VIA MEDICA

ORIGINAL ARTICLE

Cardiology Journal
2007, Vol. 14, No. 1, pp. 59–66

ISSN 1507–4145

The influence of renal function and selected cardiovascular risk factors on the thickness of the intima-media complex in the peripheral arteries

Anna Lisowska[1], Włodzimierz Jerzy Musiał[1], Piotr Lisowski[2], Małgorzata Knapp[1], Jolanta Małyszko[3], Grażyna Latocha-Korecka[1] and Hanna Bachórzewska-Gajewska[4]

[1]Department of Cardiology, Medical University, Białystok, Poland
[2]Department of Cardiac Surgery, Medical University, Białystok, Poland
[3]Department of Nephrology, Medical University, Białystok, Poland
[4]Laboratory of Invasive Cardiology, Medical University, Białystok, Poland

Abstract

Background: *Measurement of the intima-media thickness (IMT) in the peripheral arteries leads to better stratification of cardiovascular risk. This is of great importance in patients with chronic renal insufficiency, who are particularly vulnerable to developing atherosclerotic lesions. The aim of the study was to evaluate whether parameters of renal insufficiency and selected risk factors of atherosclerosis influence IMT in the peripheral arteries.*

Methods: *The study population comprised 231 patients submitted to coronary angiography with ultrasonographic assessment of the common carotid artery (CCA), carotid artery bulb (CB) and common femoral artery (CFA) made contemporaneously with evaluation of IMT and atherosclerotic plaques. Renal function as well as selected clinical and biochemical risk factors of atherosclerosis were assessed. Two subgroups were analysed: 200 patients with coronary heart disease confirmed angiographically (study group) and 31 patients without coronary lesions (control group).*

Results: *Significant negative correlation was found between glomerular filtration rate and IMT values in CCA ($p < 0.001$) as well as in CB ($p < 0.05$). Patients with abnormal glucose metabolism had significantly higher IMT values in CCA (0.95 ± 0.30* vs. *0.87 ± 0.20; $p = 0.034$). Hypercholesterolaemia did not influence the IMT values in CCA and CFA. There was no correlation between body mass index and IMT.*

Conclusions: *Patients with chronic renal insufficiency presented higher values of IMT in CCA. The measurement of IMT appears to be a valuable non-invasive method of diagnosing preclinical stages of atherosclerosis in the described group of patients.* (Cardiol J 2007; 14: 59–66)

Key words: intima-media thickness of peripheral arteries, renal function, cardiovascular risk factors

Introduction

Persons with chronic renal insufficiency, particularly those requiring renal replacement therapy, constitute the group of patients most vulnerable to developing atherosclerotic lesions in the

Address for correspondence: Dr med. Anna Lisowska
Department of Cardiology, Medical University
Skłodowskiej-Curie 24A, 15–276 Białystok, Poland
e-mail: anlila@poczta.onet.pl
Received: 18.08.2006 Accepted: 23.11.2006

cardiovascular system, irrespective of their status with regard to the traditional risk factors [1–3]. Specific cardiovascular risk factors related directly to chronic renal disease include decreased glomerular filtration rate (GFR), proteinuria, increased activity of the renin-angiotensin-aldosterone system, hypervolaemia caused by overhydration, disturbances of the calcium-phosphate metabolism, dyslipidaemia and anaemia [4]. Pathophysiology of ischaemic heart disease in patients with nephropathies is different from that in the general population in that atherosclerotic plaques are more calcified, and the process affects not only the large epicardial arteries but also the smaller arterioles. Coronary reserve is decreased, and so is the availability of nitric oxide and the activity of NO synthesis inhibitors. Hypertrophy/hyperplasia of the coronary arterioles decreases their capacity for relaxation, and the decreased number of capillaries within the myocardium disrupts oxygen diffusion [5–7]. All the abovementioned data maintain interest in the cardiovascular factors affecting patients with chronic renal insufficiency.

Various methods of assessment of the arterial system are currently available. Coronary angiography is the gold standard in diagnosing lesions of the coronary arteries. However, it is an invasive method and therefore detailed criteria of patient qualification have been drawn up [8]. Non-invasive techniques, including ultrasonographic measurement of the intima-media thickness (IMT) or of the flow-mediated dilatation (FMD), are of increasing clinical significance. New diagnostic modalities also include the detection of calcium deposits within the coronary arteries (so-called calcium scoring) or their direct visualisation with the aid of electron-beam computed tomography (EBCT) or magnetic resonance (MRI). Multi-row (even 64-row) tomography enables the coronary blood vessels to be visualised extremely precisely [9]. Non-invasive diagnostic methods are of particular importance in an asymptomatic population, since they contribute additional data to the established risk factors and permit better risk stratification of adverse cardiovascular episodes [10].

