposition to CV diseases.

The study protocol was approved by the ethics committee at the Medical University of Silesia.

Clinical assessment The clinical assessment and CV risk evaluation were based on the ESC guidelines.[18] Hypertension was determined based on blood pressure measurements or a prior diagnosis and current treatment. Dyslipidemia, diabetes, and obesity were defined as previously described.[18-20] Coronary artery disease was defined as a stenosis of 50% or greater in any major coronary artery (left main, left anterior descending, circumflex, and right coronary arteries). Peripheral artery disease was determined based on a prior diagnosis or treatment, ultrasound examination, or a history of typical symptoms (eg, intermittent claudication).

Ultrasound indices All ultrasound images were recorded by a single experienced investigator using the same settings. Once the recruitment was completed, single clips showing only the region of interest were randomly analyzed offline by one observer blinded to patient data. All the ultrasound indices were obtained using a high-resolution ultrasound (GE Vivid 9, Milwaukee, Wisconsin, United States) with a linear transducer (9–12 MHz) for carotid arteries (CAS, IMT, EMT), echocardiography transducer (1.5–4.5 MHz) for epicardial fat thickness, and abdominal transducer

TABLE 1 Clinical characteristics of the study group

Parameter		Value
Age, y, mean (SD)		61 (7.3)
Sex, female / male		118 (36) / 204 (64)
Diabetes		118 (36)
Lipid-lowering treatment		322 (100)
LDL-C, mg/dl, mean (SD)		101 (37)
HDL-C, mg/dl, mean (SD)		45 (13)
Triglycerides, mg/dl, mean (SD)		141 (83)
Hypertension		322 (100)
Smoking[a]		230 (71)
Overweight / obesity		109 (33) / 160 (49)
Risk factors[b], mean (SD)		5.4 (1.5)
Family history of CAD		122 (38)
Previous myocardial infarction		41 (12)
Previous coronary PCI / CABG		46 (14) / 0
Peripheral artery disease		77 (24)
CAD ≥50% stenosis		228 (71)
CAD	1-vessel	81 (35)
	2-vessel	76 (33)
	3-vessel	71 (32)
Coronary revascularization[c]		158 (49)

Data are presented as number (percentage) unless otherwise indicated.

a Current smoking or smoking in the past for at least 1 year

b Male sex, age >55 y, hypertension, hyperlipidemia, obesity, type 2 diabetes, chronic kidney disease, smoking

c Percutaneous or surgical coronary revascularization at the index hospitalization

SI conversion factors: to convert LDL-C and HDL-C to mmol/l, multiply by 0.0259.

Abbreviations: CABG, coronary artery bypass grafting; CAD, coronary artery disease; HDL-C, high-density lipoprotein cholesterol; LDL-C, low-density lipoprotein cholesterol; PCI, percutaneous coronary intervention

(3.5 MHz) for abdominal visceral fat (intra-abdominal thickness [IAT]).

Ultrasound indices were obtained and measured according to the guidelines[10,21-23] and as precisely described in our previous study with intra- and interobserver variability and coefficients of variation.[10] The combined PATIMA index was first developed and proposed in our previous research.[12] In the current study, it was calculated using the same formula: PATIMA [u] = (EMT/BMI × 35) + IMT + (EFT × 60), where EMT/BMI denotes EMT adjusted for body mass index (BMI). All single ultrasound measures represent different tissue components of the arterial wall and provide a different component of a patient's CV risk.

Statistical analysis Data were expressed as means with SD, number and percentage, or area under the curve values with standard error. Data with normal distribution were analyzed with the Kolmogorov–Smirnov test. Baseline clinical parameters or the ultrasound measures were compared between the subgroups using the *t* test for normally distributed continuous variables. In the case of nonnormal distribution, the Mann–Whitney test was used. A multiple comparison analysis was conducted using the analysis of variance (ANOVA) with the Bonferroni correction. Prior to the ANOVA test, the Levene test for equality of variances was performed. The differences between the subgroups were analyzed using 1-way ANOVA. To determine the best cutoff value for individual ultrasound indices, the receiver operating characteristic (ROC) curves were used, providing sensitivity, specificity, and optimal predictive values for coronary revascularization. A *P* value of less than 0.05 was considered significant. Statistical analysis was conducted using the MedCalc v 18.5 software (MedCalc, Ostend, Belgium).

