

CAROTID ARTERY DISEASE IN DIABETIC PATIENTS

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Abstract

There are two points of view on the interplay between carotid artery disease and diabetes mellitus: Diabetes mellitus has been recognized as one of the main determinants for the presence and progression of asymptomatic and symptomatic carotid artery disease; and carotid intima-media thickness has been defined as a useful tool for risk stratification of this population.

Hyperglycaemia, duration of diabetes, arterial hypertension, cholesterol and inflammatory markers have previously been determined as independent factors for carotid atherosclerosis in diabetes, and aging as its predictor in this population by our own results. This paper focuses on the particularities of risk factors in diabetic patients (especially in type 2) and evidence-based guidelines for the management and risk reduction of these patients with stroke and/or carotid artery disease.

At present, carotid ultrasound is recommended in diabetic patients with cerebrovascular symptoms. Since the prevalence of diabetes increases constantly, we attempt to address refreshment of criteria for screening of carotid artery disease in the diabetic population. It could be recommended for diabetic patients with at least one more risk factors and for diabetic patients above 60 years of age.

Key words: carotid artery disease, diabetes, stroke, carotid ultrasound, aging, prognosis.

Introduction

Diabetic vascular disease is the main reason for morbidity and mortality in diabetic patients (pts).

Two thirds of all cause of deaths in Diabetes mellitus (DM) belong to macrovascular disease, and 25% of them belong to cerebrovascular disease. 60% of the expenses for treatment of type 2 diabetes are aimed at treatment of vascular disease, and 9% of them at cerebrovascular disease [1, 1b].

Carotid artery disease and Stroke in Type 2 diabetes

Stroke and Diabetes

Diabetes Mellitus (DM) has been recognized as one of the most important factors for

the development of cerebrovascular disease, defined as ischaemic stroke or asymptomatic carotid stenosis (*Cincinnati/North Kentucky Study*) [2, 2b]. Risk of ischaemic stroke in diabetic patients is higher in every age- and race-group compared to nondiabetic groups. A three to 10-fold risk of stroke-referred diabetic pts is included in *MRFIT* and *Baltimore-Washington Cooperative Stroke Studies*. A multivariate analysis with regards to ischaemic stroke found population attributable risk of diabetes in a range of 5622% (*Northern Manhattan Stroke and Rochester Studies*). According *ARIC* follow-up diabetic pts without coronary artery disease referred have a similar relative risk of stroke as nondiabetic pts with coronary artery disease. There is a relative risk of stroke in diabetic pts from 2.1 to 5.8 [3, 3b].

There is a strong relation between type 2 diabetes and the occurrence and recurrence of stroke, according *Tokyo Metropolitan Hospital Series* and *South London Stroke Register* [4–5]. Kuusisto's study revealed type 2 diabetes as an important predictor of stroke onset in elderly people [6].

Tuomelhto's study group referred to the fact that in a population with stroke only 20% have normal glycaemia [7]. There is a prevalence of Diabetes Mellitus in a stroke population in a range of 15 to 20% [8].

Patients with ischaemic stroke and diabetes have had more frequent arterial hypertension, previous coronary artery disease and hypercholesterolaemia vs. those without diabetes. There are differences in the clinical presentation of stroke in diabetic pts. These pts referred had a higher prevalence of lacunar infarcts and lower neurological deficits at entrance [9, 10]. Lacunar syndrome in diabetics is often accompanied by asymptomatic cerebral ischaemia and arterial hypertension.

As the result of a high prevalence of atrial fibrillation and heart failure, cardiac thromboembolism could be found in pts with DM [11, 12]. *Framingham Heart* and *Manitoba Follow-up Studies* revealed diabetes with a relative risk of 1.4 to 1.8 for the occurrence of atrial fibrillation [13, 14]. Atherosclerotic aorta-origin could also be a source of brain embolism. Lammie described degenerative abnormalities, such as lipohyalinosis and fibrinoid changes, as causes of subcortical brain infarcts in diabetics [15].

Carotid artery disease in Type 2 diabetes

Extracranial and intracranial carotid artery disease and diabetic microvascular disease are the main determinants of stroke in diabetics [16]. Diabetes is associated with large- and small-artery brain atherosclerosis, causing a change of flow.

Anatomical studies found carotid artery disease in diabetics with unstable and vulnerable plaques, which could provoke thromboembolism additionally [17].

