

# THE VALUE OF THE INTIMA-MEDIA THICKNESS AS A RISK FACTOR FOR CEREBROVASCULAR DISEASE IN FIRST DEGREE RELATIVES OF DIABETIC TYPE 2 PATIENTS

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## ABSTRACT

Cerebrovascular diseases and diabetes mellitus have become in the last years the first cause of mortality and major invalidity throughout the world. Intima media thickness is a very good marker for subclinical atherosclerosis and also for predicting future cardio and cerebrovascular events.

**The aim** of this study is to try to find out the value of the intima media thickness as a risk factor for cerebrovascular disease in first degree relatives of diabetic type 2 patients.

**Material and method:** we evaluated two groups, selected by well defined criteria, divided into the witness group of 21 subjects and the study group of 41 subjects. The intima media thickness was measured with a standard method, by cervical ultrasound mode B, at the common carotid artery distal wall, both sides left and right. Other parameters measured were weight, height, and body mass index, arterial systolic and diastolic blood pressure.

**Results:** Gender distribution of subjects in the study group was predominantly male (53,6%); regarding the BMI, we could notice that 57% of the study group was overweight, but with normal blood pressure. The IMT value in the study group has varied between 0,6mm and 1,3 mm with an average of 0,82mm on the right side and between 0,5mm and 1,2mm with an average of 0,87mm on the left side. Applying the t-Student test to these values we could see no statistical significance between the two groups analyzed ( $p>0,05$ ).

**Conclusion:** in this study intima media thickness had no statistical significant value as a risk factor for cerebrovascular disease in first degree relatives of diabetic type 2 patients.

**Key words:** intima media thickness, first degree relatives, cerebrovascular disease, diabetes mellitus type 2

## INTRODUCTION

The cerebrovascular diseases (CVD) are the third leading cause of morbidity and mortality worldwide, both in Europe and the USA. In Romania, according to WHO statistics, cerebrovascular disease ranks first both in terms of mortality and major long-term disability (1). Diabetes mellitus (DM) has become an alarming and extremely dangerous reality. It is estimated that worldwide in 2006 were 264 million people with diabetes, the vast majority (90%) were type 2. The diabetes prevalence in 1995 was 135 million and the prediction for 2025 is 380 million (2,3).

Intima media thickness (IMT) is a marker of subclinical atherosclerosis representing effectively the intima and media cumulative thickness measured

through ultrasound image of the carotid axis, mode B, in longitudinal section (4). The natural course of IMT depends on age and sex, and the genetics of each individual (5). The genetic background seems to be directly involved in controlling phenotypic expression of IMT, there are studies proving that the offspring of diabetic patients type 2 IMT values of both the ACC and ACI is higher compared with relatives of people without diabetes (6).

## PURPOSE OF STUDY

In the present study we aimed to analyze the value of intima-media thickness(IMT) measured by B mode ultrasound of the common carotid artery bilaterally as an independent risk factor for ischemic

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stroke in first degree relatives of patients with type 2 diabetes.

The motivation of this study was that stroke is one of the most frequent pathologies in today's society, but also one of the neurological diseases that are well complied to primary and secondary prevention.

Stroke is characterized by an increasing prevalence, by a substantial high number of modifiable risk factors, a high rate of long-term disability, and a high economical intake both at national and international level. The relationship between stroke and type 2 diabetes is demonstrated by numerous population studies, larger or smaller. It is also known the risk of these diseases in future generations with a genetic load, with a family history of stroke or type 2 diabetes (8,9,10).

In this context we aimed to evaluate the risk of cerebrovascular disease in first degree relatives of patients known with type 2 diabetes with the help of IMT, especially for primary prevention in these subjects and to possibly include the IMT measurement in a protocol examination of patients with type 2 diabetes mellitus as a risk factor for their descendants.

