

**UNIVERSITY OF MEDICINE AND PHARMACY CRAIOVA
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**DOCTORAL THESIS
- ABSTRACT -**

The visceral adiposity index - a potential marker of
cardiovascular risk

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KEY WORDS: diabetes mellitus, visceral adiposity index, metabolic syndrome, cardiovascular risk.

INTRODUCTION

Obesity is a major risk factor for insulin resistance and diabetes mellitus (DM) type 2. Insulin resistance, mediated by obesity, correlates with the accumulation of pro-inflammatory macrophages and inflammation.

Since the association between abdominal obesity (visceral fat) and DM but also cardiovascular risk is already well known, we have proposed to highlight the latest data on insulin resistance and cardiovascular risk.

Cardiovascular disease is the leading cause of death worldwide (1). Studies conducted over time have shown that atherosclerosis, which is the basis, develops slowly and is advanced enough when symptoms occur, at which time the mortality risk is greatly increased. Although great progress has been made in the treatment of CVD, it is much more effective to identify CVD causes and implement prevention strategies.

Worldwide, metabolic diseases have become worrying in recent years, with diabetes mellitus and hypertension being the major illnesses involved (2). Obesity, manifested in recent years among the population, is the main cause of these conditions. In 2007, the WHO report indicates worldwide over 1 million overweight people, over 300 million obese and a 20-30% prevalence of metabolic syndrome. Studies have found that the existence of metabolic syndrome increases by 27-37% of the overall mortality risk and by 65-93% of the risk of cardiovascular disease (3).

All risk factors that act on the body and cause a subclinical or clinical atherosclerosis or atherosclerosis manifested by coronary disease, cerebrovascular disease, peripheral arterial disease, aortic aneurysm (4-7) create the cardiovascular or cardiometabolic risk status of the individual.

STAGE OF KNOWLEDGE (theoretical part)

CHAPTER I summarizes the main data from the literature on cardiovascular and cardiometabolic risk.

Global cardiometabolic risk is the overall risk of developing type 2 DM and/or CVD, including myocardial infarction (MI) and stroke, which is due to a bunch of risk factors (8). The cardiometabolic risk is based on the concept of continuous risk. The importance of cardiometabolic/cardiovascular risk is particular because controlling its components may affect atherogenesis and its clinical consequences: chronic ischemic heart disease (CIC), cerebrovascular disease and peripheral arteriopathy, but also DM.

The value of risk factors and chronic clinical conditions in CVT is unequal, strongly influenced by genetic factors, their timing, associated treatments, possible protective factors, etc., the future being the one that will clarify the many features and characteristics of the cardiovascular risk. The presence of more risk factors in the same person makes their effect exponential, not additive.

CHAPTER II contains notions about the visceral adiposity index (VAI) indicating the function of visceral adipose tissue, and its growth is independently correlated with cardiovascular and cerebrovascular risk.

VAI could become an easy-to-use tool in day-to-day practice that highlights the MDGs.

VAI takes into account gender (Male/Female), anthropometric measurements (AC, BMI) and biochemical tests (TG, LDL - cholesterol). VAI has no exact definition, it can be calculated using the following formulas:

$$\text{Males: VAI} = \left(\frac{\text{WC}}{39.68 + (1.88 \times \text{BMI})} \right) \times \left(\frac{\text{TG}}{1.03} \right) \times \left(\frac{1.31}{\text{HDL}} \right)$$

$$\text{Females: VAI} = \left(\frac{\text{WC}}{36.58 + (1.89 \times \text{BMI})} \right) \times \left(\frac{\text{TG}}{0.81} \right) \times \left(\frac{1.52}{\text{HDL}} \right)$$

PERSONAL RESEARCH (practical part)

1. The importance of the theme

Visceral obesity (9) is associated with increased adipocytokine production, increased proinflammatory activity (10), impaired insulin sensitivity (11), increased risk of diabetes, dyslipidemia (high cholesterol and triglycerides, low HDL) of high blood pressure and mortality rate (12-15).

The identification of a routine indicator applicable to the visceral adipocyte function with higher sensitivity and specificity than the classical parameters (such as waist circumference, BMI and lipids) could be useful for assessing cardiometabolic risk.

