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# CAROTID IMT IN TYPE 2 DIABETIC PATIENTS: A SURVEY ON FACTORS OF INFLUENCE

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A b s t r a c t: The study was aimed to determine factors of carotid intima-media thickness (CIMT) in a population of patients with type 2 diabetes (T2D).

A survey was conducted on 370 patients (mean age 60.3 ± 8.3 years and diabetes duration 8.6 ± 6.2 years) with T2D and coronary artery disease. Multivariate linear regression analysis was built to define the factors of CIMT, when age, systolic and diastolic blood pressure, weight, body mass index, waist circumference, glycaemia, urea, creatinin, triglycerides, total cholesterol, LDL-, HDL-, and non-HDL-cholesterol were put in a model.

Mean CIMT of 0.8992 ± 0.1529 mm, and its maximal value of 0.9905 ± 1.946 mm was detected in this study population. Regression analysis demonstrated that mean and maximal CIMT were independently influenced by age, blood creatinin, diastolic pressure and non-HDL cholesterol, as well.

The results have clinical value in defining target groups in patients with T2D and arterial hypertension, higher non-HDL cholesterol and blood creatinin, and those-that are older have a greater probability of detection of increased CIMT.

**Key words**: CIMT, type 2 diabetes, creatinin, age, non-HDL cholesterol.

**Contributors:** *Ljubica Georgievska-Ismail, Slavco Tosev

## *Introduction*

*Diabetes mellitus* (DM) has been recognized as an independent risk factor for carotid artery disease in the general population [1]. Its onset in pts

with DM is influenced by arterial hypertension, hyperlipidemia and inflamatory biomarkers [2, 3].

The IRAS study defined postprandial glycemia as a risk factor for carotid IMT in the non-diabetic population and hypercholesterolemia as a risk factor for CIMT in diabetic pts [4, 5]. However, not many studies have dealt with risk factors for carotid IMT value in pts with DM.

The study was aimed to determine factors of carotid intima-media thickness (CIMT) in a population of patients with type 2 diabetes (T2D).

## *Patients and methods*

A survey was conducted on 370 patients (mean age 60.3 ± 8.3 years and diabetes duration 8.6 ± 6.2 years) with T2D and coronary artery disease. The study was carried out in the Vascular Lab of the University Cardiology Clinic, Skopje, over the period 2005–2008. Type 2 diabetes was defined based on the criteria of the International Diabetes Federation. Coronary artery disease in the evaluated population is defined as symptomatic CAD, angiographically confirmed.

Evaluation for CARD was done by the HP Agilent S4500 ultrasound system. CIMT was measured by B-mode ultrasound using a linear transducer (7.5–10 MHz) and presented as the mean value of two measurements from both sides of common carotid arteries. Carotid IMT was defined as the distance from the leading edge of the first echogenic line to the leading edge of the second echogenic line on the scans, with the first line representing the lumen-intimal interface and the second line representing the collagen-containing upper layer of the adventitia. IMT with a value equal to or great than 0.8 mm was defined as increased IMT. The observer was blind to patients' risk factors.

Standard laboratory tests were performed in the evaluated patients. Blood pressure was measured with a standard sphygmomanometer in a sitting position and presented as a mean value of two readings (in mmHg). Anthropometric measurements were made with the patient wearing lightweight clothing and no shoes. Weight was presented in kilograms (kg) and Body Mass Index (BMI) in $kg/m^2$. Waist and hip circumferences were measured with a plastic tape meter at the level of the umbilicus and of the major trochanter.

Multivariate linear regression analysis was built to define the factors of CIMT when age, systolic and diastolic blood pressure, weight, body mass index, waist circumference, glycemia, urea, creatinin, triglycerides, total cholesterol, LDL- ,HDL- , and non-HDL cholesterol were put into a model.

*Results*

In the study population we found these estimated parameters (Table 1).