RESULTS

Clinical characteristics of the study group The clinical characteristics of patients are presented in TABLE 1. The study group included 322 patients (118 women and 204 men; mean [SD] age, 61 [7] years). Hypertension and dyslipidemia were reported in 100% of patients; obesity, in 49%; and diabetes, in 36%. All patients were referred for coronary angiography during the index hospitalization with the following indications[17]: high pretest clinical probability with significant symptoms and typical risk factors (25%), intermediate pretest clinical probability with significant symptoms and/or positive results of exercise stress test (29%), stress echocardiography (22%), myocardial perfusion scintigraphy (11%), and coronary computed tomography angiography (13%).

Coronary angiography showed CAD (CAS of at least 50%) in 228 patients (71%) with equal rates of 1-, 2-, and 3-vessel disease (TABLE 1). Coronary revascularization was performed in 158 patients (49%): percutaneous in 139 and surgical in 19. The main indications for coronary revascularization were as follows[17]: left main or proximal left anterior descending artery disease (percutaneous coronary intervention [PCI], 33%; coronary artery bypass grafting [CABG], 6%); any symptomatic coronary stenosis resistant to medical treatment (PCI, 44%); as well as 2- or 3-vessel disease (PCI, 11%; CABG, 6%). There were no revascularizations within the previously implanted stents (restenosis or any stent failures).

Ultrasound indices and coronary revascularization The study group was divided into 2 subgroups depending on the results of coronary angiography and the presence of indications for coronary revascularization. Patients

TABLE 2 Ultrasound indices in patients with coronary artery disease with and without indications for coronary revascularization

Ultrasound indices	Coronary revascularization		*P* values
	Yes	No	
CAS, %	37.8 (19.88)	31.1 (20.3)	0.003
Carotid IMT, μm	987 (526)	865 (238)	0.01
Carotid EMT, μm	784 (169)	802 (363)	0.58
IAT, mm	74.4 (24)	77.1 (28)	0.38
PATIMA index, u	2176 (563)	1991 (405)	0.001

Data are presented as mean (SD).

Abbreviations: CAS, carotid artery stenosis; EMT, extra-media thickness; IAT, intra-abdominal thickness; IMT, intima-media thickness; PATIMA, Periarterial Adipose Tissue Intima Media Adventitia

TABLE 3 Ultrasound indices in patients with and without indications for coronary revascularization as well as those with nonsignificant coronary artery disease

Ultrasound indices	CAD (CAS ≥50%)		No CAD (CAS <50%)	*P* value
	Indications for revascularization	No indications for revascularization		
CAS, %	37.8 (19.88)	37.1 (22.1)	25.7 (17.1)	<0.001
Carotid IMT, μm	987 (526)	950 (229)	787 (216)	<0.001
Carotid EMT, μm	784 (169)	822 (132)	783 (465)	0.6
IAT, mm	74.4 (24)	81.3 (31)	73.8 (25)	0.13
PATIMA index, u	2176 (563)	2114 (301)	1884 (446)	<0.001

Data are presented as mean (SD).

Abbreviations: see TABLES 1 and 2

with indications for coronary revascularization showed higher carotid IMT, PATIMA index, and CAS compared with those without indications. On the other hand, the groups were similar in terms of the total number of CV risk factors (mean [SD], 5.4 [1.3] vs 5.3 [1.1]; $P = 0.9$), carotid EMT, and IAT (TABLE 2). Subsequently, the study group was divided into 3 subgroups: patients referred for coronary revascularization, patients with CAD not referred for revascularization, and patients with nonsignificant CAD (<50% stenosis) (TABLE 3).

Receiver operating characteristic curve analysis and prediction of coronary revascularization Given the main aim of the study, the following parameters were used in the ROC curve analysis for predictors of coronary revascularization: age, total number of CV risk factors, maximal CAS, carotid IMT, carotid EMT/BMI, IAT, and the combined PATIMA index.