Increased thickness of the intima-media complex, detected in ultrasonography, occurs even in the early developmental stages of atherosclerosis and correlates with other traditional risk factors as well as with the clinical presentation [11–13]. Moreover, Held et al. [14] demonstrated that atherosclerotic plaques and the assessment of IMT in the carotid artery allow a patient's risk of ischaemic heart disease to be assessed.

The aim of the study was to evaluate whether parameters of renal insufficiency and selected risk factors of atherosclerosis influence IMT in the peripheral arteries.

Methods

The study population was recruited among patients of the Department of Cardiology of the Medical University of Białystok hospitalised between 2001 and 2003. The study included male patients aged from 18 to 65 years, who were qualified for coronary angiography and who at the same time underwent transthoracic echocardiography and ultrasonographic evaluation of peripheral arteries. Selected clinical parameters and biochemical risk factors of atherosclerosis as well as renal function were assessed. Criteria of exclusion were previously diagnosed diabetes mellitus, symptomatic obliterative atherosclerosis of the lower limb arteries and severe arterial hypertension.

The study population included 231 patients. On the basis of images of the coronary arteries two groups of patients were identified: the study group, comprising 200 patients with coronary heart disease confirmed in angiography, and the control group of 31 patients with no significant coronary lesions detected. Coronary artery narrowing of over 50% of the vessel lumen was considered significant. Detailed patient characteristics are presented in Table 1.

Clinical evaluation of each patient included measurement of arterial pressure, resting ECG and exercise test, transthoracic echocardiography, coronary angiography and ultrasonography of the carotid and femoral arteries. Laboratory tests included total cholesterol, LDL and HDL cholesterol fractions, serum triglycerides, plasma fibrinogen, platelet count and oral glucose tolerance test. Indications for coronary angiography were assessed on the basis of a patient's clinical presentation and the results of accessory investigations according to the standards of the Polish Cardiac Society. Coronary angiography was performed in a routine manner via the femoral artery.

Carotid and femoral artery ultrasonography was performed using the Sonos 5500 device with a linear probe of 3–11 MHz frequency. Additionally, the software enabling evaluation of the peripheral arteries in B-mode presentation was used, as described previously [15]. The parameters evaluated included the thickness of IMT and the presence of atherosclerotic plaques within the vessel.

The common carotid artery (CCA) was evaluated 10 mm from its bulb and the common femoral

Table 1. Patient characteristics.

	Study group (n = 200)	Control group (n = 31)	p
Age (years)	52.8 ± 8.4	45.9 ± 10.5	< 0.001
Smoking	137 (68.5%)	11 (35.5%)	< 0.001
Body mass index [kg/m^2]	27.6 ± 3.8	26.8 ± 3.3	NS
Systolic blood pressure [mm Hg]	142.7 ± 20.6	136.1 ± 19.9	NS
Diastolic blood pressure [mm Hg]	92.1 ± 13.4	85.6 ± 11.5	< 0.05
Total cholesterol [mg%]	181.7 ± 37.1	174.0 ± 32.9	NS
LDL cholesterol [mg%]	112.2 ± 33.5	104.0 ± 28.9	NS
HDL cholesterol [mg%]	38.3 ± 8.6	44.5 ± 13.5	0.05
Triglycerides [mg%]	156.0 ± 65.0	120.3 ± 36.2	< 0.01
Diabetes*	39 (19.5%)	1 (3.2%)	< 0.01
Abnormal fasting glycaemia*	8 (4%)	0 (0%)	0.0001
Impaired glucose tolerance*	65 (32.5%)	5 (16.1%)	0.0001
Creatinine [mg%]	1.065 ± 0.20	1.012 ± 0.18	NS
Glomerular filtration rate [ml/min]	97.3 ± 25.1	109.9 ± 30.0	0.01
Fibrinogen [mg%]	423.2 ± 110.8	364.8 ± 124.4	< 0.01
Platelets [× 1000/mm^3]	231.8 ± 80.3	198.1 ± 54.1	< 0.05
Ejection fraction (%)	46.2 ± 8.3	52.0 ± 13.3	< 0.01

*Disturbances of glucose metabolism diagnosed during hospitalisation.

artery (CFA) 10 mm before the origin of the deep femoral artery. In each of the vessel segments assessed two measurements of IMT were performed and their results were averaged. Maximal measured IMT values were considered. Atherosclerotic plaques were defined as focal IMT values of over 1.3 mm.