Table 1

*Values of estimated risk factors*

| Parameters | Mean. | Std. Dev. |
|---|---|---|
| Sys.TA (mmHg) | 144.26 | 19.56 |
| Waist (cm) | 96.97 | 8.00 |
| Hip | 52.96 | 6.43 |
| High | 169.07 | 7.59 |
| Weight (kg) | 82.38 | 12.61 |
| BMI (kg/m2) | 28.75 | 4.07 |
| GL (mmol/L) | 8.49 | 2.47 |
| HOL. | 5.39 | 1.37 |
| HDL | 1.05 | 0.44 |
| NON.HDL | 4.28 | 1.36 |
| LDL | 3.37 | 1.00 |
| TR | 1.98 | 1.04 |

We measured a mean value of CIMT (CIMTx) of 0.8992 ± 1.529 mm, and its maximal value (CIMTm) = 0.9905 ± 1.946 mm (Figure 1).

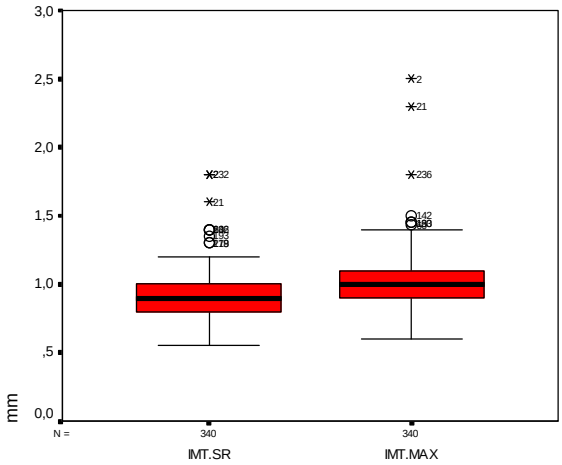


*Figure 1 – CIMT values in study population*

Multiple regression analysis (shown in Table 2) demonstrated that mean and maximal values of CIMT were independently associated with age (Figure 2), blood creatinin and diastolic pressure. Maximal value CIMT was influenced by non-HDL cholesterol, also (Figure 3).

Table 2

*Multiple regression analysis for factors of CIMT*

| Model | | Beta | Sig | 95% CI (B) | 95% CI(B) |
|---|---|---|---|---|---|
| IMT mean | Const | | 0.000 | .293 | .699 |
| | Age | 0.154 | 0.004 | .001 | .005 |
| | Creatinin | 0.136 | 0.011 | .000 | .001 |
| | Diast.press | 0.111 | 0.036 | .000 | .004 |
| IMT max | Const | | 0.001 | .173 | .669 |
| | Non HDL | 0.190 | 0.000 | .013 | .043 |
| | Creatinin | 0.142 | 0.007 | .000 | .001 |
| | Age | 0.136 | 0.010 | .001 | .006 |
| | Diast.press | 0.104 | 0.048 | .000 | .004 |