Patients with Diabetes mellitus referred with a higher value of carotid intima-media thickness (CIMT) vs. non diabetics. Glycaemic control measured as fasting glycaemia or HbA1C has been found as independent factors

for CIMT value in diabetics (*RIAD*) [18–19]. In the *AIR*-population-based study on atherosclerosis and insulin resistance, increased CIMT and plaque size were found in advanced stages of impaired (lost) glucose control. In the *DIWA* study CIMT was greater in women with known type 2 diabetes vs. those with normal glucose tolerance [19b]. This study did not observe an association between impaired glucose tolerance and increased CIMT or carotid plaque occurrence.

Carotid IMT is related to diabetes duration and plasma cholesterol in patients with type 2 diabetes, and with postprandial glycaemia in the general population (*IRAS*). *IRAS* and *ARIC* studies referred to a mean value of CIMT of 0.91 and 0.89 mm in a population with type 2 diabetes [20–21]. That is comparable with results from our data of 340 patients with type 2 diabetes, presenting a mean CIMT 0.89 ± 1.59 mm and max CIMT of 0.99 ± 1.95 mm.

Diabetes mellitus is an independent factor for high grade carotid stenosis in the general population [22]. Type 2 diabetes is a factor that determinates the progression of carotid atherosclerosis, measured as a progression of CIMT and the occurrence of plaque in the internal carotid artery [23–24].

The pathogenesis of carotid artery disease in a type 2 diabetes population is based on a cluster of metabolic factors such as: insulin resistance, hyperlipidaemia, obesity and arterial hypertension [27–28]. Independent factors for carotid artery disease in diabetics are arterial hypertension, hypercholesterolaemia and inflammatory markers CRP and fibrinogen [25–26].

Non HDL-cholesterol is found as an independent predictor for ischaemic stroke and total cardiovascular risk in the type 2 diabetic population [29, 30]. Non HDL-cholesterol correlates with CIMT value in type 2 diabetics [31]. The *IRAS* study revealed a positive relation of carotid atherosclerosis with LDL-cholesterol, and an inverse relation with HDL-cholesterol. Metabolic syndrome amplifies LDL-cholesterol associated increasing for carotid atherosclerosis in the general population [32]. LDL-cholesterol independently influences increasing CIMT and the occurrence of carotid plaques in population-based studies where diabetic patients are included [34]. High blood

pressure and abdominal obesity are factors influencing the CIMT [35–36]. Pts with diabetic nephropathy revealed greater CIMT than those without. Renal involvement accelerates carotid atherosclerosis in a population with type 2 diabetes [37–38]. Bilateral carotid stenosis is probably a determinate from a complex mechanism based on the atherothrombotic process and involvement of many risk factors.

Prognostic implications

Diabetes has been defined as a stronger risk factor for stroke-related mortality than arterial hypertension or hyperlipidaemia. Diabetes mellitus causes 16% of stroke mortality in men and 30% in women [39].

Prognosis of pts with a stroke and Diabetes mellitus is dependent on glycaemia and glycated haemoglobin [40–42]. Hyperglycaemia that was found in an acute phase of stroke is recognized as important factor for cerebral damage through oxidative and inflammatory mechanisms [43]. Strong evidence between glycaemia and risk of cerebrovascular events in diabetics has not been found. On the other hand HbA1C, as a parameter of glycometabolic control, is an independent factor for future cerebrovascular events [45]. Duration of diabetes is also an important predictor of stroke in type 2 diabetes (*Copenhagen Stroke Study, Finnish Study*) [44, 46]. In many studies surviving stroke pts with diabetes have been shown to have a worse outcome. According to the *Cincinnati/North Kentucky Study* diabetic pts are more likely to survive with disability after an ischaemic stroke. No published data has found a unique profile for ischaemic stroke in diabetics. Studies by Lithner and Toni reported that stroke severity was similar in diabetics and nondiabetics [47–48]. But Kiers and Pulsinelli reported a poorer outcome of stroke in diabetic pts [49–50].

