ORIGINAL ARTICLE

Arterial structure and function in patients with acute coronary syndrome after 1-year treatment

Agata Schneider[1], Joanna Gawęcka[1], Andrzej Minczykowski[1], Tomasz Krauze[1], Przemysław Guzik[1], Jarosław Piskorski[2], James Heathers[3], Andrzej Wykrętowicz[1]

1 Department of Cardiology-Intensive Therapy, Poznan University of Medical Sciences, Poznań, Poland
2 Institute of Physics, University of Zielona Góra, Zielona Góra, Poland
3 Department of Psychology, University of Sydney, Sydney, Australia

KEY WORDS

arterial stiffness, intima–media thickness, myocardial infarction

ABSTRACT

INTRODUCTION The modification of arterial stiffness and intima–media thickness (IMT) is controversial in patients with clinically significant atherosclerosis.

OBJECTIVES We evaluated the effects of 1-year pharmacological therapy on arterial stiffness and IMT in survivors of non-ST-segment elevation myocardial infarction (NSTEMI) who were treated according to current clinical guidelines.

PATIENTS AND METHODS A total of 298 patients with NSTEMI (median age, 64 years; 85 women) were enrolled to this study. Local (carotid) arterial stiffness and IMT were measured noninvasively before discharge and after 12 months of contemporary pharmacological treatment according to current clinical guidelines. The study group was divided into patients with normal systolic blood pressure (BP) (<140 mm Hg) and those with increased systolic BP (≥140 mm Hg) at 12 months. The results were presented as median (25th–75th percentile).

RESULTS There were no significant changes in local arterial stiffness between patients with normal and those with increased systolic BP (8.9 m/s [7.9–10.9 m/s] vs 8.7 m/s [7.8–10.1 m/s] at baseline and 9.6 m/s [8.3–11.0 m/s] vs 10.4 m/s [9.1–12.4 m/s] at 12 months, $P = 0.67$ and $P = 0.05$, respectively); however, a significant reduction in IMT was found in both groups (777 μm [664–896 μm] vs 715 μm [619–841 μm] at baseline and 818 μm [720–962 μm] vs 760 μm [674–897 μm] at 12 months, $P = 0.0003$ and $P = 0.001$, respectively). Arterial stiffness and IMT were affected by age and mean BP; however, adjustment for these variables did not affect the obtained results in multivariate models.

CONCLUSIONS The 1-year pharmacological treatment of patients after NSTEMI was associated with a significant reduction in IMT but had no effect on the properties of the arterial structure.

Correspondence to:
Agata Schneider, MD, PhD,
Katedra i Klinika Intensywnej Terapii Kardiologicznej i Chorób Wewnętrznych,
Uniwersytet Medyczny
im. Karola Marcinkowskiego,
ul. Przybyszewskiego 49,
60-355 Poznań, Poland,
phone: +48 61 869 13 91,
e-mail: aamille@wp.pl
Received: November 29, 2016.
Revision accepted: February 14, 2017.
Published online: February 15, 2017.
Conflict of interest: none declared.
Pol Arch Intern Med. 2017; 127 (3): 184-189
doi:10.20452/pamw.3939

INTRODUCTION In recent years, arterial structure and function have been the subject of intensive clinical research. It has been demonstrated that carotid intima–media thickness (IMT) represents a useful phenotype for subclinical atherosclerosis.[1,2] A number of studies showed that the degree of IMT can predict various clinical cardiovascular (CV) events.[3] Consequently, IMT measurement is increasingly used in clinical trials as a surrogate endpoint.[4,5] Large artery stiffening is a hallmark of aging, and this process is further amplified by hypertension and diabetes.[6] Arterial stiffness contributes to CV complications and is also regarded as a useful predictor of future CV events.[7,8] Several studies indicated that arterial stiffness and IMT may be reduced by antihypertensive treatment, although it was also suggested that antihypertensive drugs may affect arterial compliance irrespective of blood-pressure lowering.[9-12] These studies are thought to determine when the modification of subclinical atherosclerosis may result in risk reduction of future CV events (eg, coronary artery disease). However, few studies have investigated the effects of the most

current multiple drug therapy on the indices of arterial structure and function in an unselected "real-world population" of patients with established atherosclerotic heart disease. Therefore, we assessed whether a 12-month treatment according to current guidelines[13] for secondary prevention of myocardial infarction (MI) affects arterial stiffness and IMT in consecutive patients admitted with the diagnosis of acute coronary syndrome (ACS).