This study aims to identify the utility of the visceral adiposity index (IAV) in the estimation of visceral adipocytic dysfunction associated with cardiometabolic risk. This could be crucial in preventing cardiometabolic risk that is identified as an important condition associated with premature mortality, decreased quality of life and increased costs.

2. Objectives of the research

- Inclusion of subjects in the study, batch establishment.
- Identify the presence of cardiometabolic risk factors and determine their prevalence in each of the 3 sub-groups.
- Evaluation of visceral adiposity index.
- Cardiovascular risk assessment (Framingham score) in the 3 sub-groups.
- Highlighting causal relationships between VAI and cardiometabolic risk factors.
- Correlations VAI - cardiovascular risk (Framingham score).
- Drawing up the conclusions.

3. Material and methods

3.1 STUDY DESIGN

3.1.1 General dates

- Period of study

The study was conducted over 3 years (2011-2014) and included patients with diabetes mellitus, prediabetes and subjects without diabetes or prediabetes.

- Lot and sampling mode

The study is an epidemiological, transversal, noninterventional type and was performed by analyzing 300 subjects divided into three subgroups as follows:

- Subgroup 1 including 100 patients with prediabetes
- Subgroup 2 including 100 patients with type 2 diabetes
- Subgroup 3 (control) consisting of 100 individuals randomly recruited without diabetes or prediabetes

- Inclusion criteria: Caucasian subjects; patients diagnosed with DZ and prediabetes according to World Health Organization (WHO) criteria, International Diabetes Federation (IDF) and American Diabetes Association (ADA) (with minor changes) (16). At least two fasting blood glucose values of ≥ 126 mg/dl are required after at least 8 hours of fasting; blood glucose ≥ 200 mg/dl at any time of the day in the presence of specific clinical signs (polyuria, polydipsia, polyphagia); HbA1c $\geq 6.5\%$; glycaemia 2 hours after glucose loading ≥ 200 mg / dl); Patients diagnosed with prediabetes (glucose lowering or glucose tolerance): blood glucose = 110-125 mg/dl, glucose at 2 hours after glucose loading = 140-199 mg/dl, HbA1c = 5.7-6.4%.

- Exclusion criteria: acute metabolic imbalance, acute or chronic diseases, drug treatments that could have a secondary effect on glucose metabolism.

- Data collection: Patients with diabetes who met the inclusion and exclusion criteria were recruited from those who presented themselves at the specialized

ambulatory of the Craiova County Emergency Clinical Hospital. The first 3 patients with type 2 DM were counted daily up to 100. Next, the next 100 subjects without diabetes were included in the outpatient clinic at County Clinical Emergency Hospital Craiova and at the Municipal Clinical Hospital Filantropia with diabetes suspected of having undergone oral glucose tolerance test (OGTT); the prediabetic patients were enrolled in the study in the order of OGTT and overlapped in age and sex over the 100 patients with DM. The control group was obtained with the support of 4 family doctors, including the first patients overlapping age and sex over the 100 patients with DM who had normal OGTT and normal HbA1c.

- **Informed consent** has been fully acknowledged by each participant in the study after having been given all the necessary information to make a decision for or against to participate in the study. The study was conducted in accordance with the ethical principles laid down in the Helsinki Declaration, in line with good clinical practice, respecting the right to integrity, confidentiality, the option to withdraw the subject at any time from the study.

3.1.2 Recorded anamnestic data:

- Demographic data: age, gender, nationality, religion, marital status, level of studies, occupation.
- Pathological personal history: diabetes mellitus, treated/untreated hypertension, dyslipidemia.
- The lifestyle analysis

3.1.3 Clinical data

Anthropometric data: weight, height, body mass index, waist circumference, blood pressure.

Hypertension was classified according to ESH / ESC 2013 guidelines for HTA management (17). Hypertensive subjects with high blood pressure values were considered during the examination, patients with normal blood pressure but who

were on antihypertensive therapy or who knew HTA history (controlled by lifestyle optimization, weight loss).

The diagnosis of dyslipidemia was established according to the NCEP - ATP III (2009) classification. Dyslipidaemic subjects were those patients with altered lipid fraction values at the time of examination, patients with normal lipid values but who were undergoing hypolipidemic therapy or who had a history of dyslipidemia.

The diagnosis of metabolic syndrome was established according to the criteria proposed by IDF, NCEP ATP III, harmonized (2009), requiring a minimum of 3 criteria.