Furthermore, hyperglycaemia and advanced glycation products could damage the brain structure. These are the reasons that population-based studies by Leibson, Ott suggested that diabetes has been associated with vascular dementia. More consistent are the results of the *Honolulu Asia-Aging Study*, providing evidence of the association between diabetes, genetic base and the occurrence of dementia [51]. Older individuals with type 2 diabetes have an

elevated risk of brain vascular damage and neurovegetative changes. Those with longest diabetes duration and treated with insulin referred more brain changes. Pathological brain changes in diabetic pts might be a basis for a higher risk of dementia [52].

Risk stratification schemes in pts with a stroke considered age, previous history of stroke, TIA, coronary artery disease or heart failure, and traditional risk factors such as diabetes or arterial hypertension. According to the AFI scheme diabetic pts are considered as high risk pts, independent of their age. The American College of Chest Physicians classified diabetic pts as a medium risk population. They are at high risk if another risk factor is present [53]. The Joint Task Force of American Heart Association (AHA)/American College of Cardiology (ACC)/European Society of Cardiology (ESC) classified diabetic and age > 75 years as moderate risk factors together with arterial hypertension, heart failure and left ventricular ejection fraction < 35% [54]. Diabetes and age are determinants of Framingham and CHADS prediction scores for stroke. The latter considered age > 75 years as an independent risk factor for the prediction of future stroke [55, 56].

Treatment of carotid artery disease and/or stroke in diabetic patients

Diabetic pts with cerebrovascular disease should be treated for risk factors: arterial hypertension and hyperlipidaemia (Table 1).

Arterial hypertension is independently associated with the rate of mortality and myocardial infarction and future stroke in type 2 diabetes [57–58]. Regulation of blood pressure in diabetics is more useful than in nondiabetics regarding total cardiovascular risk [59].

Recent studies have reported that aggressive blood pressure reduction significantly reduced stroke. Therefore, a tighter control of blood pressure is required to prevent stroke in diabetic patients as compared with non-diabetic subjects. The desirable target pressure is less than 130/80 mmHg.

Angiotensin Converting Enzyme (ACE) inhibitors have been found useful to be administered to these pts, according to the *HOPE* and *PROGRESS* study [60]. *LIFE* study found the same trend when angiotensin receptor bloc-

kers (ARB) were used [61]. Cochrane, a collaboration librarian who conducted an independent MEDLINE search from 2006 to 2007, recommended an ACE inhibitor/diuretic combi-

nation in patients with cerebrovascular disease, and an ACE inhibitor and ARB in patients with diabetes mellitus [62].

Table 1

Recommendation for diabetic pts, aimed at primary and secondary prevention of stroke

CLASS OF RECOMMENDATION	RECOMMENDATION
I	Treatment of arterial hypertension
IIa	ACE inhibitors administration
I	Statins
I	Acetyl salicylic acid
IIb	Clopidogrel in certain cases
IIa	Glycometabolic control

Treatment in older patients should be almost the same as in younger patients, although blood reduction should be attempted safely and step by step. The use of Ca antagonists is recommended as first-line drugs by Kawamura, as ACE inhibitor, for achieving it [63].

Antithrombotic therapy is indicated for the prevention of stroke in diabetics. The first choice is Acetyl Salicylic Acid (ASA) in a low dose [61]. *Clopidogrel* reduces the future relative risk in these pts [62]. Clopidogrel is administered in case of Aspirin intolerance or in combination with ASA in pts with recurrent stroke. Dual antithrombotic therapy has been recognized as less safe regarding bleeding if it is administered for a long-term period (*MATCH*, *CHARISMA trials*) [63–65]. In the CAPRIE study on patients with multiple vascular bed involvement, the annual events rate in patients who received ASA was 19.84%, compared with a rate of 17.39% in individuals receiving clopidogrel. This group, including those with carotid artery disease, also derived greater benefit from Clopidogrel treatment than did low-risk patients. The CAPRIE trial included 3,866 patients with diabetes. The events rate was higher in this group than in the population as a whole. As with other high-risk populations, patients with diabetes derived a greater benefit from clopidogrel than from ASA therapy. Clopidogrel prevented 21 more events per 1000 diabetic patients treated than did ASA. The events rate in patients with diabetes receiving

insulin was higher than in diabetic patients as a whole, and these patients also achieved an even greater benefit with clopidogrel treatment than did diabetic patients as a whole. In insulin-treated diabetic patients, the rate was 21.5% for those receiving ASA and 17.7% for those receiving clopidogrel – a relative risk of 16.7%. Clopidogrel prevented 38 more events per 1000 diabetic patients receiving insulin than did ASA.