PATIENTS AND METHODS

Study population

The study included consecutive patients who were admitted for percutaneous coronary intervention due to ACS manifesting as NSTEMI within 12 hours from symptom onset and who presented more than 50% of coronary artery narrowing. Subjects with cardiogenic shock, advanced and refractory chronic heart failure, atrial fibrillation or flutter, chronic renal disease on dialysis, and known neoplasm or chronic condition with life expectancy of less than 1 year were excluded from the study. For the purpose of this study, blood pressure (BP) measurements and ultrasound assessments were performed between 48 and 72 hours after admission, and then at 12-month follow-up in all patients who survived. Patients were discharged with a detailed description of their medical record and prescribed medication.[13] Further treatment was supervised by their family physician. The University Ethics Committee approved the study protocol, and written informed consent was obtained from all participants.

Blood pressure, local carotid stiffness, and intima–media thickness

In all patients, brachial BP was measured using an oscillometric method (M-785; Omron Healthcare Company, Limited, Kyoto, Japan) in the supine position, after a 5-minute rest, on both arms. The higher reading from one of the arms was taken for further analysis. The BP results were obtained from a single measurement on each arm. All patients underwent an ultrasound examination of the left common carotid artery, using high-resolution 4–13 MHz linear probe (MyLabClass C, Esoate, Genova, Italy). All investigations were performed with the patient in the supine position with head elevation. The common carotid artery 1 cm before the bulb was used for measurements. All measurements were performed with the dedicated ArtLab software using radiofrequency data technology (QIMT^{RF} for IMT and QAS^{RF} for arterial stiffness, Esoate, Genova, Italy). The QIMT algorithm allows the automatic detection of IMT, and real time feedback helps obtain the best possible measurements (with SD <20 μm); 6 successive measurements are continuously averaged. For the measurements of quality arterial stiffness (QAS), the left common carotid artery image 1 cm before bifurcation is obtained. The system cyclically computes 6 successive measurements of both the arterial distension and diameter (with SD <35 μm). The vessel distension and diameters are measured several times on each cardiac cycle. The average is calculated for each cardiac cycle. The local stiffness of the arterial wall is expressed as QAS = local pulse wave velocity (PWV):

$$PWV = \frac{1}{\sqrt{\rho \cdot DC}} = \sqrt{\frac{D^2 \cdot \Delta p}{\rho(2D \cdot \Delta D + \Delta D^2)}}$$

where: D = diastolic diameter, ΔD = change of diameter in systole, DC = distensibility coefficient, Δp = local pulse pressure, and ρ = blood density.

Statistical analysis

Distribution of continuous data was analyzed by the Shapiro–Wilk test. Since most of the data did not have normal distribution, their summary was reported as median and interquartile range. Qualitative characteristics were reported as standard descriptive statistics. Differences between the groups were estimated with the paired and nonpaired Wilcoxon test for continuous variables, and the Fisher exact test for dichotomized variables. The Spearman correlation coefficient was calculated for the analysis of relations between patients' age, hemodynamic parameters, subclinical atherosclerosis, and arterial stiffness. Since not all patients presented with systolic BP of less than 140 mm Hg during the follow-up visit at 12 months, we performed the post hoc analysis. Patients were assigned either to the group with systolic BP of less than 140 mm Hg or with systolic BP of 140 mm Hg or higher. A general linear regression model was used to compare the differences between the adjusted means of the indices of subclinical atherosclerosis and arterial stiffness at baseline and at 12 months. All analyses were performed with SPSS (version 23.0, IBM Corp, Armonk, New York, United States).