Patient's age, clinical CV risk factors, and IAT were not predictive for coronary revascularization (FIGURE 1). All the other ultrasound parameters, including maximal CAS, carotid IMT, carotid EMT/BMI, and combined PATIMA index were predictors of coronary revascularization. Moreover, a comparison of the 4 ROC curves did not show significant differences in the area under the ROC curve values, with CAS and IMT showing the best sensitivity for revascularization (TABLE 4, FIGURE 2).

DISCUSSION In the present study of patients with high and very high CV risk scheduled for coronary angiography, we found that baseline CAS, carotid parameters (IMT and EMT/BMI), and the combined PATIMA index offer a similar significant predictive value for coronary revascularization. Although the total number of clinical risk factors is the basis for CV risk estimation and CAD prevention, it does not predict the need for coronary revascularization in patients with at least high CV risk. To the best of our knowledge, this is the first study showing the predictive value of the main vascular indices for coronary revascularization and not only for the presence or severity of CAD.

There have been several studies showing that carotid atherosclerosis[1,14,24,25] or carotid IMT[3,4,26,27] are associated with CAD or clinical prognosis. Our previous studies showed also that carotid EMT (index of perivascular adipose tissue) and the combined PATIMA vascular index are associated with the presence and severity of CAD.[12] Moreover, we found that carotid IMT, EMT, and the combined PATIMA index are associated with the complexity of CAD assessed by the SYNTAX score.[15] All the ultrasound indices used in our study correspond to different vascular or tissue components. They reflect some common CV risk factors, but they also show some differences in terms of risk stratification. This is supported by our results, which revealed that CAS as well as IMT, EMT, and PATIMA index have a similar predictive value for coronary revascularization.

The relationship between a particular index and different aspects of CAD is complex. The association with the presence or the severity of coronary stenosis is a simple finding, while the association with the complexity is more advanced, but it does not have to result in revascularization in a patient. There are several different risk factors found in clinical assessment, laboratory tests, or imaging studies,[16] which are associated with vascular disease. However, in clinical practice, we need indices that would show a closer association with treatment outcomes or a change in clinical prognosis. Even the well-known Duke Treadmill Score obtained in an exercise test was shown to have a weak correlation with CAD and coronary revascularization.[28] Baseline vascular indices assessed in our study showed potential utility for the prediction of coronary revascularization, which is

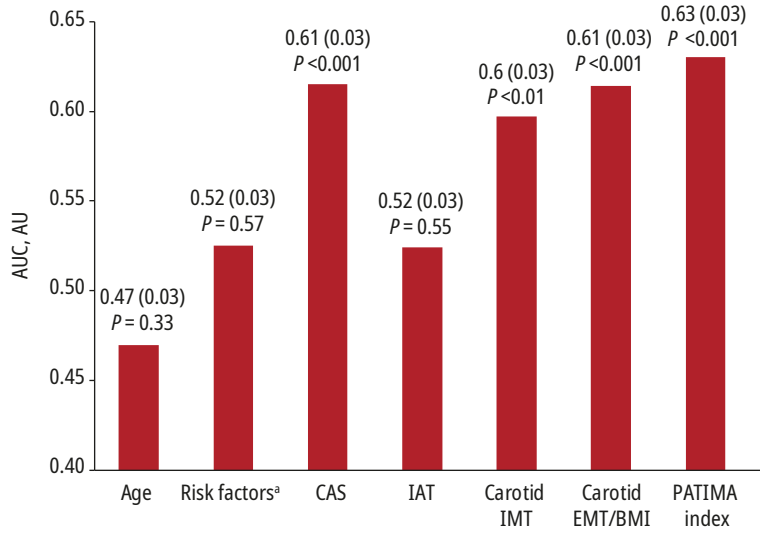

FIGURE 1 Comparison of the receiver operating characteristic curves: prediction of coronary revascularization. Data are presented as mean (SD).

a Total number of cardiovascular risk factors

Abbreviations: AUC, area under the receiver operating characteristic curve; EMT/BMI, extra-media thickness adjusted for body mass index; NS, nonsignificant; others, see TABLE 2