Renal function was assessed through measurement of creatinine level and GFR, calculated according to the Cockcroft-Gault method: GFR = (140 – age) × × body mass [kg]/72 × serum creatinine level. The following classification of chronic renal insufficiency stages was adopted (according to the Kidney Disease Outcomes Quality Initiative, K/DOQI):

— stage 1: GFR > 90 ml/min;
— stage 2: GFR of 60–90 ml/min — occult renal insufficiency;
— stage 3: GFR of 30–60 ml/min — overt compensated renal insufficiency;
— stage 4: GFR of 15–30 ml/min — advanced renal insufficiency;
— stage 5: GFR < 15 ml/min — end-stage renal insufficiency.

Creatinine levels below 1.5 mg/dl in men were described as normal.

Statistical analysis

The measurement results were submitted to statistical analysis. Arithmetical mean values and standard deviation were calculated for measurable characteristics, and quantity percentage distributions were determined for qualitative characteristics. Pearson's correlation coefficients were calculated for continuous characteristics of normal distribution and Spearman's coefficients for characteristics of non-normal distribution.

The normal distribution was verified using Kolmogarov's test. For intergroup comparisons of characteristics of normal distribution, Student's *t*-test was used, and in cases of non-normal distribution the Mann-Whitney test was used. Intergroup comparisons of qualitative data were performed using the χ^2 test. The level of statistical significance was designated as $p < 0.05$. Calculations were performed using the SPSS 8.0 PL and Statistica 6.0 PL software.

All the patients gave their consent for participation in the study. The approval of the local Ethical Committee was obtained.

Results

As presented in Table 1, patients in the study group were older, heavier smokers, had higher diastolic blood pressure, lower levels of HDL cholesterol and higher levels of triglycerides and fibrinogen and higher platelet counts. They more often experienced disturbances of glucose metabolism. Ejection fraction in echocardiography was significantly lower in the study group compared to the control group. There were no significant differences in creatinine levels between the two groups but patients in the study group had significantly lower GFRs.

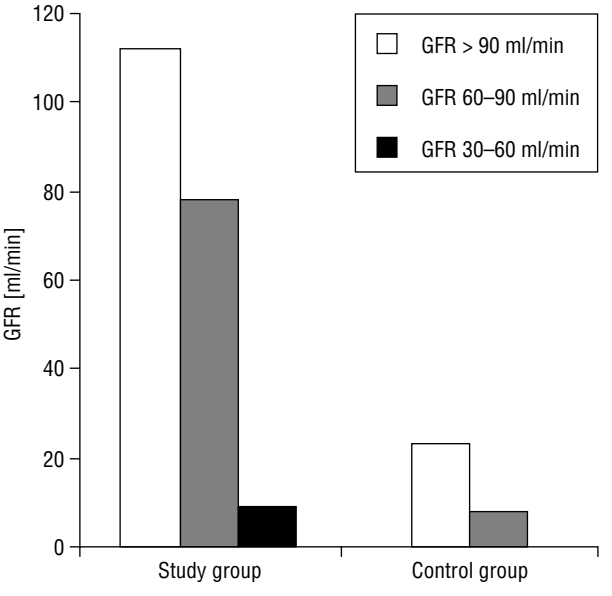

Figure 1. Glomerular filtration rates (GFR) in patients from the study and the control group.

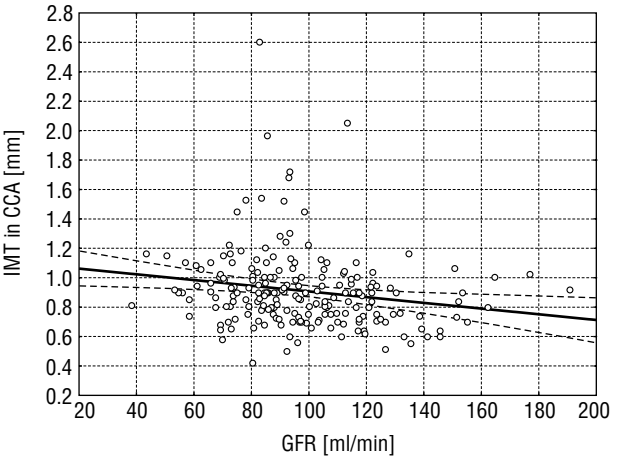

Figure 2. Results of intima-media thickness (IMT) measurement in the common carotid artery (CAA) and glomerular filtration rates (GFR) in patients from the study group.