3.1.4 Biochemical data

Venous blood was harvested from which the following tests were performed: blood glucose, insulinemia, serum creatinine, total cholesterol, HDL-cholesterol, triglycerides. OGTT was performed in all patients included in the prediabetal subplot, who had either glucose-lowering (IFG) or low glucose tolerance (IGT) and all patients without DM or prediabetes (132 patients at who had OGTT, a number of 100 had normal values, the rest of 32 had either prediabetes or diabetes). Venous blood was harvested by peripheral venipuncture in vacuence with 3 mL EDTA. Harvesting took place in the morning, after fasting for at least 12 hours.

3.1.5 Calculation of the visceral adiposity index (IAV), according to gender according to the formulas below:

$$\text{Males: VAI} = \left(\frac{\text{WC}}{39.68 + (1.88 \times \text{BMI})} \right) \times \left(\frac{\text{TG}}{1.03} \right) \times \left(\frac{1.31}{\text{HDL}} \right)$$

$$\text{Females: VAI} = \left(\frac{\text{WC}}{36.58 + (1.89 \times \text{BMI})} \right) \times \left(\frac{\text{TG}}{0.81} \right) \times \left(\frac{1.52}{\text{HDL}} \right)$$

3.1.6 Cardiovascular Risk Assessment (Framingham Score)

The Framingham score quantifies the risk of fatal or non-fatal CV events at 10 years. The parameters used are: age, sex, smoker / non-smoker condition, total cholesterol and HDL-cholesterol value, treated or untreated systolic blood pressure.

The stratification of cardiovascular risk was performed in the three categories:

- low risk (<10%),
- moderate risk (10-20%),
- high risk (> 20%)

3.2 Statistical analysis of data

The data obtained were recorded as a Microsoft Excel spreadsheet and analyzed for each of the three batches using Microsoft Excel (Microsoft Corp., Redmond, WA, USA) together with XLSTAT 2014 for Microsoft Excel (Addinsoft SARL, Paris, France) and IBM SPSS Statistics 17.0 (IBM Corporation, Armonk, NY, USA) to analyze the relationships between clinical and paraclinical data of patients. For statistical analysis, the SPSS (Statistical Package for Social Sciences) version 17.0 for Windows was used.

In the present paper we used fundamental statistical indicators to characterize the numerical data used: arithmetic mean and standard deviation, as well as spreading indicators, minimum, maximum, median, quartiles (percentiles).

The Pearson and Spearman method was used to analyze correlations between linear parameters.

The Student test was used to compare the groups for the continuous variables, and the Chi square test (χ^2) for the category data.

The ANOVA test analyzed the differences of the averages of some parameters continuously by categories, and when the data were not homogeneous and the ANOVA could not be applied, the Kruskal-Wallis, nonparametric, benchmarking test was used.

The value of p was interpreted as follows:

- $p < 0.05$, significant result
- $p < 0.001$, high significant result
- $p > 0.05$, insignificant result

4. RESULTS

Each subgroup comprised patients equally divided by age and gender.

The decades of age in which the patients of each subgroup were framed are shown in the table below.

Decades of age and sex distribution of the three subgroups

Decade	No. Men	No. Women
20 - 39 years	1 (2%)	1 (2%)
40 – 59 years	17 (34%)	17 (34%)
60 – 79 years	32 (64%)	32 (64%)
TOTAL	50 (100%)	50 (100%)

I. Evaluation of cardiovascular risk factors

1. Lifestyle

Regard to the **number of meal / day** we found that in the control group both women and men consume at least 3 main meals / day in equal proportions (50%). In the prediabet group, 53.7% of men and 46.3% of women consume more than or equal to 3 main meals / day, whereas in the diabetes group this is usually found in 53.9% women and 46.1% % men.

Patients with prediabetes and diabetes consumes 3 main meals / day greater than those in the control group due to the education that these patients frequently receive during regular checkups.

In the control group, women and men consume **fruits and vegetables** daily in 50% vs 50%. In prediabetes and diabetes, men consume more fruits and vegetables per day than women, namely 51.6% men and 48.4% women and in the prediabetes group 52.1% men and 47.9% women.

Both women and men were registered in all three groups with more non-smokers and former smokers than smokers, which is a good thing.