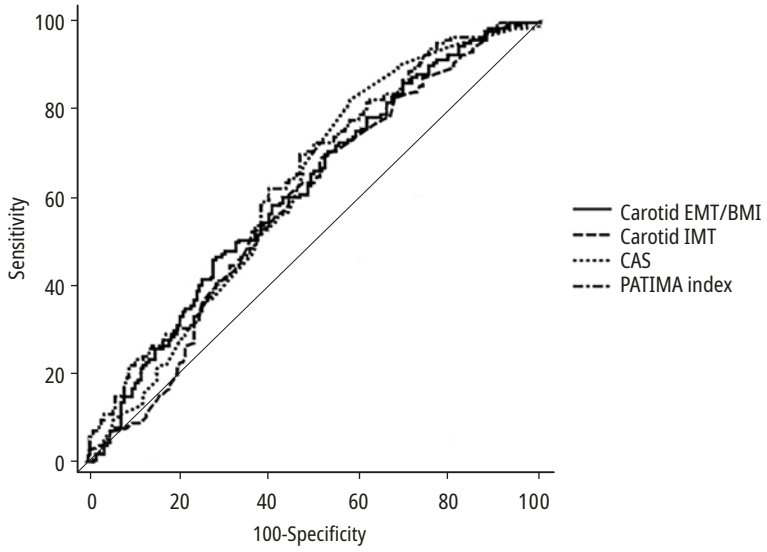

FIGURE 2 Receiver operating characteristic curve analysis: prediction of coronary revascularization

Abbreviations: see TABLE 2 and FIGURE 1

much more challenging. We may assume that increased ultrasound indices in patients with stable CAD indicate a stronger need for coronary angiography with a higher probability of revascularization. The ESC guidelines on CV disease prevention[16,18] underlined the need for new data supporting the use of vascular carotid indices in the prediction of treatment outcome, as there is a clear gap in the available evidence. Our study partially fills this gap by providing some novel data concerning the differences in ultrasound indices (CAS, EMT, and PATIMA index), with higher values observed in patients referred for coronary revascularization than those with nonsignificant CAD.

Among all the ultrasound vascular indices, carotid IMT is historically the most important one, with the largest body of evidence.[29] It is currently perceived as a marker of atherosclerosis (its development and progression) as well as a predictor of CV events.[4] It has been used as an endpoint in studies assessing the efficacy of some pharmacologic interventions.[4,8] However, neither carotid IMT nor other major vascular indices were used as predictors of treatment outcome. Our previous study[30] showed that increased perivascular visceral fat index (carotid EMT) is associated with worse lipid goal attainment, which could help identify patients requiring more aggressive lipid-lowering treatment. Carotid IMT failed to show any associations with lipid management. A direct comparison with other studies or concepts of combined indices in relation to the efficacy of treatment is impossible, as there have been no other studies in this field.

Clinical perspectives To the best of our knowledge, we present the first results concerning the predictive value of CAS and major vascular indices for coronary revascularization. The severity of CAS, carotid IMT, EMT, and the combined PATIMA index may improve the stratification of patients before they are scheduled for coronary angiography. Given the differences in the complexity of measurements of those indices (with the most complex being PATIMA, followed by EMT, IMT, and CAS) and that the

TABLE 4 Receiver operating characteristic curve analysis for ultrasound indices as predictors of coronary artery disease

Ultrasound indices	Coronary revascularization					
	AUC (SE)	Optimum value	Sensitivity, %	Specificity, %	PPV, %	NPV, %
Carotid EMT/BMI	0.61 (0.032)	27.6	46	71	60	58
Carotid IMT	0.59 (0.031)	760	77	41	56	65
CAS	0.61 (0.031)	20	80	42	57	70
PATIMA index	0.63 (0.031)	1947	70	52	58	65

Abbreviations: NPV, negative predictive value; PPV, positive predictive value; SE, standard error; others, see TABLE 2 and FIGURE 1

predictive values of the indices were similar, it seems that the simple assessment of CAS severity or carotid IMT should be recommended in clinical practice.

Limitations Our results cannot be generalized as they concern mainly patients with high and very high CV risk and with clinical characteristics similar to those of our study group. Ultrasound indices or carotid artery ultrasound parameters are reliable only if they are obtained by experienced observers. A long-term prospective follow-up of the study group after revascularization is lacking; thus, we cannot draw conclusions on the association between ultrasound indices and clinical prognosis.