Renal function and IMT

In both groups there were few patients with creatinine levels > 1.5 mg/dl (4% patients in study group and 3.2% patients in the control group). In the study group a GFR of over 90 ml/min was observed in 56% patients (112 persons), a GFR of 60–90 ml/min in 39% patients (78 persons), and values of 30–60 ml/min in 4.5% patients (9 persons). In the control group as many as 74.2% men had GFR values over 90 ml/min, and only 25% patients had filtration rates between 60–90 ml/min; there were no patients with a GFR below 60 ml/min (Fig. 1). There was significant negative correlation between GFR and IMT values measured in CCA ($p < 0.001$) (Fig. 2) and in the bulb of CCA ($p < 0.05$). In the control group no such correlation was observed. Nor was there any significant relationship between GFR values and the incidence of atherosclerotic plaques in the peripheral arteries. Moreover, filtration rates were lower in patients with three-vessel disease compared to the rates observed in patients with one or two-vessel stenosis ($p < 0.05$). Of the traditional cardiovascular risk factors analysed, it was only the occurrence of diabetes and the level of glycosylated haemoglobin that correlated with decreased GFR ($p < 0.05$).

Disturbances in glucose metabolism and IMT

In the study group, the oral glucose tolerance test (OGTT) revealed abnormalities of glucose metabolism in 112 patients (56%), of whom 8 (4%) had abnormal fasting glycaemia, 65 (32.5%) had impaired glucose tolerance and 39 subjects (19.5%) had type 2 diabetes (diagnostic criteria according to WHO) (tab. 2). In the control group disturbed glucose metabolism was diagnosed in 6 patients, including 5 persons with impaired glucose tolerance and a man diagnosed with diabetes. Twenty five patients (80.6%) in the control group showed no alteration in glucose metabolism. Individuals with abnormal OGTT results had significantly higher values of IMT in CCA (0.95 ± 0.30 *vs.* $0.87 \pm \pm 0.20$; $p = 0.034$). No significant differences in IMT values were observed in CCA bulb (1.31 ± 0.53 *vs.* 1.31 ± 0.57; $p = NS$) and in CFA (1.31 ± 0.62 *vs.* $1.36 \pm \pm 0.68$; $p = NS$) between the patients with abnormal glucose metabolism and the healthy subjects (Fig. 3).

Age, body mass, arterial pressure and IMT

The study group consisted of 125 individuals (62.5%) aged over 50 years and 75 (37.5%) aged below 50 years. Statistically significant differences were observed between the two age subgroups with respect to IMT in CCA (0.95 ± 0.3 *vs.* 0.85 ± 0.2; $p = 0.002$) and IMT in CCA bulb (1.41 ± 0.6 *vs.* 1.15 ± 0.3; $p = 0.001$). Patients above and below 50 years of age did not differ significantly with respect to IMT values in the femoral arteries.

Normal body mass index values (BMI < 25) were observed in 51 patients in the study group, 102 patients were overweight (BMI of 25–30), and obesity was diagnosed in 47 subjects (BMI > 30). There was no correlation between BMI and IMT values, despite the fact that 51% patients in the study group were overweight and 23.5% obese.

Table 2. Intima-media thickness (IMT) in the peripheral arteries and disturbances in glucose metabolism.

	Patients with normal OGTT (n = 88)	Patients with abnormal OGTT (n = 112)	p
Age (years)	51.6 ± 8.6	53.8 ± 8.1	NS
IMT of CCA [mm]	0.87 ± 0.20	0.95 ± 0.30	0.034
IMT of CCA bulb [mm]	1.31 ± 0.57	1.31 ± 0.53	NS
IMT of CFA [mm]	1.31 ± 0.62	1.36 ± 0.68	NS
Plaques in CCA	3 (3.4%)	10 (9%)	NS
Plaques in CCA bulb	30 (34%)	48 (43%)	NS
Plaques in CFA	48 (54.5%)	52 (46%)	NS
Body mass index [kg/m^2]	26.8 ± 3.6	28.2 ± 3.8	0.02
Triglycerides [mg%]	143.7 ± 59.9	165.6 ± 67.4	0.01
Total cholesterol [mg%]	179.2 ± 40.5	183.7 ± 34.3	NS
HDL cholesterol [mg%]	39.0 ± 8.7	37.8 ± 8.5	NS
LDL cholesterol [mg%]	111.4 ± 37.2	112.7 ± 30.5	NS
Insulin level in OGTT 0 min [μUI/ml]	7.75 ± 2.7	10.8 ± 5.7	0.02
Insulin level in OGTT 120 min [μUI/ml]	40.0 ± 35.5	112.4 ± 101.3	0.0001