In the control group, **smokers** were 72% men and 28% women, in the prediabetes group 62% of men were smokers and 37.8% women, while in the diabetes group 65.5% were males and 34.5% women without statistically significant differences between subgroups ($p > 0.05$).

Also, there were no statistically significant differences between women and men in the number of cigarettes smoked daily ($p = 0.953$), over 80% stating that they smoked 10-20 cigarettes / day.

The percentage of former smokers was higher among men, but there was no significant difference between the three groups ($p = 0.329$).

Daily alcohol consumption was significantly higher among males ($p = 0.047$) than among women. In the control group, 72.9% of men consumed alcohol, 62.3% of men in the prediabetes group consisted of alcohol, while in the diabetes group the percentage of men consuming alcohol was 71.1%. However, there were no significant differences between male sex groups in terms of alcohol consumption.

Regarding **sleep**, in all three subgroups, we found, in larger proportions, a sleep duration of at least 6 hours / day.

Higher percentages were observed among males compared to women in terms of hours of daily sleep (≥ 6 hours), in all three subgroups, but no significant differences ($p > 0.05$).

Regarding **physical activity**, there were no significant differences between the 3 subgroups and between men and women, about 80% of the subjects underwent physical activity, walked at least 30 min / day, more than 4 times / week.

2. Obesity

Concerning BMI patients, the average in subgroup 1 was 31,43 Kg / m², 29,04 Kg / m² in subgroup 2 and 27,82 Kg / m² in subgroup 3, with statistically significant differences between the 3 subgroups ($p < 0.001$).

The mean waist circumference in the subgroup of prediabetic patients was 105.99 cm, in the diabetic subgroup 101.54 cm and in the control group 96.74 cm, with statistically significant differences between lots ($p < 0.001$).

Analyzing the prevalence of obesity among patients in the studied subgroups, there was a higher percentage among women with diabetes (66%), followed by the 40% prediabetes subsubgroup and 28% respectively in the control subgroup.

In men, the same aspect was seen but lower than women, respectively 42% in the subgroup with diabetes, 24% in the prediabetes subgroup and 10% in subjects in the control subgroup, statistically significant gender difference ($p = 0, 0001$).

3. Hypertension

The mean of systolic arterial pressure in the prediabetic subgroup was 142.19 ± 39.97 mmHg, in the diabetes subgroup was 139.84 ± 19.61 mmHg and in the control was 139.98 ± 20.22 mmHg with no statistically significant differences between the three sub-groups ($p = 0.806$).

The mean of diastolic arterial pressure in the prediabetes subgroup was 79.90 ± 13.83 mmHg, in the subgroup with diabetes was 75.55 ± 10.48 mmHg and in the control subgroup was 80.94 ± 10.13 mmHg without statistically significant differences between the three sub-groups ($p = 0.680$).

The absence of statistically significant differences between subgroups is explained by adequate compliance and treatment of hypertensive patients. The prevalence of hypertension in the subgroup of diabetes was 76% in males and 84% in females, women and men in the prediabetes subgroup scored equal to 56%. In the control subgroup, men recorded a higher percentage than women, respectively 62% vs 56%.

Overall, in all 300 patients, the hypertension prevalence was 65%, higher than the 40.4% prevalence of high blood pressure in the romanian population in SEPHAR II and 61.7% in the PREDATORR study.

The higher percentage of people with hypertension may be due to the fact that there is a large percentage of people aged 60-79 years in each subgroup, a structure imposed by the random criteria of subject inclusion; therefore, the percentage of subjects with hypertension in the analyzed subgroups does not

represent the hypertension prevalence in these subject categories, with no weighted data.

4. Dyslipidemia

In terms of total cholesterol, the mean value in the prediabetes subgroup was 192.92 ± 39.60 mg / dl, in the diabetes subgroup was 219.63 ± 54.75 mg / dl, while in the control group was 220.72 ± 65.24 mg / dl, with statistically significant differences between the three sub-groups ($p < 0.001$). Lower total cholesterol in patients with prediabetes and diabetes is probably explained by careful monitoring by periodic control and appropriate treatment as needed.