AHA/ACC/ESC Guidelines recommended oral anticoagulant therapy for pts with permanent or paroxysmal atrial fibrillation and a history of stroke or TIA. Pts with more than one moderate risk factor for thrombo-embolism (Diabetes mellitus included) should also be treated with an anticoagulant drug. Chronic oral anticoagulant therapy should be administered to diabetic patients with atrial fibrillation and the presence of a risk factor for thrombo-embolism (class IIA). Aspirin and anticoagulants are recommended for diabetic pts with atrial fibrillation to prevent stroke (class I). The target value of INR should be from 2 to 3, independently of age or other risk factors. A lower INR target (1.6–2) may be considered in pts with a high risk of bleeding [61].

The negative influence of glycaemia in nondiabetic pts presenting with a stroke is also well documented, as it was in diabetics. It is important to detect diabetes early and to regulate glycaemia in pts with a stroke [67]. But there is not sufficient data from controlled stu-

dies that glycaemic control will be beneficial for newly diagnosed diabetic pts with a stroke.

Appropriate antidiabetic treatment will improve the prognosis of diabetic pts with a stroke (*UKPDS*). Group intensive blood-glucose control with sulfonylurea or insulin compared with conventional treatment and risk of complications in pts with type 2 diabetes (*UKPDS 33*). There is evidence-based data that lifestyle modification could reduce the progression of impaired glucose tolerance to diabetes, as much as risk factors for stroke: arterial hypertension, obesity and dyslipidaemia. It is important and could be achieved for better a prognosis for stroke pts [69].

Statins achieve a significant reduction in total and LDL-cholesterol and have important plaque-stabilizing properties. The Heart Protection Study referred to a stroke reduction in the diabetic population when Simvastatin was used [70]. There is evidence-based data regarding stroke reduction using statins. Acute stroke in diabetic pts should be treated on the same principles as the general population. Thrombolysis is effective if administered in the first four hours. Optimization of circulation and glycometabolic control are part of conservative treatment. In the acute phase the value of blood pressure should be reduce up to 25% from its initial value [61].

The aim of carotid revascularization is to prevent a stroke by removing an obstruction of blood flow to the brain and preventing artery-to-artery thrombembolism [70b]. There are no differences in guidelines for carotid revascularization between the diabetic and non-diabetic population. There is a high probability of carotid restenosis after endarterectomy and future vascular events in patients with DM, as referred to in studies: *USFS*, *ELOCAS*, *SAPHIRE* [71–72]. Diabetics referred a higher rate of mortality and intracerebral haemorrhage, but not myocardial infarction, in the perioperative period after carotid endarterectomy [73]. The rate for perioperative stroke and death after carotid endarterectomy in pts older than 75 years is 7.5%. Approved indications for carotid revascularization are: carotid stenosis > 50% with a history of stroke or TIA. Pts with stroke in development and carotid stenosis > 70% could benefit from revascularization, but this indication is not approved. Symptomatic ulce-

rative carotid artery disease with carotid stenosis > 50% should be treated according to the mentioned indications. There are diffident indications for revascularization in the presence of: progressive stroke with carotid stenosis > 50%, acute dissection of internal carotid artery, acute carotid occlusion in first 6 hours, and history of TIA with carotid stenosis < 70% [74].

The Cochrane systematic review including randomized trials: *NASCET*, *ECST*, *ACAS* and *ACST* supports carotid endarterectomy for symptomatic carotid stenosis > 50%, and asymptomatic carotid stenosis > 60% [75]. The American Heart Association suggests a 6% upper limit for perioperative risk in symptomatic pts, and 3% in asymptomatic pts. Pts with tortuous carotid arteries, presence of calcified plaques, lumen diameter of internal carotid artery smaller than 3 mm are served with endarterectomy as the first line of carotid revascularization.

Published data regarding carotid stenting (*CaRESS*, *SAPPHIRE*, *CABERNET*, *ARCHeR*, *CAPTURE*, *BEACH*, *ALKK*, *CASES-PMS*, *CREATE*) show this revascularization procedure as not inferior to endarterectomy. Studies: *CAVATAS*, *Wallstent*, *EVA-3S* did not imply the use of distal protection devices and demonstrated a significant proportion of neurological complications after carotid stenting (Picture 1).