Conclusions We showed for the first time that the severity of CAS as well as carotid vascular indices (IMT, EMT, and combined PATIMA index) may predict coronary revascularization in patients with high or very high CV risk. Although the selected indices represent different tissue components or aspects of atherosclerosis, their predictive value is similar. Clinical assessment and the number of CV risk factors do not add predictive value in this group of patients.

ARTICLE INFORMATION

CONTRIBUTION STATEMENT MH conceived the concept and design of the study, performed ultrasound examinations and analyzed all ultrasound data, as well as drafted the manuscript. MB, AK, MM, and LM analyzed patients' clinical data, including coronary angiography. MH, MB, and ZG contributed to the interpretation of data and manuscript drafting. All authors revised the manuscript critically for important intellectual content and approved the final version of the manuscript. All authors take responsibility for all aspects of the reliability and freedom from bias of the data presented and their discussed interpretation.

CONFLICT OF INTEREST None declared.

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REFERENCES

1 Kozlov S, Balachonova T, Machmudova H, et al. Carotid atherosclerosis, endothelial disfunction, and arterial stiffness in young and middle-aged men with coronary artery disease. Int J Vasc Med. 2012; 950130.

2 Neumann FJ, Sousa-Uva M, Ahlsson A, et al. 2018 ESC/EACTS Guidelines on myocardial revascularization. Eur Heart J. 2019; 40: 87-165.

3 Katakami N, Kaneto H, Shimomura I. Carotid ultrasonography: a potent tool for better clinical practice in diagnosis of atherosclerosis in diabetic patients. J Diabetes Investig. 2014; 5: 3-13.

4 Nezu T, Hosomi N, Aoki S, Matsumoto M. Carotid intima-media thickness for atherosclerosis. J Atheroscler Thromb. 2016; 23: 18-31.

5 O'Leary DH, Polak JF, Kronmal RA, et al. Distribution and correlates of sonographically detected carotid artery disease in the Cardiovascular Health Study. The CHS Collaborative Research Group. Stroke. 1992; 23: 1752-1760.

6 Burke GL, Evans GW, Riley WA, et al. Arterial wall thickness is associated with prevalent cardiovascular disease in middle-aged adults. The Atherosclerosis Risk in Communities (ARIC) Study. Stroke. 1995; 26: 386-391.

7 Allan PL, Mowbray PI, Lee AJ, Fowkes FG. Relationship between carotid intima-media thickness and symptomatic and asymptomatic peripheral arterial disease. The Edinburgh Artery Study. Stroke. 1997; 28: 348-353.

8 Nair SB, Malik R, Khattar RS. Carotid intima-media thickness: ultrasound measurement, prognostic value and role in clinical practice. Postgrad Med J. 2012; 88: 694-699.

9 Skilton MR, Sérusclat A, Sethu AH, et al. Noninvasive measurement of carotid extra-media thickness associations with cardiovascular risk factors and intima-media thickness. JACC Cardiovasc Imaging. 2009; 2: 176-182.

10 Haberka M, Gasior Z. Ultrasound extra-media thickness is related to anthropometric and clinical parameters of metabolic syndrome: a novel index of perivascular adipose tissue. Atherosclerosis. 2015; 239: 169-177.

11 Haberka M, Sosnowski M, Zuziak-Pruska J, Gasior Z. Extra-media thickness and epicardial fat: comparison of a novel carotid artery ultrasound index and a well-established cardiac magnetic resonance fat quantification method. Nutr Metab Cardiovasc Dis. 2015; 25: 763-770.

12 Haberka M, Gasior Z. A carotid extra-media thickness, PATIMA combined index and coronary artery disease: comparison with well-established indexes of carotid artery and fat depots. Atherosclerosis. 2015; 243: 307-313.

13 Wofford JL, Kahl FR, Howard GR, McKinney WM. Relation of extent of extracranial carotid artery atherosclerosis as measured by B-mode ultrasound to the extent of coronary atherosclerosis. Arterioscler Thromb. 1991; 11: 1786-1794.

14 Simon A, Chironi G, Levenson J. Performance of subclinical arterial disease detection as a screening test for coronary heart disease. Hypertension. 2006; 48: 392-396.

15 Haberka M, Lelek M, Bochenek T, et al. Novel combined index of cardiometabolic risk related to periarterial fat improves the clinical prediction for coronary artery disease complexity. Atherosclerosis. 2018; 268: 76-83.