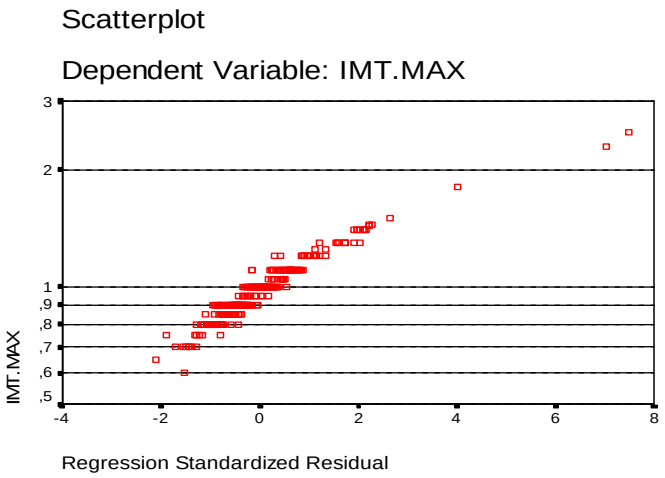


*Figure 2 – Linear regression depenedence of CIMTm from age of pts*

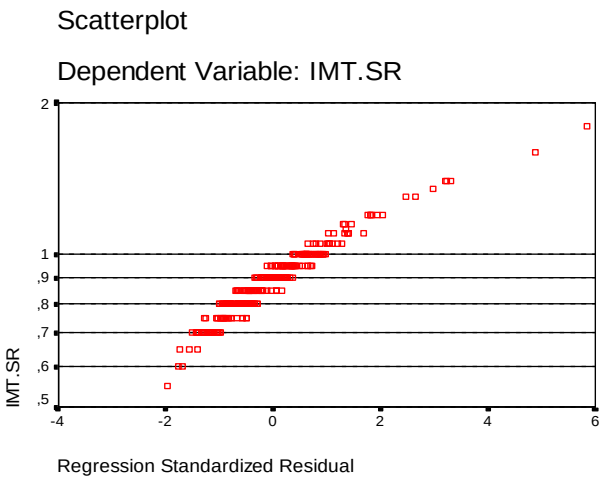


*Figure 3 – Linear regression depenedence of CIMTx from non-HDL cholesterol*

## *Discussion*

Previous studies referred to increased mean CIMT in the diabetic population vs. those in the general population (Table 3). IRAS and ARIC studies referred to CIMT value = 0.91 and 0.88 mm in populations with diabetes and metabolic syndrome [6, 7]. These values are comparable with CIMT values derived from our study.

Every change of blood creatinin value of 1 mmol/L is responsible for increasing CIMT by 14%, according to our results. Patients with manifest nephropathy were excluded from the study.

Some previous studies referred to the fact that carotid atherosclerosis is more prominent in pts with early diabetic nephropathy and T2D [8–12]. Blood creatinin value represents kidney function and its impairment. Diabetic nephropathy even in an early phase is a marker for general atherosclerosis. Therefore there is a connection with CIMT. Another explanation is that nephropathy and carotid atherosclerosis share the same risk factors: arterial hypertension, which is very frequent and a component of metabolic syndome. A third explananation is that kidney impairment accelerates carotid atherosclerosis in the type 2 diabetic population [13–15]. The most logical explanation is that increasing of CIMT is a part of the process of atherosclerosis and could predict diabetic nephropathy in its early phases.

Table 3

*Studies on CIMT in populations with T2DM and/or coronary artery disease*

| *Author* | *No pts* | *Age* | *CIMT (mm)* |
|---|---|---|---|
| **Folsom** | 263 (244) | 45 ± 64 | 0.8498 + 0.0127 (0.7347 + 0.0098) |
| **Hedbland** | 170 (130) | 59 ± 6 | 0.86 + 0.0169 (0.81 + 0.0173) |
| **Wakenknecht** | 272 | 57 ± 8 | 0.890 + 0.00166 |
| **Ishizaka** | 166 | 60 ± 9 | 0.82 + 0.0194 |
| **Wei** | 185 | 54 ± 8 | 0.84 + 0.02 (0.73 + 0.01) |
| **Henry** | 301 | 67 ± 8 | 0.88 + 0.0098 |
| **Taniwaki** | 271 | 51 ±10 | 1.004 + 0.0266 |
| **El-Bargouri** | 250 | 51 ± 8 | 0.798 + 0.0152 (0.797 + 0.0185) |
| **Yamasaki** | 252 | 30 ± 6 | 1.087 + 0.0334 |
| **Rajala** | 54 | 62 ± 2 | 0.99 + 0.0422 |
| **Niskanen** | 84 | 67 ± 1 | 1.21 + 0.04 |
| **Geroulakis** | 97 | 49 ± 7 | 0.83 + 0.0234 |
| **Toumilehro** | 44 | 70 ± 8.9 | 1.28 + 0.1447 |
| **Temelkova** | 71 | 57 ± 1 | 0.98 + 0.03 |
| **Guvener** | 70 | 58 ± 11 | 0.74 + 0.0239 |
| **Bonora** | 56 | 57 ± 8 | 1.44 + 0.020 |
| **Pujia** | 54 | 54 ± 10 | 0.765 + 0.0176 |
| **Visona** | 29 | 53 ± 6 | 0.90 + 0.0216 |
| **Keven** | 19 | 48 ± 9 | 0.91 + 0.0252 |
| **Sugurdadomir** | 44 | 66 | 0.87 + 0.0281 |
| **Mohami** | 140 | 55 ± 13 | 0.87 + 0.0281 |
| **Bosevski** | 340 | 60.3 ± 8.3 | 0.8965 + 0.1601 |
| **Lorenz*** | 5052 | 19–90 | |
| **Hodis*** | 100 | 54 | |

*Studies are meta-analysis for CIMT.