Picture 1 – Ultrasound scan of stent in internal carotid artery and measurement of out flow velocities (own collection)

This procedure is recommended for high risk pts selected with anatomical characteristics and medical comorbidities [76]. Anatomical criteria include: non accessible lesions for surgery, restenosis after endarterectomy, bilateral carotid stenosis, intracranial stenosis or pre-

vious neck surgery or radiation. Comorbidities such as unstable angina, heart failure, planned by-pass surgery, met the high risk categorization. Advanced age > 75 years is a selection criterion for a high risk patient [74–75]. Ongoing trials (*TACIT*, *CREST*) will give more insight into control of pt's specific risk factors (Diabetes mellitus included), vs. optimal medical therapy and carotid endarterectomy /or stenting.

Carotid ultrasound in the diabetic population

The concept of total cardiovascular risk in diabetic patients is based on the results of *Framingham*, *PROCAM*, *Multiple Risk Factors Study* [77]. When diabetic patients refer with an absolute risk of future coronary/or cerebrovascular events > 20%, or a relative risk > 5% compared to the general population, it is necessary to implement the European Society for Cardiology's and American Diabetes Association's Guidelines for treatment or secondary prevention. *Framingham*, *UKPDS* and *FINDRISC* scores are user-friendly worldwide [79–80]. These tools do not consider asymptomatic vascular disease in their aim to stratify a risk in diabetic patients.

Prognosis of pts with type 2 diabetes depends on the presence of diabetic vascular disease. Two thirds of deaths result from macrovascular complications, and 25–50% of them are due to carotid and peripheral arterial disease [81–83]. The *London Cohort Study* defined glycaemia, HbA1C, peripheral arterial disease and carotid stenosis as predictors for the prognosis of T2D pts [84].

The American Heart Association, in order to estimate the cardiovascular risk in type 2 diabetes, recommends screening for asymptomatic vascular disease and its treatment [85].

The recommendation of screening consists of noninvasive determination of the ankle-brachial index and imaging of carotid arteries in order to assess CIMT. Exercise test and Multisliced Computer Tomography (MCT) of vessels have additional prognostic value in this population [86].

Carotid ultrasound is recommended to be used in stroke and carotid bruits [87]. As a result of the low prevalence of carotid artery disease in diabetic pts (4.5%), expenses for devices, training and general screening is not wi-

dely recommended. The clinical role of carotid screening is controversial, as the *Asymptomatic Carotid Atherosclerosis Study* showed a non-significant risk reduction in death and stroke risk after endarterectomy of asymptomatic carotid stenosis. The probability of finding carotid artery disease in type 2 diabetic pts is higher when peripheral arterial disease is diagnosed [87b].

There is a positive trend in the increase of diabetes prevalence worldwide. There is increasing evidence that diabetic cardiovascular complications are the most common cause of death and disability in these pts.

Duval *et al.* suggest refreshment of criteria for indication for carotid examination in diabetics [87].

Carotid ultrasound should be used in every diabetic pt, not only if cerebrovascular symptomatology present, but also in the presence of: coronary artery disease, arterial hypertension, hyperlipidaemia, age > 60 years, smoking, renal failure, long diabetes duration and uncontrolled diabetes [88].

Results of studies dealing with the prognostic role of carotid ultrasound in diabetic or type 2 diabetic populations indicate widening the indications for carotid screening, also.

IMT, measured at the level of common or internal carotid arteries (CIMT), has a prognostic role in determining global cardiovascular risk in the general population and the population with coronary artery disease [89, 89b]. CIMT represents the cumulative effect of predisposing factors of risks, which is why it could predict future risk [90]. Through measuring CIMT we can follow the effects of therapy in relation to the presented risk factors [91].

CIMT is significantly greater in diabetic pts than in nondiabetic pts. *IRAS* and *ARIC* studies referred to a mean CIMT of 0.91 and 0.88 mm in the diabetic population (Picture 2).

There is a higher rate of CIMT progression in pts with DM on standard therapy, vs. those with intensive therapy. In his systematic review Bots deals with the use of statin and antihypertensive drugs, aiming to attenuate the rate of progression of CIMT and to reflect the cardiovascular risk [92].

The presence of carotid plaques is a superior factor influencing the prognosis of coronary artery disease more than CIMT [94–95].