As expected, the mean HDL-cholesterol was lower in prediabetic patients (49.32 ± 12.54 mg / dl) and diabetes (53.09 ± 12.77 mg / dl) versus the control group 56.82 ± 18.76 mg / dl, with statistically significant differences between the 3 subgroups ($p < 0.002$).

The mean LDL-cholesterol in the prediabetes subgroup was 137.45 ± 49.09 mg / dl, in the diabetes subgroup was 111.82 ± 38.06 mg / dl, while in the control group it was of 136.60 ± 49.06 mg / dl, with statistically significant differences between the three subgroups ($p < 0.001$). Here again, lower LDL-cholesterol in patients with diabetes can be explained by appropriate patient treatment.

The mean triglyceride level in the prediabetes subgroup was 141.10 ± 83.33 mg / dl, in the diabetes subgroup 158.77 ± 79.00 mg / dl, while in the control group was $140, 88 \pm 9.82$ mg / dl, with no statistically significant difference between the 3 subgroups ($p = 0.250$).

The prevalence of dyslipidemia in the diabetic group was 83.7% in males and 72% in females, 44% in male and 58% in females in prediabetes group, while in the control group males had a prevalence of 46% and 56% women. Thus there is a statistically significant difference between the 3 sub-groups ($p = 0.001$), but insignificant between the female and the male sex.

Globally analyzing all 300 studied patients, the prevalence of dyslipidaemia was 69.9%, with no significant gender differences (65.3% females vs. 64.7% males),

a prevalence close to 80% at the level of the romanian population obtained in the PREDATORR study.

5. Glycemic status

The A1c hemoglobin mean in the control subplot was $5.43\% \pm 0.38$, in the prediabetes subgroup was $5.86\% \pm 0.19$ and in the subgroup of diabetic patients was $7.14\% \pm 1, 57$, reflecting good metabolic control of patients with diabetes.

6. Metabolic syndrome

In women, there were statistically significant differences ($p < 0.05$) among the 3 sub-groups with respect to the presence of MS: in the control subgroup, MS was found in 24% of women, 36% in the prediabetes subgroup, while, in the diabetes group was present in 44% of women.

In men, in the control subgroup MS was found in 14% of men, in the prediabetes subgroup at 34%, while, in the diabetes subgroup was present in 38% of males, statistically significant difference ($p < 0, 05$).

Although women showed metabolic syndrome in a higher percentage than men in all three sub-groups, the differences were statistically insignificant ($p = 0.701$).

MS prevalence among the 300 studied patients was 32.3%.

II. Evaluation of visceral adiposity index

By calculating VAI, we obtained an average of 4.99 for prediabetes patients, greater than 6.22 for patients with diabetes and the smallest mean of 4.88 being found in the control subgroup, significant difference statistically between sublots ($p = 0.039$).

III. Cardiovascular risk assessment by Framingham score

In the subgroup of prediabetes patients, most patients (56%) were moderate in the cardiovascular risk category, 24% at high risk and 20% at low risk.

Most patients in the group with Type 2 DM, 70% had high cardiovascular risk, 20% moderate, and only 10% of patients with type 2 DM had a low cardiovascular risk.

In the control subgroup, most patients (64%) were in the low cardiovascular risk category, 32% in the moderate risk category and only 4% at high risk.

IV. Statistical Correlations VAI - Cardiovascular Risk Factors

IV.1 Cardiometabolic pro-risk lifestyle did not statistically correlate with the value of VAI in terms of main meal / day meals, fruit and vegetables, alcohol consumption or smoking, sleep or physical activity.

IV.2 Obesity

No positive linear correlation of the VAI value with the BMI value ($R = 0.15$, $p = 0.135$) was shown in the control group.

In the prediabetes group, the VAI value correlated positively with the BMI value ($R = 0.272$, $p = 0.006$), the same situation also occurring in the diabetic group ($R = 0.217$, $p = 0.03$).

So, we can say that for people with prediabetes and diabetes, higher BMI is predictive of a higher VAI.

Regarding the abdominal circumference, no positive linear correlation of the VAI value with the WC value ($R = 0.25$, $p = 0.012$) was shown in the control group. In the prediabetic group, the VAI value correlated positively with the WC value ($R = 0.377$, $p < 0.001$), the same situation occurring in the diabetes group ($R = 0.368$, $p < 0.001$).

Thus, we can say that for people with prediabetes and diabetes, the higher VAI value is predictive of a higher WC value.