The *Malmo* study referred to age as an independent factor for increased CIMT in the general population [16]. Studies of the influence of age on CIMT in the diabetic population are lacking. Because of structural changes during ageing, CIMT has been thickened in the older population. How important it is in imparied gluco-metabolic conditions is not well understood. Ageing by one year is responsible for an increase of CIMT by 15%, according to our results. The systematic review by Brohall presents DM as an independent risk factor for CIMT, which is equivalent to ageing by 10 years [17].

Our multivariate analysis reaveled non HDL-cholesterol and diastolic blood pressure as independent risk factors for CIMT in the T2D population. Arterial hypertension and hyperlipidaemia were defined as independent risk factors for advanced carotid artery disease in T2D patients, earlier [18]. Sands trial has shown vascular remodelling and CIMT thickening due to arteial hyper-

tension and hyperlipidemia in the general population [19]. Our results confirm the predictivity of these risk factors for CIMT in type 2 diabetic patients.

## *Conclusion*

Our data revealed age, blood creatinin, non HDL cholesterol and diastolic pressure as indepenedent risk factors for CIMT in the T2D population. The results have clinical value in defining target subgroups in patients with T2D: and arterial hypertension, higher non-HDL cholesterol and blood creatinin, and that older ones to have a greater probability of showing symptoms of increased CIMT.

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Резиме

## ЗАДЕБЕЛУВАЊЕТО НА КАРОТИДНАТА ИНТИМА-МЕДИЈА КАЈ ПАЦИЕНТИТЕ СО ТИП 2 ДИЈАБЕТЕС: ПОПРЕЧНА СТУДИЈА ЗА ФАКТОРИТЕ НА ВЛИЈАНИЕ

**Бошевски М., Соработници***

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Студијата имаше за цел одредување на фактори на ризик кои влијаат на вредноста на задебелувањето на каротидната интима-медија (кИМЗ) кај пациентите со тип 2 дијабетес (Т2Д).

Беше изведена попречна студија на 370 пациенти (средна возраст 60,3 ± 8,3 години и времетрање на дијабетес 8,6 ± 6,2 години). Мултиваријантна линеарна регресиона анализа беше направена со цел да се дефинираат факторите на кИМЗ откако возраста, систолниот и дијастолниот крвен притисок, тежината, индексот на телесна маса, обемот на струкот, гликемијата, уреата, креатининот, триглицеридите, вкупниот холестерол, ЛДЛ-ХДЛ- и нон-ХДЛ холестеролот беа внесени во моделот.

Беше одредена средна вредност на кИМЗ од 0,8992 ± 0,1529 мм и нејзина максимална вредност од 0,9905 ± 1,946 мм. Регресионата анализа ги прикажа возраста, креатининот, дијастолниот притисок и нон-ХДЛ холестеролот за независни фактори на кИМЗ.

Резултатите имаат клиничко значење во дефинирањето на целни потгрупи на пациенти со Т2Д и: артериска хипертензија, висок нон-ХДЛ холестерол и креатинин, како и оние повозрасните каде што очекуваме поголема веројатност за одредување на зголемена вредност на задебелувањето на каротидната интима-медија.

**Клучни зборови**: кИМЗ, тип 2 дијабетес, креатинин, возраст, нон- ХДЛ холестерол.

**Соработници:** *Љубица Георгиевска-Исмаил, Славчо Тошев

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Table 1. Values of estimated risk factors

| Parameters | Mean. | Std. Dev. |
|---|---|---|
| Sys.TA (mmHg) | 144,26 | 19,56 |
| Waist (cm) | 96,97 | 8,00 |
| Hip | 52,96 | 6,43 |
| High | 169,07 | 7,59 |
| Weight (kg) | 82,38 | 12,61 |
| BMI (kg/m2) | 28,75 | 4,07 |
| GL (mmol/L) | 8,49 | 2,47 |
| HOL. | 5,39 | 1,37 |
| HDL | 1,05 | 0,44 |
| NON.HDL | 4,28 | 1,36 |
| LDL | 3,37 | 1,00 |
| TR | 1,98 | 1,04 |