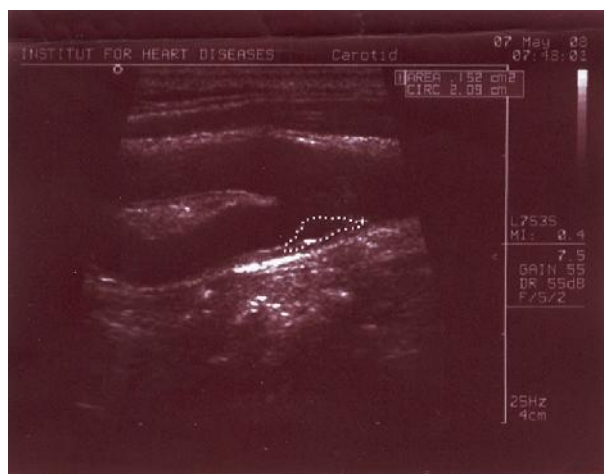
All of these studies included a significant part of the diabetic subpopulation.



Picture 2 – Ultrasound scan of increased IMT in common carotid artery (own collection)

Lee and Matsumoto referred to a strong relation between increased CIMT and carotid plaques with an ischaemic stroke in type 2 diabetics [96].

Studies: *Kuopio Ischemic Heart Disease Risk Factor*, *Rotterdam, Cardiovascular Health*, *Malmo Diet Study*, *ARIC*, *LILAC*, *CAPS*, and meta-analysis of Lorenz presented carotid plaques and stenosis as superior predictors for future coronary and cerebrovascular events including mortality (Picture 3) [98–99].



Picture 3 – Ultrasound scan of echolucent plaque on carotid bulb

The prevalence of carotid artery disease in the DM population, defined as presence of plaque, is over 50% [99b]. Advanced carotid atherosclerosis is related to glycaemia, and lipid profile, as well to over all cardiovascular risk in these pts [100–101]. Ultrasound measu-

rements of progression of carotid IMT, carotid plaque area and volume (three dimensional acquisitions for the last ones), are correlated with type 2 diabetes and vascular events. Use of this method is of clinical usefulness and has a future perspective [103–104]. Ragi recommended CIMT and MCT for coronary calcium to estimate the risk in diabetic pts without presence of vascular disease. CIMT value > 1 mm, and or calcium score > 400 put these pts at high risk, where medical therapy is necessary [105].

Carotid artery disease is related to the presence of coronary artery disease in the type 2 diabetic population [106] the incremental value of carotid ultrasound in prognosis of pts with type 2 diabetes who are asymptomatic for coronary artery disease is presented by a few studies in the last two years [107–109]. The systematic review by Brohall presented CIMT with a prognostic value for future cardiovascular events [110]. There is a two- to four-fold relative risk of future events regarding 0,1 mm CIMT.

Measurements of CIMT may provide good prognostic information during atherosclerosis screening programmes in the type 2 diabetic population. Our unpublished data presented maximal CIMT as a predictor for cardiovascular mortality (Fig. 1) and carotid stenosis for cardiovascular events with two-fold risk (OR 2,246 95% CI 0,487–10,359. Our results have made a contribution in this way.

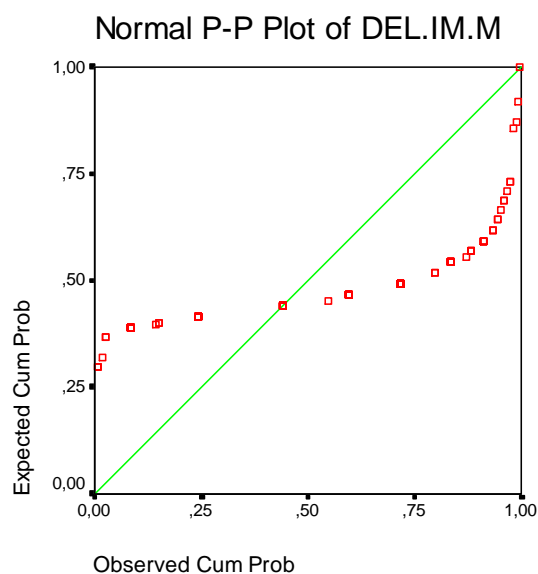


Figure 1 – Regression probability of occurrence of cardiovascular death in type 2 diabetes depends on maximal value of CIMT

ARIC, IRAS, CHT studies referred to progression of CIMT of 0.05–0.07 mm annually. Studies dealing with type 2 diabetic population referred for progression of CIMT of 0.1 mm annually.