OGTT — oral glucose tolerance test; IMT — intima-media thickness; CCA — common carotid artery; CFA — common femoral artery

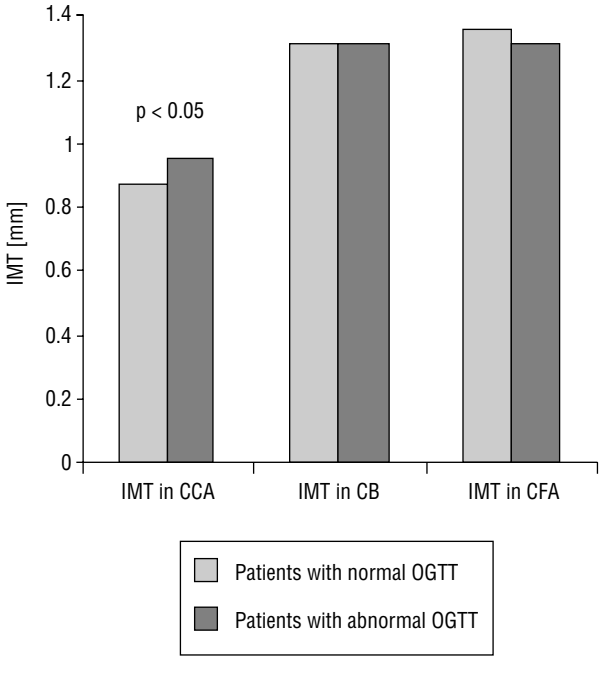

Figure 3. Results of intima-media thickness (IMT) measurement in common carotid artery (CCA), carotid bulb (CB) and common femoral artery (CFA) and disturbances in glucose metabolism.

Elevated systolic arterial pressure of ≥140 mm Hg was noted in 121 patients (60.5%) in the study group and 127 subjects (63.5%) had diastolic pressure values greater than 90 mm Hg. The IMT measurement values correlated with diastolic pressure ($p = 0.048$).

Disturbances in lipid metabolism and IMT

Total cholesterol levels of > 200 mg% were found in 57 patients (29%), and LDL cholesterol levels of > 100 mg% with HDL cholesterol < 40 mg% were observed in 122 patients (61%). Triglyceride levels of over 150 mg% were noted in 90 individuals (45%). Elevated total and LDL cholesterol had no influence upon the thickness of the intima-media complex in CCA and CFA.

Discussion

Previously published data, including the authors' own observations, suggest the occurrence of significantly greater IMT values in the peripheral arteries in patients with important coronary artery stenoses as compared to individuals with no abnormalities in coronary angiography [16, 17]. These findings confirm the role of IMT measurement in the peripheral arteries in predicting the development of atherosclerotic lesions in the coronary arteries. The aim of the present study was to analyse the potential relationship between IMT values in CCAs and selected cardiovascular risk factors, with particular emphasis on parameters of renal function.

Patients with chronic renal insufficiency run a significantly greater risk of developing cardiovascular complications. Greater IMT values in the carotid arteries were observed in patients before dialysis [18], in those requiring dialysis and in recipients of renal grafts [19, 20] as compared to subjects

with normal renal function. Only the group studied by Konings [21] failed to show this correlation.

In the population presented here a high percentage of patients with abnormal renal function were observed among male subjects with coronary heart disease verified through angiography. Stage 2 of chronic renal insufficiency (a GFR of 60–89 ml/min) was identified in almost 40% of patients and stage 3 (GFR of 30–59 ml/min) in 4.5% patients. Additionally, a significant correlation was found between decreased GFR and increased thickness of the intima-media complex in CCA and its bulb. However, our study, in contrast to those of other authors [22], demonstrated no relationship between creatinine levels and IMT values in the peripheral arteries. This is compatible with the current recommendations of the Kidney Disease Outcomes Quality Initiative (K/DOQI), which suggests calculating GFR instead of using creatinine level measurements for assessment of renal function.