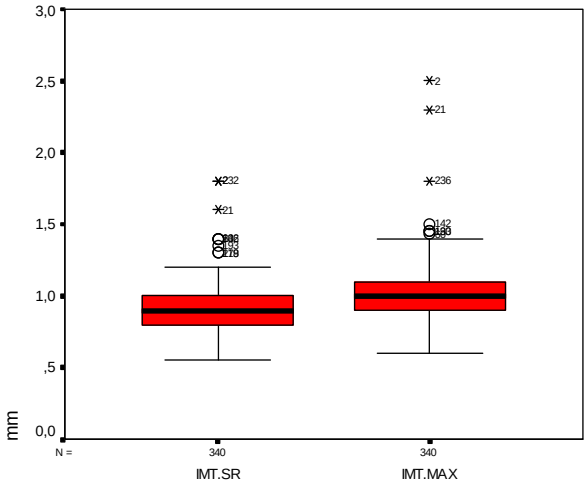


Figure 1. CIMT values in study population
Графикон 1. Вредности на КИМТ во испитувната популација

Table 2. Multiple regression analysis for factors of CIMT
Табела 2. Мултиваријантна регресиона анализа за фактори на КИМТ

| Model | | Beta | Sig | 95% CI (B) | 95% CI(B) |
|---|---|---|---|---|---|
| IMT mean | Const | | 0,000 | ,293 | ,699 |
| | Age | 0,154 | 0,004 | ,001 | ,005 |
| | Creatinin | 0,136 | 0,011 | ,000 | ,001 |
| | Diast.press. | 0,111 | 0,036 | ,000 | ,004 |
| IMT max | Const | | 0,001 | ,173 | ,669 |
| | Non HDL | 0,190 | 0,000 | ,013 | ,043 |
| | Creatinin | 0,142 | 0,007 | ,000 | ,001 |
| | Age | 0,136 | 0,010 | ,001 | ,006 |
| | Diast.press | 0,104 | 0,048 | ,000 | ,004 |

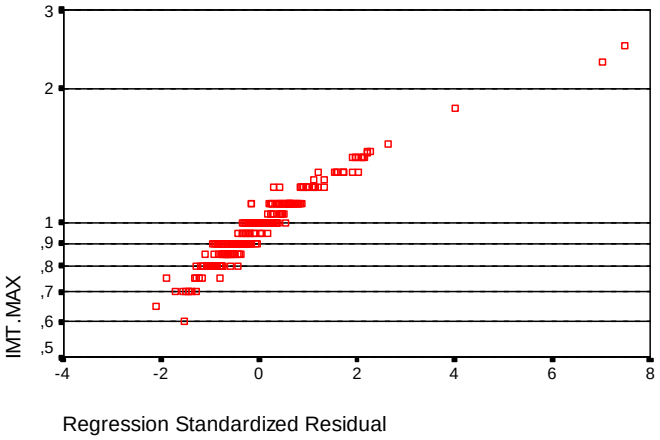


Figure 2. Linear regression depenedence of CIMTm from age of pts
Графикон 2. Линеарна регресиона зависност на макс. КИМТ од возраста на пациентот.

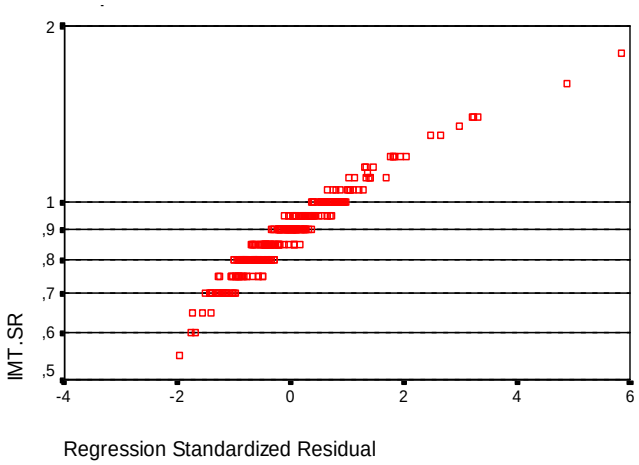


Figure 3. Linear regression depenedence of CIMTx from non-HDL cholesterol
Графикон 3. Линеарна регресиона зависност на средната вредност КИМТ од нон-ХДЛ холестеролот.