RESULTS

Characteristics of the study population

A total of 298 consecutive patients with ACS were included (85 women and 213 men; median age, 64 years). The baseline clinical characteristics of the patients are presented in TABLE 1. All patients received treatment recommended by the current guidelines (secondary prevention of MI). Apart from double antiplatelet therapy, 97% of the patients were treated with angiotensin-converting enzyme inhibitor (ACEI) or angiotensin receptor blocker (ARB); 92%, with β-blocker; 24%, with diuretics; and 32%, with aldosterone antagonist. At 12-month follow-up (TABLE 2), 84% of the patients still received ACEI (P <0.0001) and 6%—ARB (P = 0.1); 91% of the patients received β-blocker (P = 0.8); 99%, statin (P = 0.01); 26%, diuretic (P = 0.9); and 27%, aldosterone antagonist (P = 0.4).

Hemodynamic parameters and arterial function and structure

The analysis of hemodynamic data performed in all patients showed that systolic, diastolic, and mean BP were significantly higher at 12 months (TABLE 3), although the median values of systolic and diastolic BP were within the reference

TABLE 1 Clinical characteristics and measurements. Data on medication collected at discharge.

Parameter	Value
Continuous data, median (25th–75th percentile)	
Age, y	64 (57–71)
Creatinine, mg/dl	0.88 (0.75–1.0)
Cholesterol, mg/dl	194 (163–237)
High sensitivity troponin T, ng/l	177 (44–705)
LVEF, %	54 (45.8–60.3)
Categorical data, n (%)	
Male sex	213 (71.5)
History of myocardial infarction	97 (32.6)
Hypertension	243 (81.5)
Diabetes	98 (32.9)
Current tobacco use	115 (38.6)
Aspirin	294 (98.7)
Clopidogrel	282 (94.6)
ACEI or ARB	288 (96.6)
β-blocker	279 (93.6)
Statin	292 (98.0)
Diuretic	76 (25.5)
Long-acting nitrate	49 (16.4)
Aldosterone antagonist	73 (24.5)

Abbreviations: ACEI, angiotensin-converting enzyme inhibitor; ARB, angiotensin receptor blocker; LVEF, left ventricular ejection fraction

TABLE 2 Distribution of treatment after discharge and at 12-month follow-up

Medications	Discharge	Follow-up after 12 months	*P* value[a]
ACEI	94	84	<0.0001
ARB	3	6	0.1
β-blockers	92	92	0.8
CCB	17	15	0.5
Diuretics	24	26	0.3
Statins	95	99	0.01
ASA	99	97	0.06
Clopidogrel	95	90	0.001
Aldosterone antagonist	32	27	0.004

Data are presented as percentage of patients.

a Fisher exact test

Abbreviations: ASA, acetylsalicylic acid; CCB, calcium channel blocker; others, see TABLE 1

ranges. Similarly, local arterial stiffness of the carotid artery was significantly higher at 12 months. In contrast, the IMT and cholesterol concentrations were significantly reduced at 12 months.

Clinical, hemodynamic, and arterial parameters measured during the follow-up visit at 12 months in patient groups divided according to BP are shown in TABLE 4. Patients with a systolic BP of 140 mm Hg or higher were significantly older and all their hemodynamic parameters as well as QAS were significantly higher in comparison with the baseline values. On the other hand, the IMT was significantly reduced in comparison with the baseline values. In contrast, patients with a systolic BP of less than 140 mm Hg at the follow-up visit showed a nonsignificant difference in systolic and mean BP. Moreover, the QAS did not differ significantly, while the IMT was significantly reduced in comparison with the baseline value. Cholesterol concentrations were significantly lower in both subgroups in comparison with baseline data. Additionally, we analyzed the arterial structure and function in patients with previous MI versus those with no previous MI. No significant differences were shown either for the IMT or for QAS (data not shown).