## MATERIAL AND METHOD

We evaluated a total of 62 patients divided into two groups: 41 subjects in the study group and 21 subjects in the control group. Criteria for inclusion in the control group were:

- family history, that is a sibling or parent with a history of stroke
- the absence of type 2 diabetes in first-degree relatives
- aged 20-50 years
- absence of cardiovascular pathology and/or cerebrovascular and in the study group:

- family history, namely a first degree relative (parents and/or brothers/sisters) with type 2 diabetes
- age between 20-50 years
- the absence of cardiovascular and/or cerebrovascular pathology.

As exclusion major criteria for both groups were:

- the IMT > 1.5 mm
- carotid stenosis or occlusion
- older than 50 years.

## IMT measurement

Before being examined, all subjects were informed about the research method and signed informed consent. The groups were examined with the Siemens Acuson X300, using a 7.5 MHz linear probe in the neurosonology laboratory belonging to the Neurology Clinic, Rehabilitation Hospital of Iasi, in dim light and quiet conditions. All measurements were performed with subjects in the supine position with slight hyperextension of the neck, head up to around 20° and possibly as necessary rotated 30° left or/and right.

The examination ultrasound method was on the longitudinal section, mode B on both left and right common carotid arteries. IMT measurement was performed at the distal wall of the ACC, 10 mm of the bifurcation, in an area without atherom plaques. On the device monitor it was used the "frozen" mode and position of the cursor was placed at the intima-lumen and intima – adventitious interface, the distance between the two lines hyperechogenic was recorded as intima-media thickness or IMT. Three measurements were performed on each common carotid artery; the value used for subsequent statistical analysis was the average of 3 measurements on each side.

IMT higher average values than of 0.9 mm were considered elevated. We have not considered val-

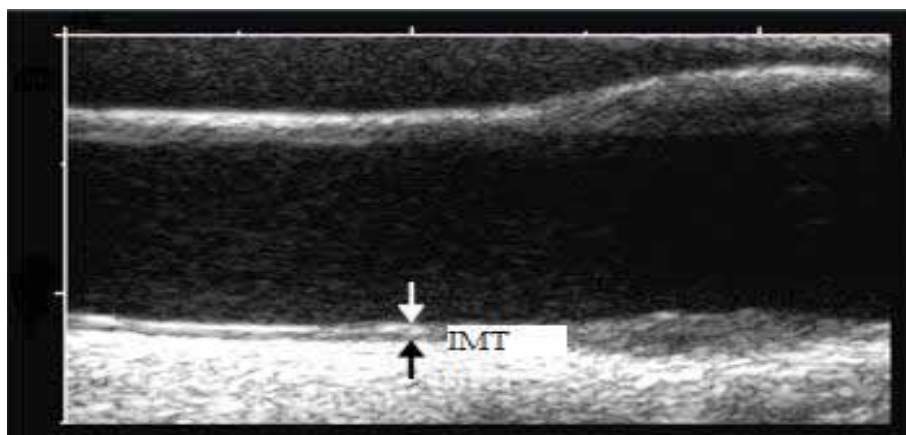


Figure 1. IMT image on ultrasound mode B

ues greater than or equal to 1.6 mm (which represent plaque in formation). Note that all measurements were made by the same examiner to eliminate interexaminator differences in measurement.

### Measurement of other parameters

IMT has a natural evolution, which depends on sex, age and associated pathology (diabetes, hypertension, etc). There is an increased IMT value with age without necessarily becoming pathological. The ARIC study provided data on the mean IMT by age and sex for ACC and bifurcation. The estimated annual rate of progression of IMT was 0.010 mm per year for both sexes. Other studies have published values of 0.12 mm or 0.3 – 0.4 mm. At any age male subjects had higher values of IMT and the progression rate was higher at the bifurcation where the arterial wall is subjected to a level of high hemodynamic stress. Perhaps more from the neurologist's point of view we are interested in the relationship between IMT and stroke (11,12).