Табле 3. Студии за kIMT во популациите со Т2ДМ и/или КАБ
Table 3. Studies on CIMT in populations with T2DM and/or coronary artery disease

| *Author* | *No pts* | *Age* | *CIMT (mm)* |
|---|---|---|---|
| **Folsom** | 263 (244) | 45±64 | 0,8498+0,0127 (0,7347+0,0098) |
| **Hedbland** | 170(130) | 59±6 | 0,86+0,0169 (0,81+0,0173) |
| **Wakenknecht** | 272 | 57±8 | 0,890+0,00166 |
| **Ishizaka** | 166 | 60±9 | 0,82+0,0194 |
| **Wei** | 185 | 54±8 | 0,84+0,02 (0,73+0,01) |
| **Henry** | 301 | 67±8 | 0,88+0,0098 |
| **Taniwaki** | 271 | 51±10 | 1,004+0,0266 |
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| **Yamasaki** | 252 | 30±6 | 1,087+0,0334 |
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| **Niskanen** | 84 | 67±1 | 1,21+0,04 |
| **Geroulakis** | 97 | 49±7 | 0,83+0,0234 |
| **Toumilehro** | 44 | 70±8,9 | 1,28+0,1447 |
| **Temelkova** | 71 | 57±1 | 0,98+0,03 |
| **Guvener** | 70 | 58±11 | 0,74+0,0239 |
| **Bonora** | 56 | 57±8 | 1,44+0,020 |
| **Pujia** | 54 | 54±10 | 0,765+0,0176 |
| **Visona** | 29 | 53±6 | 0,90+0,0216 |
| **Keven** | 19 | 48±9 | 0,91+0,0252 |
| **Sugurdadomir** | 44 | 66 | 0,87+0,0281 |

| | | | |
|---|---|---|---|
| **Mohami** | 140 | 55+13 | 0,87+0,0281 |
| **Bosevski** | 340 | 60,3+ 8,3 | 0,8965+0,1601 |
| **Lorenz*** | 5052 | 19-90 | |
| **Hodis*** | 100 | 54 | |

*Studies are meta-analysis for CIMT.

## Задебелувањето на каротидната интима-медија кај пациентите со тип 2 дијабетес: Попречна студија за факторите на влијание

***Резиме***

Студијата имаше за цел одредување на фактори на ризик кои влијаат на вредноста на задебелувањето на каротидната интима-медија (кИМЗ) кај пациентите со тип 2 дијабетес (Т2Д).

Беше изведена попречна студија на 370 пациенти (средна возраст 60,3 ± 8,3 години анд времетрање на дијабетес 8,6 ± 6,2 години). Мултиваријантна линеарна регресиона анализа беше направена со цел на дефинирање на факторите на кИМЗ откако возраста, систолниот и дијастолниот крвен притисок, тежината, индексот на телесна маса, обемот на структо, гликемијата, уреата, креатининот, триглицеридите, вкупниот холестерол, ЛДЛ- ХДЛ- и нон-ХДЛ холестеролот беа внесени во моделот.

Беше одредена средна вредност на кИМТ од 0,8992 ± 0,1529 мм и нејзина максимална вредност од 0,9905 ± 1,946 мм. Регресионата анализа ги прикажа возраста, креатининот, дијастолниот притисок и нон-ХДЛ холестеролот за независни фактори на кИМЗ.

Резултатите имаат клиничко значење во дефинирањето на целни подргупи на пациенти со Т2Д и: артериска хипертензија, висок нон-ХДЛ холестерол и креатинин, како и оние повозрасните каде очекуваме поголема веројатност за одредување на зголемена вредноста на задебелувањето на каротидната интима-медија.