In the whole study group, the QAS correlated significantly with systolic BP and age (r = 0.47, P <0.0001 and r = 0.43, P <0.0001, respectively; TABLE 5). Similarly, the IMT correlated significantly with age and systolic BP (r = 0.2, P <0.0001 and r = 0.2, P <0.0001, respectively; TABLE 5). Further analysis demonstrated that when the mean arterial stiffness was adjusted for age and mean BP, it did not differ significantly from the baseline value in any of the subgroups (FIGURE 1A). In contrast, the mean IMT adjusted for age and mean BP remained significantly lower compared with the baseline values in both subgroups (FIGURE 1B). In a multivariate regression model with clinical characteristics obtained on enrollment, only age and BP significantly affected the IMT (data not shown).

DISCUSSION Our study demonstrated that treatment according to the current guidelines had no significant effect on local arterial stiffness but was associated with a significant decrease in IMT in patients with NSTEMI.

Patients with established coronary heart disease are strongly encouraged to implement lifestyle changes that affect modifiable risk factors such as obesity, physical inactivity, or smoking. Moreover, treatment with aspirin or other antiplatelet drugs, statins, ACEIs or ARBs, and β-blockers also has proven benefit in secondary prevention of future CV complications.[13] The mechanisms by which these drugs exert beneficial effects are not fully understood and most probably are not limited to simple reduction of BP and cholesterol levels.

In recent years, particular interest was focused on new CV risk factors such as arterial stiffness and IMT. Several studies have demonstrated that increased arterial stiffness can predict CV complications, such as MI, stroke, or need for revascularization.[14] It is also regarded as a measure of target organ damage in patients with hypertension.[15-17] Stiffness can be measured at different arterial locations including the carotid-femoral segment or locally on the carotid or femoral artery. Moreover, general indices of arterial stiffness such as systemic arterial compliance or stiffness index derived from digital volume plethysmography are also used in clinical practice.[18] These different indices underscore that stiffness is not uniformly

TABLE 3 Hemodynamic, arterial, and laboratory parameters at 12 month follow-up.

Parameter	Baseline	After 12 months	*P* value[a]
Systolic BP, mm Hg	130 (116–146)	137 (126–150)	<0.0001
Diastolic BP, mm Hg	75 (68–83)	80 (73–87)	<0.0001
Mean BP, mm Hg	94 (86–103)	99 (91–108)	<0.0001
PP, mm Hg	54 (44–67)	57 (46–70)	0.04
IMT, µm	797 (685–914)	740 (644–863)	<0.0001
QAS, m/s	9.2 (7.9–10.9)	9.6 (8.4–11.5)	0.001
Cholesterol, mg/dl	194 (163–235)	150 (150–171)	<0.0001

Data are shown as median and the 25th – 75th percentile.

a Unpaired Wilcoxon test

Abbreviations: BP, blood pressure; IMT, intima–media thickness; PP, pulse pressure; QAS, quality arterial stiffness

TABLE 4 Clinical, hemodynamic, and arterial parameters according to blood pressure measured at follow-up visit at 12 months

Parameter	BP control <140 mm Hg (n = 163)		*P* value[a]	BP control ≥140 mm Hg (n = 135)		*P* value[a]	Comparison at baseline *P* value[b]
	A – baseline	B – at 12 months	A vs B	C – baseline	D – at 12 months	C vs D	A vs C
Hypertension, n (%)	123 (75)			120 (88)			0.004[c]
Diabetes, n (%)	54 (33)			44 (33)			1.0[c]
Age, y	62 (56–70)			65 (60–73)			0.001
Systolic BP, mm Hg	125 (113–137)	128 (117–132)	0.4	136 (123–151)	151 (145–165)	<0.0001	<0.0001
Diastolic BP, mm Hg	74 (67–81)	76 (69–82)	0.04	77 (70–85)	86 (77–93)	<0.0001	0.009
Mean BP, mm Hg	90 (82–100)	93 (85–98)	0.48	97 (89–105)	107 (102–115)	<0.0001	<0.0001
PP, mm Hg	51 (42–59)	48 (40–56)	0.005	60 948–72)	71 (59–80)	<0.0001	<0.0001
IMT, µm	777 (664–896)	715 (619–841)	0.0003[d]	818 (720–962)	760 (674–897)	0.001[d]	0.007[d]
QAS, m/s	8.9 (7.9–10.9)	8.7 (7.8–10.1)	0.67[d]	9.6 (8.3–11.0)	10.4 (9.1–12.4)	<0.0001[d]	0.05[d]
Cholesterol, mg/dl	195 (164–238)	150 (150–171)	<0.0001	193 (157–235)	150 (150–171)	<0.0001	0.78