Multivariate analysis showed that patient age and GFR are independent factors influencing IMT values in CCA. This observation is in agreement with the results published by Ishimura et al. [23]. On the other hand, Litwin et al. [24] observed significantly greater IMT values in children with chronic renal insufficiency, which emphasises the role of IMT measurement as an early marker of atherosclerosis development in patients with impaired renal function.

The present study shows no correlation between GFR and the occurence of atherosclerotic plaques in the peripheral arteries, which probably resulted from the fact that a major part of the study group consisted of patients with mild or moderate renal insufficiency. Reports in the literature that demonstrate a high incidence of atherosclerotic plaques are based on patients with end-stage renal disease [25].

As with the findings of Rubenfire et al. [26], a close correlation between IMT and patient age, abnormalities of glucose metabolism and diastolic blood pressure was confirmed in the present study. The influence of patient age upon the thickness of the intima-media complex in CCA was also reported by Gariepy et al. [27]. Although almost half the patients in the study group were overweight and 23.5% were obese, there was no relationship between BMI and IMT values, as reported by the above-mentioned authors. Zanchetti et al. [28] emphasised the influence of systolic (but not diastolic) blood pressure upon IMT values in the carotid arteries. In the study presented here, no such influence was attributable to systolic pressure, which could be explained by the fact that antihypertensive agents had previously been administered to over half the patients. Similarly, elevated total and LDL cholesterol in the study group did not correlate with IMT values in CCA. Such findings have been reported by other authors [29] but the patients observed had significant hypercholesterolaemia, whereas in the present population approximately 60% of patients had mild lipid abnormalities (moderately elevated LDL and decreased HDL cholesterol).

Smoking significantly influenced IMT values in CFA and the incidence of atherosclerotic plaques in this vessel but not the IMT in CCA, findings which were similarly to those of Salonen and Salonen [30]. In the present population, fibrinogen levels correlated with IMT in CCA but not in CFA, as reported by the above-mentioned authors.

The results of the Insulin Resistance Atherosclerosis Study (IRAS) demonstrated that IMT in CCA was 70 μm greater in diabetic patients than in normoglycaemic subjects [31]. The Atherosclerosis Risk in Communities Study (ARIC) confirmed a positive but not significant correlation between IMT in the carotid artery and postprandial glycaemia [32], as was also observed by Sun et al. [33]. A confirmed diagnosis of diabetes correlated with the occurrence of atherosclerotic plaques in the carotid artery but impaired glucose tolerance had no influence on increased risk of atherosclerosis [34]. In the population presented here patients with abnormal glucose metabolism demonstrated through OGTT (abnormal fasting glycaemia, impaired glucose tolerance and diabetes) showed significantly greater thickness of the intima-media complex in CCA only but not in the carotid bulb or CFA. Lack of significantly increased IMT in the peripheral arteries outside CCAs could be explained by the fact that the patients observed had no previous disturbances of glucose metabolism and therefore atherosclerotic lesions in their peripheral arteries were not advanced. According to data published in the literature, diabetes increases the risk of adverse cardiovascular events from twofold to fourfold [35]. Moreover, the progression of IMT in the carotid arteries was observed to be twice as rapid in diabetic patients, and this was not slowed down by hypoglycaemic treatment [31]. Early identification of diabetic subjects and assessment of cardiovascular risk factors, including the value of IMT in CCA, could therefore lead to the application of primary prophylaxis, thus preventing the occurrence of vascular complications.

To sum up, it should be noted that increased IMT in CCA in patients with traditional risk factors allows them to be designated to the high-risk group

and warrants administration of adequate therapy aimed at modifying these risk factors. Aggressive therapy for risk factors in patients with peripheral arterial disease was previously demonstrated to delay the progressive accumulation of intima-media plaques [36] or even to reduce IMT [37], which on clinical grounds reduced the incidence of adverse cardiovascular episodes.

Conclusions

1. The present study confirms the close relationship between IMT values in the CCAs and selected cardiovascular risk factors, including patient age, abnormalities of glucose metabolism, diastolic blood pressure and fibrinogen level.
2. There was a significant negative correlation between GFRs and IMT values in CCA and its bulb.
3. Measurement of IMT in CCA and its bulb might be a valuable non-invasive tool in assessment of the preclinical stage of atherosclerosis in patients with impaired renal function. This would permit identification of patients at particularly high risk of cardiovascular events and early introduction of prophylactic measures.