16 Piepoli MF, Hoes AW, Agewall S, et al. 2016 European Guidelines on cardiovascular disease prevention in clinical practice: The Sixth Joint Task Force of the European Society of Cardiology and Other Societies on Cardiovascular Disease Prevention in Clinical Practice. Eur Heart J. 2016; 37: 2315-2381.

17 Montalescot G, Sechtem U, Achenbach S, et al. ESC Guidelines on the management of stable coronary artery disease. The Task Force on the management of stable coronary artery disease of the European Society of Cardiology. Eur Heart J. 2013; 34: 2949-3003.

18 Perk J, De Backer G, Gohlke H, et al. European Guidelines on cardiovascular disease prevention in clinical practice: The Fifth Joint Task Force of the European Society of Cardiology and Other Societies on Cardiovascular Disease Prevention in Clinical Practice (constituted by representatives of nine societies and by invited experts). Atherosclerosis. 2012; 223: 1-68.

19 Definition and diagnosis of diabetes and intermediate hyperglycaemia. Report of a WHO/IDF Consultation. World Health Organization. 2006 http://www.who.int/diabetes/publications/Definition%20and%20diagnosis%20of%20diabetes_new.pdf. Accessed December 2018.

20 Use of glycated hemoglobin (HbA1c) in the diagnosis if diabetes mellitus. Abbreviated report of a WHO consultation. World Health Organization. 2011 http://www.who.int/diabetes/publications/diagnosis_diabetes2011/en/. Accessed December 2018.

21 Touboul PJ, Hennerici MG, Meairs S, et al. Mannheim carotid intima-media thickness and plaque consensus (2004–2006–2011). Cerebrovasc Dis. 2012; 34: 290-296.

22 Iacobellis G, Assael F, Ribaudo MC, et al. Epicardial fat from echocardiography: a new method for visceral adipose tissue prediction. Obes Res. 2003; 11: 304-310.

23 Leite CC, Wajchenberg BL, Radominski R, et al. Intra-abdominal thickness by ultrasonography to predict risk factors for cardiovascular disease and its correlation with anthropometric measurements. Metabolism. 2002; 51: 1034-1340.

24 Cicorella N, Zanolla L, Franceschini L, et al. Usefulness of ultrasonographic markers of carotid atherosclerosis (intima-media thickness, unstable carotid plaques and severe carotid stenosis) for predicting presence and extent of coronary artery disease. J Cardiovasc Med (Hagerstown). 2009; 10: 906-912.

25 Hallerstam S, Larsson PT, Zuber E, Rosfors S. Carotid atherosclerosis is correlated with extent and severity of coronary artery disease evaluated by myocardial perfusion scintigraphy. Angiology. 2004; 55: 281-288.

26 Ikeda N, Kogame R, Iijima M, Nakamura K. Carotid artery intima-media thickness and plaque score can predict the SYNTAX score. Eur Heart J. 2012; 33: 113-119.

27 Stein JH, Korcarz CE, Hurst RT, et al; American Society of Echocardiography Carotid Intima–Media Thickness Task Force. Use of carotid ultrasound to identify subclinical vascular disease and evaluate cardiovascular disease risk: a consensus statement from the American Society of Echocardiography Carotid Intima–Media Thickness Task Force. Endorsed by the Society for Vascular Medicine. J Am Soc Echocardiogr. 2008; 21: 93-111.

28 Dzenkeviciute V, Sapoka V, Kasiulevicius V, et al. Value of Duke treadmill score in predicting coronary artery lesion and the need for revascularization. Kardiol Pol. 2017; 75: 439-444.

29 Allan PL, Mowbray PI, Lee AJ, Fowkes FG. Relationship between carotid intima media thickness and symptomatic and asymptomatic peripheral arterial disease. The Edinburgh Artery Study. Stroke. 1997; 28: 348-353.

30 Haberka M, Okopień B, Gąsior Z. Obesity, ultrasound indexes of fat depots and lipid goal attainment in patients with high and very high cardiovascular risk: a novel approach towards better risk reduction. Nutr Metab Cardiovasc Dis. 2016; 26: 123-133.