Data are shown as median and the 25th–75th percentile unless otherwise indicated.

a Paired Wilcoxon test, b Unpaired Wilcoxon test, c Fisher exact test, d General linear regression model

Abbreviations: see TABLE 3

TABLE 5 Correlation between age, hemodynamic parameters, subclinical atherosclerosis, and arterial stiffness

Parameter	Age		Mean BP		PP	
	rho	*P* value	rho	*P* value	rho	*P* value
QIMT	0.23	0.0001	0.11	0.05	0.2	0.006
QAS	0.38	<0.0001	0.3	<0.0001	0.46	<0.0001

Abbreviations: QIMT, quality intima–media thickness; others, see TABLE 3

distributed along the arteries. Moreover, these various parameters have different associations with incident CV complications.

A comprehensive assessment of various indices of arterial stiffness with incidence of CV events and all-cause mortality showed that local carotid and femoral stiffness were independently associated with CV sequelae, including death.[19] It was also hypothesized that modification of arterial stiffness may influence future CV events. Studies performed so far have reported conflicting results on the effect of antihypertensive treatment on arterial stiffness. Mourad et al[20] reported that age-related increase in pulse pressure (surrogate measure of arterial stiffness) is not prevented by conventional antihypertensive therapy. Tropeano et al[10] demonstrated pressure-independent reduction in carotid stiffness after long-term use of ACEIs in diabetic patients with hypertension. Raff et al[9] showed that olmesartan improves segmental arterial stiffness and lowers central systolic and ambulatory BP in patients with metabolic syndrome. It should be noted that various populations with different risk profiles were represented in the above studies. Moreover, local versus segmental arterial stiffness was estimated, and short (6 weeks) versus long-term (7 months) drug treatment was applied.