References

1. Baigent C, Burbury K, Wheeler D. Premature cardiovascular disease in chronic renal failure. Lancet, 2000; 356: 147–152.
2. Foley RN, Parfrey P, Samak MJ. Clinical epidemiology of cardiovascular disease in chronic renal failure. Am J Kidney Dis, 1998; 32: 112–119.
3. Uhlig K, Levey AS, Sarnak MJ. Traditional cardiac risk factors in individuals with chronic kidney disease. Semin Dial, 2003; 16: 118–127.
4. Parfrey P, Foley R. The clinical epidemiology of cardiac disease in chronic renal failure. J Am Soc Nephrol, 1999; 10: 1606–1615.
5. Schwarz U, Buzello M, Ritz E et al. Morphology of coronary atherosclerotic lesions in patients with end-stage renal failure. Nephrol Dial Transplant, 2000; 15: 218–223.
6. Amann K, Ritz E. Microvascular disease — the Cinderella of uraemic heart disease. Nephrol Dial Transplant, 2000; 15: 1493–1503.
7. Kielstein JT, Boger RH, Bode-Boger SM et al. Marked increase of asymmetric dimethylarginine in patients with incipient primary chronic renal disease. J Am Soc Nephrol, 2002; 13: 170–176.
8. Silber S, Albertsson P, Aviles FF et al. Guidelines for percutaneous coronary interventions. The Task Force for Percutaneous Coronary Interventions of the European Society of Cardiology. Eur Heart J, 2005; 26: 804–847.
9. Zagrodzka M, Szmit S, Janaszek-Sitkarska H et al. Angiografia klatki piersiowej metodą tomografii komputerowej u pacjentów po zawale serca i pomostowaniu tętnic wieńcowych z podejrzeniem zatorowości płucnej. Kardiologia po Dyplomie, 2006; 4: 79––88.
10. Patel S, Rajaram V, Pandya S et al. Nowe nieinwazyjne markery zastępcze miażdżycy. Kardiologia po Dyplomie, 2004; 3: 22–33.
11. Bots ML, Hoes AW, Koudstaal PJ, Hofman A, Grobbee DE. Common carotid intima-media thickness and risk of stroke and myocardial infarction: the Rotterdam study. Circulation, 1997; 96: 1432–1437.
12. Salonen JT, Salonen R. Ultrasound B-mode imaging in observational studies of atherosclerotic progression. Circulation, 1993; 87 (suppl. 3): II56–II65.
13. Folsom AR, Eckfeldt JH, Weitzman S et al. Relation of carotid artery wall thickness to diabetes mellitus, fasting glucose and insulin, body size and physical activity. Atherosclerosis Risk in Communities (ARIC) Study Investigators. Stroke, 1994; 25: 66–73.
14. Held C, Hjemdahl P, Eriksson SV, Bjorkander I, Forslund L, Rehnqvist N. Prognostic implications of intima-media thickness and plaques in the carotid and femoral arteries in patients with stable angina pectoris. Eur Heart J, 2001; 22: 62–72.
15. Lisowska A, Musiał W, Prokop J et al. Ultrasonograficzna ocena kompleksu błona wewnętrzna-błona środkowa tętnic obwodowych: przydatność kliniczna. Pol Przegl Kardiol, 2003; 4: 451–456.
16. Lisowska A, Musiał WJ, Knapp M et al. Carotid and femoral atherosclerotic lesions in patients with coronary heart disease confirmed by angiography. Kardiol Pol, 2005; 63: 636–642.
17. Kabłak-Ziembicka A, Tracz W, Przewłocki T et al. Association of increased carotid intima-media thickness with the extent of coronary artery disease. Heart, 2004; 90: 1286–1290.
18. Zoungas S, Branley P, Kerr PG et al. Atherosclerosis and folic acid supplementation trial in chronic renal failure: baseline results. Nephrology, 2004; 9: 130–141.
19. Nasri H, Baradaran A. Association of serum lipoprotein(a) with ultrasonographically determined early atherosclerotic changes in the carotid and femoral arteries in kidney transplanted patients. Transplant Proc, 2004; 36: 2683–2686.
20. Brzosko S, Hryszko T, Lebkowska U et al. Plasma tissue-type plasminogen activator, fibrinogen and