IV. 3 Hypertension

Regarding the diagnosis of hypertension, none of the 3 analyzed subgroups showed a correlation between the presence of hypertension and the VAI value, which can be translated by the fact that the VAI value does not differ depending on

the presence or absence of hypertension ($p = 0.552$, $p = 0.793$, $p = 0.814$), respectively the presence of hypertension is not predictive of an increased VAI.

IV.4 Dyslipidemia

Regarding dyslipidemia, a positive linear correlation of the VAI value with the presence of dyslipidemia ($p = 0.103$) was not found in the control group.

In the prediabetic group, the VAI value was positively correlated with the presence of dyslipidemia, patients with dyslipidemia having an average VAI of 5.84 higher than the 3.93 value of non- dyslipidemic patients, a statistically significant difference ($p = 0.017$). The same situation was also found in the diabetes group, the mean value in patients with dyslipidemia was 6.57, higher than the 4.27 of patients without dyslipidemia, statistically significant difference ($p = 0.04$).

In the case of prediabetes and diabetes patients, an increased value of VAI has been shown to be predictable for the presence of dyslipidemia.

IV.5 Glycemic status

We analyzed the linear correlation between the VAI value and the A1c value by the Pearson evaluation method and we noticed that a positive linear correlation of the VAAI value with the A1c value ($R = 0.025$, $p = 0.809$) was shown at the control group , while for prediabetic group ($R = 0.199$, $p = 0.04$) and diabetes ($R = 0.202$, $p = 0.04$) the VAI value correlated positively, statistically significant.

Thus, we can assert that a higher value of VAI is predictive of a higher A1c value.

IV.6 Metabolic syndrome

Regarding metabolic syndrome, a positive linear correlation of the VAI value with the presence of MS was revealed in the control group, the median value of VAI in individuals with MS was 7.73 compared to the value of 2.78 registered in individuals without MS , statistically significant difference ($p < 0.001$).

In the prediabetic group, the VAI value was positively correlated with the presence of MS, MS patients with an average VAI of 6.57 greater than the 3.26 of non-MS patients, statistically significant difference ($p < 0.001$).

The same situation was also found in the diabetes group, the mean value in patients with MS with a value of 6.47, higher than the 1.69 value of non-MS patients, statistically significant difference ($p < 0.001$).

In this case, in all subgroups, the increased VAI has been shown to be predictable for MS.

V. Correlations VAI - Cardiovascular Risk Assessed by Framingham Score

By correlating the mean VAI with the cardiovascular risk category evaluated by the Framingham score, there were high statistical differences ($p = 0.001$). Thus, the low cardiovascular risk category was associated with an average VAI of 4.238, the moderate cardiovascular risk category with a mean VAI of 4.704, and a value of 6.148 in the high cardiovascular risk category.

In conclusion, the higher the VAI value, the more the cardiovascular risk increases.

CONCLUSIONS

- The increased prevalence of cardiovascular risk factors seen in the individuals surveyed in this transversal study is worrying as it involves increased cardiometabolic risk and draws attention to the need for a multifactorial, intensive, early-established clinical management.
- Contrary to our expectations, life style analysis (main meals / daily meals, daily consumption of vegetables, fruits and sweets, number of hours of sleep / day, daily physical activity) did not offer significant differences between the 3 subgroups or between the sexes .
- Both women and men were registered in all three sub-groups with more non-smokers and former smokers than smokers, which is encouraging.
- Daily alcohol consumption was significantly higher among males in all three subgroups.
- By analyzing the prevalence of obesity among the patients of the subgroups studied, there was a higher percentage among women with DM (66%), followed by the prediabetes subgroup with 40%, respectively 28% in the control subgroup. In men, the same aspect was seen but lower than women, respectively 42% in the subgroup with DM, 24% in the prediabetes subgroup and 10% in subjects from the control subgroup, statistically significant difference between gender ($p = 0, 0001$).
- There were no statistically significant differences between the SBP and DBP, the absence of these differences is explained by the appropriate compliance and treatment of hypertensive patients. The prevalence of hypertension in the diabetic subgroup was higher in males than in females, in the prediabetes subgroup women and men recorded equal percentages, and in the control subgroup males had a higher percentage than females.
- No significant differences were found between the sexes in the mean value of total cholesterol, HDL cholesterol, LDL cholesterol or triglycerides. The lower value of TC, LDL cholesterol and TG in prediabetes and DM patients is probably explained by careful monitoring by periodic monitoring and appropriate treatment as needed. The prevalence of dyslipidemia in the diabetic group was 83.7% in males and 72% in females, 44% in male and 58% in females, while in the control group males had a

prevalence of 46% and 56% women. Thus, there was a statistically significant difference between the three subgroups ($p = 0.001$), but insignificant between females and males.