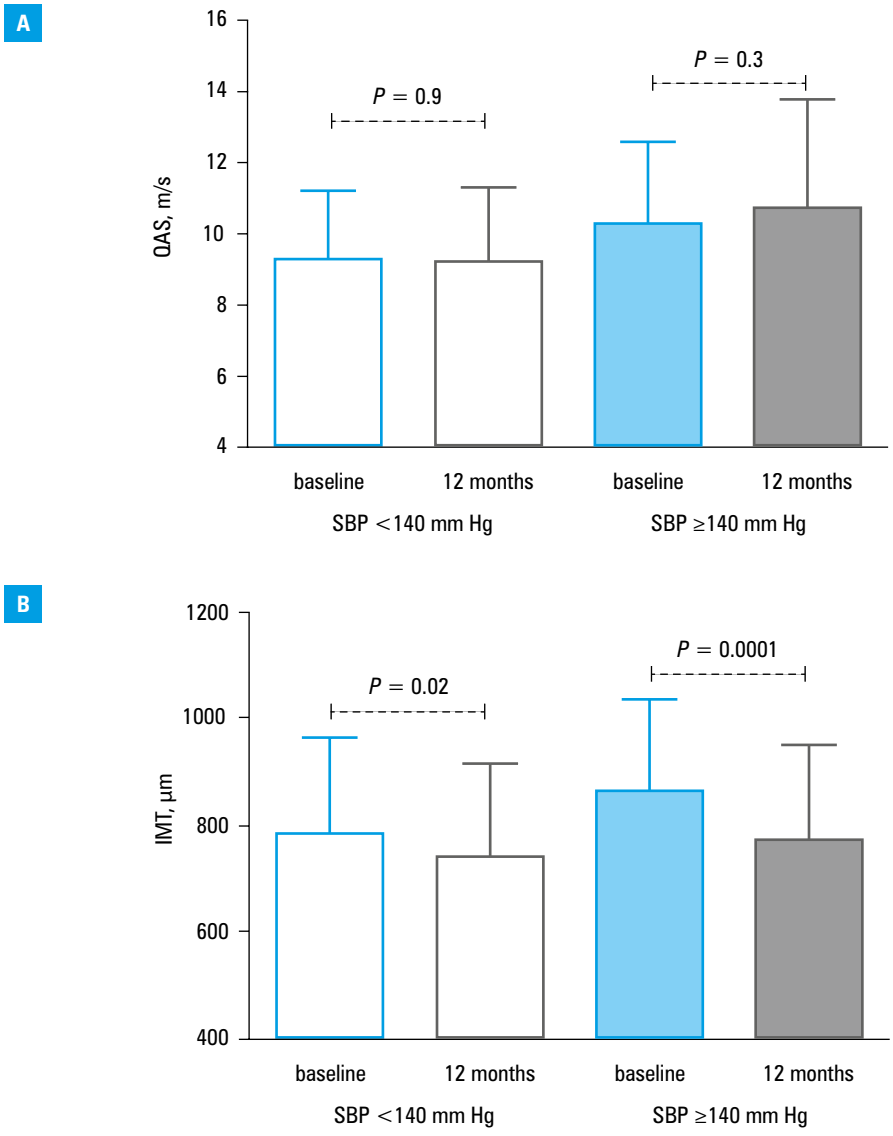

FIGURE 1 **A** – quality arterial stiffness (QAS) at baseline and at 12-month follow-up adjusted for age and mean blood pressure in patients with a systolic blood pressure (SBP) of less than 140 mm Hg or of 140 mm Hg or higher at follow-up; **B** – intima–media thickness (IMT) at baseline and at 12-month follow-up adjusted for age and mean blood pressure in patients with an SBP of less than 140 mm Hg or 140 mm Hg or higher at follow-up; results shown as mean and standard error of the mean

In our current study, 298 survivors of NSTEMI were evaluated after 12 months of treatment according to the guidelines. Most of the patients received the most contemporary pharmacological treatment at discharge and the majority of the patients continued it throughout the 12-month follow-up. Local carotid arterial stiffness was estimated by echo-tracking. After 12 months of treatment, median systolic and diastolic BP were significantly higher (although within the reference ranges), and local arterial stiffness was also significantly higher in comparison with the baseline values. The study population was further subdivided into those with a systolic BP of less than 140 mm Hg and of 140 mm Hg or higher at follow-up visit at 12 months. Arterial stiffness was significantly (borderline) higher in patients with higher systolic BP at the follow-up visit. This population also more often suffered from hypertension in the past. It is well known that arterial stiffness is correlated with age and BP.[21,22] Similarly, in our study, arterial stiffness correlated strongly and significantly with age and BP. We therefore compared arterial stiffness in the subgroups after adjustment for both covariates. We used the mean arterial pressure in the model because it determines mean arterial transmural pressure, which in turn determines arterial stiffness. We noted that after adjustment for both explanatory variables, arterial stiffness did not differ significantly at 12 months in any of the subgroups.