Hodis presented that a change in CIMT of 0.03 mm annually is associated with a relative risk of 2.2 for future coronary events. This meta-analysis was done on high risk patients [111]. According to Lorenz's meta-analysis every change of CIMT by 0.1 increases the relative risk of coronary or cerebrovascular events by 10 to 30% [99]. CIMT progression, *a priori*, is determined from the same risk factors as coronary artery disease. It is not surprising that it can determine a predictive role in coronary events [112]. Aging could additionally influence the progression of carotid atherosclerosis (EVA, CAPS) [113–116].

Influence of Aging and Diabetes On Carotid Artery Disease

The risk of stroke increases with age. The annual risk increases from 1.5% in subjects aged 50–59 years to 23.5% for those aged 80–89 [117]. This was confirmed by multivariate analysis, made by the *AF Investigators Group*, which revealed increasing age, diabetes, and arterial hypertension and previous stroke as factors for stroke onset [118].

The subgroup of old people in the type 2 diabetic population presented a high risk of ischaemic stroke [119]. Age, according to the *DAI* study, has been presented as an independent predictor of ischaemic stroke in type 2 diabetes [120].

The results of the Hoorn study showed that DM accelerated the aging of arterial vessels [116]. DM is associated with an increasing prevalence of CAD, equivalent to the aging of vessels by 20 years, or 10 years in men.

The occurrence of carotid plaques depends on the aging of pts. The *Malmo* study defined age as an independent factor for increased CIMT in the general population [117]. CIMT depends on diabetes duration. The hazard ratio and CIMT value are multiplicities in older pts with long diabetes duration.

Unpublished data from our Vascular Centre' study included 340 pts with type 2 diabetes. Results revealed a correlation between ma-

ximal value of CIMT and age in type 2 diabetics by Pearson analysis ($r = 0.498$, $p = 0.03$) (Figure 2). After the multivariate linear regression model was built, aging by 1 year has influenced an increase in CIMT by 13.6% to 15.4%.

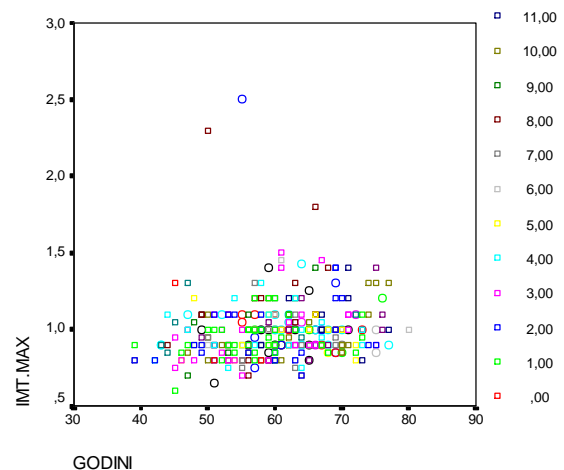


Figure 2 – Pearson correlation of maximal value of CIMT and age in type 2 diabetic pts

A systematic review by Brohall showed the presence of DM as equivalent to carotid ageing by 10 years [19b].

An age-dependent increase in carotid diameter can reflect age-associated changes in the carotid wall structure (alterations in the content and integrity of the structural matrix proteins, namely elastin and collagen). It is also worth noting, that in our healthy middle-aged population, an independent effect of age on carotid luminal diameter was observed much more in men than in women [123b].

Zunker and Mast described structural alteration in small penetrating brain arteries and arterioles, where medial smooth muscle first hypertrophied and was then replaced by extracellular matrix and plasma proteins. This is an aging phenomenon, but is exacerbated by diabetes mellitus and arterial hypertension [119–120].

Conclusion

Carotid ultrasound measurement of IMT or detection of plaque or stenosis could provide prognostic information on asymptomatic type 2 diabetic patients, who at age > 60 years presented a greater risk factor. Old people in the type 2 diabetic population presented a high prevalence of carotid artery disease and referred a high risk of ischaemic stroke. Although there is

a likelihood of a higher prevalence of comorbidities in older patients, their treatment should be almost the same as in younger patients.

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