time on dialysis prior to transplantation are related to carotid intima-media thickness in renal transplant recipients. Transplant Proc, 2003; 35: 2931–2934.
21. Konings CJ, Dammers R, Rensma PL et al. Arterial wall properties in patients with renal failure. Am J Kidney Dis, 2002; 39: 1206–1212.
22. Bax L, van der Graaf Y, Rabelink AJ, Algra A, Beutler JJ, Mali WP, the SMART Study Group. Influence of atherosclerosis on age-related changes in renal size and function. Eur J Clin Invest, 2003; 33: 34–40.
23. Ishimura E., Shoji T Emoto M et al. Renal insufficiency accelerates atherosclerosis in patients with type 2 diabetes mellitus. Am J Kidney Dis, 2001; 38 (4 suppl. 1): S186–S190.
24. Litwin M, Wuhl E, Jourdan C et al. Altered morphologic properties of large arteries in children with chronic renal failure and after renal transplantation. J Am Soc Nephrol, 2005; 16: 1494–1500.
25. Savage T, Clarke AL, Giles M, Tomson CR, Raine AE. Calcified plaque is common in the carotid and femoral arteries of dialysis patients without vascular disease. Nephrol Dial Transplant, 1998; 13: 2004–2012.
26. Rubenfire M, Rajagopalan S, Mosca L. Carotid artery vasoreactivity in response to sympathetic stress correlates with coronary disease risk and is independent of wall thickness. J Am Coll Cardiol, 2000; 36: 2192–2197.
27. Gariepy J, Salomon J, Denarie N et al. Sex and topographic differences in associations between large-artery wall thickness and coronary risk profile in a French working cohort: the AXA Study. Arterioscler Thromb Vasc Biol, 1998; 18: 584–590.
28. Zanchetti A, Crepaldi G, Bond M et al. Systolic and pulse blood pressures (but not diastolic blood pressure and serum cholesterol) are associated with alterations in carotid intima-media thickness in the moderately hypercholesterolaemic hypertensive patients of the Plaque Hypertension Lipid Lowering Italian Study. PHYLLIS study group. J Hypertens, 2001; 19: 79–88.
29. Bolinder G, Noren A, de Faire U, Wahren J. Smokeless tobacco use and atherosclerosis: an ultrasonographic investigation of carotid intima media thickness in healthy middle-aged men. Atherosclerosis, 1997; 132: 95–103.
30. Salonen JT, Salonen R. Ultrasound B-mode imaging in observational studies of atherosclerotic progression. Circulation, 1993; 87(suppl. II): 56–65.
31. Wagenknecht L, Zaccaro D, Espeland MA, Karter AJ, O'Leary DH, Haffner SM. Diabetes and progression of carotid atherosclerosis. The Insulin Resistance Atherosclerosis Study (IRAS). Arterioscler Thromb Vasc Biol, 2003; 23: 1035–1041.
32. Vitelli LL, Shahar E, Heiss G, McGovern PG, Brancati FL, Eckfeldt JH, Folsom AR. Glycosylated hemoglobin level and carotid intimal-medial thickening in nondiabetic individuals: the Atherosclerosis Risk in Communities Study. Diabetes Care, 1997; 20: 1454–1458.
33. Sun Y, Lin CH, Lu CJ, Yip PK, Chen RC. Carotid atherosclerosis, intima media thickness and risk factors — an analysis of 1781 asymptomatic subjects in Taiwan. Atherosclerosis, 2002; 164: 89–94.
34. De Michele M, Panico S, Celentano E et al. Association of impaired glucose homeostasis with preclinical carotid atherosclerosis in women: impact of the new American Diabetes Association criteria. Metabolism, 2002; 51: 52–56.
35. Folsom AR, Szklo M, Stevens J, Liao F, Smith R, Eckfeldt JH. A prospective study of coronary heart disease in relation to fasting insulin, glucose and diabetes. The Atherosclerosis Risk in Communities (ARIC) Study. Diabetes Care, 1997; 20: 935––942.
36. Crouse JR 3rd, Tang R, Espeland MA, Terry JG, Morgan T, Mercuri M. Associations of extracranial carotid atherosclerosis progression with coronary status and risk factors in patients with and without coronary artery disease. Circulation, 2002; 106: 2061–2066.
37. Furberg C, Adams H, Applegate W et al. Effect of lovastatin on early carotid atherosclerosis and cardiovascular events. Asymptomatic Carotid Artery Progression Study (ACAPS) Research Group. Circulation, 1994; 90: 1679–1687.