Several randomized controlled trials demonstrated that lipid-modifying therapy delays the annual rate of change in IMT or leads to its reduction.[23-25] Despite differences in ultrasound assessment of IMT across clinical trials, there is a consistent finding of a relationship between the rate of change of this marker and lipid-lowering therapy. Moreover, there is evidence that such treatment affects clinical endpoints. IMT is affected not only by lipid-lowering drugs. The Diabetes Interventions and Complications Research Group demonstrated that intensive type 1 diabetes treatment resulted in decreased progression of IMT 6 years after the study.[26] It is well known that hypertension promotes carotid intima–media thickening. Wang et al[11] performed a meta-analysis of randomized controlled trials that evaluated the effects of antihypertensive drugs versus placebo on carotid IMT. It was shown that ACEIs, ARBs, or calcium channel blockers decreased intima–media thickening in the presence

of similar BP reduction. Our results support these findings. The IMT was significantly reduced at 12 months. Moreover, both subgroups showed a significant reduction in IMT. IMT correlates with patients' age and BP; therefore, we compared the results after adjustment for both covariates. We observed that IMT was significantly reduced after 12 months of treatment according to the guidelines, independently of both explanatory variables.

Taken together, our study demonstrated that contemporary drug treatment of the survivors of NSTEMI is associated with a reduction of the IMT and has no effect on arterial stiffness.

Our study has several limitations. We assessed local carotid stiffness but the obtained results at a particular arterial segment cannot be extrapolated to any other arterial location. Long-term effects of the treatment were estimated, theoretically involving arterial wall remodeling, but the role of reduced distension pressure cannot be excluded. Finally, most of the patients were treated with combination therapy, thus the obtained results are not attributable to any particular drug.

Acknowledgments This project was supported in part by an unrestricted research grant from the Polish National Science Centre (Kraków, Poland; DEC-2011/03/B/NZ7/06 241; to AW).

Contribution statement AW conceived the idea for the study. AW, AS, and PG contributed to the design of the research. All authors were involved in data collection. AW, AS, AM, and PG analyzed the data. AW coordinated funding for the project. All authors edited and approved the final version of the manuscript.

REFERENCES

1 Bots ML, Hoes AW, Koudstaal PJ, et al. Common carotid intima-media thickness and risk of stroke and myocardial infarction: the Rotterdam Study. Circulation. 1997; 96: 1432-1437.

2 Kaźmierski M, Michalewska-Włudarczyk A, Krzych LJ. Intima-media thickness and flow-mediated dilatation in the diagnosis of coronary artery disease in perimenopausal women. Pol Arch Med Wewn. 2010; 120: 181-188.

3 Lorenz MW, Markus HS, Bots ML, et al. Prediction of clinical cardiovascular events with carotid intima-media thickness: a systematic review and meta-analysis. Circulation. 2007; 115: 459-467.

4 Espeland MA, O'leary DH, Terry JG, et al. Carotid intimal-media thickness as a surrogate for cardiovascular disease events in trials of HMG-CoA reductase inhibitors. Curr Control Trials Cardiovasc Med. 2005; 6: 3.

5 Taylor AJ, Villines TC, Stanek EJ, et al. Extended-release niacin or ezetimibe and carotid intima-media thickness. N Engl J Med. 2009; 361: 2113-2122.

6 Zoungas S, Asmar RP. Arterial stiffness and cardiovascular outcome. Clin Exp Pharmacol Physiol. 2007; 34: 647-651.

7 Waldstein SR, Rice SC, Thayer JF, et al. Pulse pressure and pulse wave velocity are related to cognitive decline in the Baltimore Longitudinal Study of Aging. Hypertension. 2008; 51: 99-104.

8 Sutton-Tyrrell K, Najjar SS, Boudreau RM, et al. Elevated aortic pulse wave velocity, a marker of arterial stiffness, predicts cardiovascular events in well-functioning older adults. Circulation. 2005; 111: 3384-3390.

9 Raff U, Walker S, Ott C, Schneider MP, et al. Olmesartan improves pulse wave velocity and lowers central systolic blood pressure and ambulatory blood pressure in patients with metabolic syndrome. J Clin Hypertens. 2015; 17: 98-104.