At first glance, after scrolling of vascular risk factors that correlate with increased IMT we might state that there is an increased risk of stroke due to their presence, but studies over the years have shown that IMT is an independent risk factor for cerebral ischemic events, even in the absence of plaque, with correlations even with subtypes of stroke (13,14).

Thus, in this study we also correlated the IMT with other risk factors, namely sex, age, blood pressure, body mass index, smoker or non-smoker status.

## RESULTS

In the control group we included 21 subjects from urban areas, of which 11 subjects were male and 10 female. Following history taking the distribution of first-degree relatives of the subjects included in the control group was revealed, relatives without type 2 diabetes, but with ischemic type of cerebrovascular pathology (patients hospitalized in the Neurology Clinic, Hospital of Rehabilitation Iasi), with predominance of mothers having stroke (57,1%). The age of the subjects included in the control group was quite diverse, ranging from 26 to 50 years: two subjects in the age group 41-50 years, 11 subjects in the age group 31-40 years and 8 subjects in the age group 21-30 years.

With regard to smoking we have established their status as 1 equal to a smoker and nonsmoker equal to 0. Thus, the distribution of smoking status in the

control group showed an increased number of smokers (71.42%).

Weight status was calculated with the body mass index standard formula (BMI) and according to the chart the distribution was performed to underweight, normal, overweight and obese.

**Table 1. Standard value of BMI**

|             | <b>BMI value</b>              |
|-------------|-------------------------------|
| Underweight | ≥ 18 kg/m <sup>2</sup>        |
| Normal      | 18,5 – 24,9 kg/m <sup>2</sup> |
| Overweight  | 25 – 29,9 kg/m <sup>2</sup>   |
| Obese       | ≥ 30 kg/m <sup>2</sup>        |

Thus, in the control group 24% of subjects were obese, 38% overweight and 38% normal weight.

In the study group were included 41 subjects whose first-degree relatives were clinically diagnosed with type 2 diabetes in a medical facility (clinic or outpatient ambulatory) without cardiovascular or cerebrovascular pathology. Thus, the study group distribution by gender was: 22 male subjects and 18 female subjects. The age of the subjects ranged between 22 and 50 years. Distribution of first degree relatives was: 23 subjects had the mother with diabetes type 2 and 17 subjects had the father diagnosed with type 2 diabetes.

Weight status was calculated as for the control group, with the same formula and chart accepted by relevant international forums. Thus, 13% of subjects were obese, 57% overweight and only 30% of normal weight.

The blood pressure values were within normal limits in both groups, one subject in the study group had high blood pressure values at the time of the examination; he was subsequently monitored and the blood pressure values returned to normal.

Measuring the most important parameter in the groups, the intima-media thickness average value had the following characteristics:

- in the study group:
  - the right common carotid artery IMT ranged from 0.6 mm to 1.3 mm, with a wide variance of the series of values (20.99%), most patients with values between Q25-Q75 quartile, namely between 0.7 to 1, the average of the group being 0.82 mm;
  - the left common carotid artery IMT ranged from 0.5 mm to 1.2 mm, with a wide variance of the series of values (21.85%), most patients with values in the range 0.7-1; group average being 0.87 mm;

- in the control group:
  - the right common carotid artery IMT ranged from 0.6 mm to 1.4 mm, with the largest variance of the series of values (23.04%), most patients with IMT values between Q25-Q75 quartile- range from 0.8 to 1, the average of the group being 0.91 mm;
  - the left common carotid artery IMT ranged from 0.6 mm left to 1.4 mm, with a wide variance of the series of values (20.47%), most patients with values in the range 0.8-1; group average was 0.95 mm.