- The assessment of glycemic status in the 3 subgroups was reflected by a mean of glycosylated hemoglobin in the control subplot of $5.43\% \pm 0.38$, in the prediabetes subgroup of $5.86\% \pm 0.19$, and in the subgroup of patients with diabetes about $7.14\% \pm 1.57$.
- Women showed the metabolic syndrome (MS) higher than men in all 3 subgroups, but the differences were statistically insignificant ($p = 0.701$). MS prevalence among the 300 studied patients was 32.3%.
- The VAI assessment concluded a higher mean value in diabetic patients followed by those with prediabetes, the lowest mean value being found in the control subgroup, a statistically significant difference between subgroups.
- Cardiovascular risk assessment with the Framingham score confirmed, as expected, that diabetes patients, followed by those with prediabetes, had the highest risk, the lowest risk being seen in patients of the control subgroup.
- Cardiometabolic pro-risk lifestyle did not statistically correlate with the VAI value, either in terms of main meals / day meals, fruit and vegetables, alcohol or smoking, sleep or physical activity.
- The VAI value has been positively correlated with the BMI and CA value only within the prediabetic and diabetic subgroup, but not in the control subgroup, thus indicating that the higher VAI value for prediabetes and diabetes is predictive of a higher BMI value.
- The diagnosis of hypertension did not correlate with the VAI value in any of the 3 analyzed subgroups, which may be due to the fact that the VAI value does not differ depending on the presence or absence of hypertension, or the presence of hypertension is not predictive of an increased value of VAI.
- The diagnosis of dyslipidemia did not correlate with the VAI value in the control subgroup but was linearly positive for prediabetic and diabetic subpopulations, thus proving that an increased VAI value is predictable for the presence of dyslipidemia in these patients.
- The VAI value and the HbA1c value correlated positively statistically significantly positive in patients with pre-diabetes and diabetes but not in control patients, so we

can assert that a higher VAI value is predictive of a higher value of HbA1c.

- The diagnosis of MS was positively correlated with the VAI value in all 3 studied subgroups ($p < 0.001$), thus proving that an increased VAI value is predictable for MS.

- By correlating the mean VAI with the cardiovascular risk category evaluated by the Framingham score, there were high statistically significant differences ($p = 0.001$). Thus, the low cardiovascular risk category was associated with an average VAI of 4.238, the moderate cardiovascular risk category with a mean VAI of 4.704, and a value of 6.148 in the high cardiovascular risk category.

THE NEWS AND PERSPECTIVES OPENED BY THE THESIS

VAI can be a useful and easy tool in estimating cardiometabolic risk. In the present study, the results showed that the higher the IAV value, the more cardiometabolic risk increases.

This hypothesis has been an object of research in the international specialized literature, but without data at national level so far, basically this being the novelty of the present study.

From the present study, the following directions of continuation of research can be profiled:

- ▶ Extending the study lot to increase the statistical power of the results, a larger number of enrolled patients would allow for wider comparisons to be made on sublots. It would be very useful for the consortium to include representative samples from different counties of Romania in order to draw a clear picture of the cardiometabolic risk population at our country because there is very little data on the health status of the population in Romania. Very interesting would be if samples were selected for the urban and rural areas so that the two environments of origin could be compared because of extremely interesting results. Extending the study at national level can be materialized because it does not require major financial investments (a nutrition and physical activity assessment questionnaire, anthropometric indices, blood pressure measurement and minimal lab analyzes).
- ▶ Assessing stress and depression can be important goals to analyze, as these parameters are also considered as cardiovascular risk factors.
- ▶ Patient tracking may be the goal of a future study to draw conclusions about the long-term relationship between risk factors and cardiovascular disease, which are absolutely necessary to confirm the importance of risk factors.

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