10 Tropeano AI, Boutouyrie P, Pannier B, et al. Brachial pressure-independent reduction in carotid stiffness after long-term angiotensin-converting enzyme inhibition in diabetic hypertensives. Hypertension. 2006; 48: 80-86.

11 Wang JG, Staessen JA, Li Y, et al. Carotid intima-media thickness and antihypertensive treatment: a meta-analysis of randomized controlled trials. Stroke. 2006; 37: 1933-1940.

12 Krasińska B, Miazga A, Cofta S, et al. Effect of eplerenone on the severity of obstructive sleep apnea and arterial stiffness in patients with resistant arterial hypertension. Pol Arch Med Wewn. 2016; 126: 330-339.

13 Roffi M, Patrono C, Collet JP, et al. 2015 ESC Guidelines for the management of acute coronary syndromes in patients presenting without persistent ST-segment elevation. Eur Heart J. 2016; 37: 267-315.

14 Vlachopoulos C, Aznaouridis K, Stefanadis C. Prediction of cardiovascular events and all-cause mortality with arterial stiffness: a systematic review and meta-analysis. J Am Coll Cardiol. 2010; 55: 1318-1327.

15 Leoncini G, Ratto E, Viazzi F, et al. Increased ambulatory arterial stiffness index is associated with target organ damage in primary hypertension. Hypertension. 2006; 48: 397-403.

16 Cecelja M, Chowienczyk P. Dissociation of aortic pulse wave velocity with risk factors for cardiovascular disease other than hypertension: a systematic review. Hypertension. 2009; 54: 1328-1336.

17 Milewska A, Krauze T, Piskorski J, et al. Association between high arterial stiffness and left ventricular filling pressures in patients with acute myocardial infarction. Pol Arch Med Wewn. 2015; 125: 814-822.

18 Alty SR, Angarita-Jaimes N, Millasseau SC, et al. Predicting arterial stiffness from the digital volume pulse waveform. IEEE Trans Biomed Eng. 2007; 54: 2268-2275.

19 Van Sloten TT, Schram MT, van den Hurk K, et al. Local stiffness of the carotid and femoral artery is associated with incident cardiovascular events and all-cause mortality: the Hoorn study. J Am Coll Cardiol. 2014; 63: 1739-1747.

20 Mourad JJ, Blacher J, Blin P, et al. PHASTE study. Conventional antihypertensive drug therapy does not prevent the increase of pulse pressure with age. Hypertension. 2001; 38: 958-961.

21 Millasseau SC, Kelly RP, Ritter JM, et al. Determination of age-related increases in large artery stiffness by digital pulse contour analysis. Clin Sci (Lond). 2002; 103: 371-377.

22 Olszanecka A, Pośnik-Urbańska A, Kawecka-Jaszcz K, et al. Subclinical organ damage in perimenopausal women with essential hypertension. Pol Arch Med Wewn. 2010; 120: 390-398.

23 Ikeda K, Takahashi T, Yamada H, et al (for the PEACE Investigators). Effect of intensive statin therapy on regression of carotid intima-media thickness in patients with subclinical carotid atherosclerosis (a prospective, randomized trial: PEACE (Pitavastatin Evaluation of Atherosclerosis Regression by Intensive Cholesterol-lowering Therapy) study). Eur J Prev Cardiol. 2013; 20: 1069-1079.

24 Riccioni G. Statins and carotid intima-media thickness reduction: an up-to-date review. Curr Med Chem. 2009; 16: 1799-1805.

25 Nohara R, Daida H, Hata M, et al. Effect of intensive lipid-lowering therapy with rosuvastatin on progression of carotid intima-media thickness in Japanese patients: Justification for Atherosclerosis Regression Treatment (JART) study. Circ J. 2012; 76: 221-229.

26 Nathan DM, Lachin J, Cleary P, et al. Diabetes Control and Complications Trial; Epidemiology of Diabetes Interventions and Complications Research Group. Intensive diabetes therapy and carotid intima-media thickness in type 1 diabetes mellitus. N Engl J Med. 2003; 348: 2294-2303.