Figure 2. Distribution of left IMT in the study group

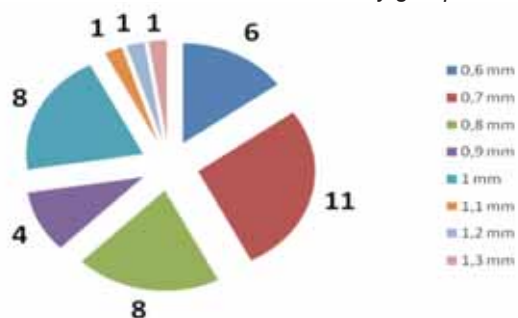


Figure 3. Distribution of right IMT in the study group

Another statistical method used was the t-Student test. Thus, applying the Student t-test on the mean values of intima-media thickness on both groups, IMT was slightly higher in the control group, but the differences were not statistically significant ( $p > 0.05$ ).

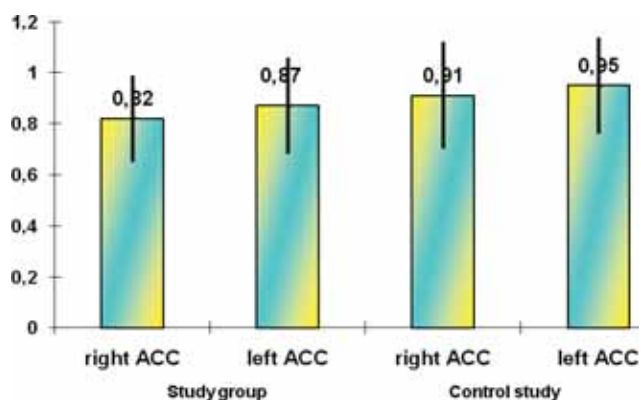


Figure 4. Mean IMT values in both groups

### CONCLUSIONS

Subclinical atherosclerosis is the early, asymptomatic form of atherosclerosis. It is measured by markers such as carotid intima-media thickness (IMT), leg-arm index, arterial calcification score and arterial stiffness. IMT is a significant independent predictor of atherosclerosis at several vascular levels, demonstrating both high sensitivity and specificity in the detection of early atherosclerosis (15,16).

In the present study we aimed to analyze the value of intima-media thickness(IMT) measured by B mode ultrasound at the common carotid artery bilaterally as an independent risk factor for ischemic stroke in first degree relatives of patients with type 2 diabetes.

Thus, making the above measurements we obtained the necessary data which was statistically processed, but the differences between the study and the control group were not statistically significant, which entitles us to state that the value of the IMT can not be used as an independent risk factor for stroke in first-degree relatives of patients with type 2 diabetes. Although Duval & Altman concluded that the value of IMT is a good prognostic indicator for heart disease and stroke in diabetic patients, it appears that this indicator may not be extended with its prognostic value to the relatives of these patients (17).

Table 2. Statistical indicators of IMT on the study group

| Parameter            | Media | Min | Max | Std. dev | Std. err | CV%   | Median | Q25 | Q75 |
|----------------------|-------|-----|-----|----------|----------|-------|--------|-----|-----|
| <b>Study group</b>   |       |     |     |          |          |       |        |     |     |
| Right ACC            | 0,82  | 0,6 | 1,3 | 0,17     | 0,11     | 20,99 | 0,82   | 0,7 | 1   |
| Left ACC             | 0,87  | 0,5 | 1,2 | 0,19     | 0,12     | 21,85 | 0,87   | 0,7 | 1   |
| <b>Control group</b> |       |     |     |          |          |       |        |     |     |
| Right ACC            | 0,91  | 0,6 | 1,4 | 0,21     | 0,22     | 23,04 | 0,91   | 0,8 | 1   |
| Left ACC             | 0,95  | 0,6 | 1,4 | 0,19     | 0,20     | 20,47 | 0,95   | 0,8 | 1   |

In conclusion, we believe that further studies are needed of a higher caliber and with both clinical and paraclinical by cervical ultrasound evaluation, ex-

tended on a longer period of time to ascertain the value of IMT in cerebrovascular pathology in the offspring of patients with type 2 diabetes.

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