

REVIEW

VISCERAL ADIPOSITY INDEX (VAI) – A POTENTIAL MARKER OF CARDIOMETABOLIC RISK

Sigina R. GÂRGAVU¹, Diana CLENCIU², Maria M. ROȘU¹, Tiberiu Ș. ȚENEA COJAN³, Andrei COSTACHE¹, Ionela M. VLADU³✉, Maria MOȚA³

¹The County Clinical Emergency Hospital of Craiova

²The Municipal Hospital of Filantropia

³The University of Medicine and Pharmacy of Craiova

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ABSTRACT

The importance of cardiovascular/cardiometabolic risk is a special one, because it may influence atherogenesis and its clinical consequences: ischemic heart disease, cerebrovascular disease, peripheral artery disease, but also diabetes mellitus (DM). To evaluate the cardiometabolic risk associated with visceral obesity, a useful indicator for the clinical practice was searched. The visceral adiposity index (VAI) could become an easy-to-use tool to evaluate the cardiometabolic risk in everyday practice. VAI indicates the function of visceral adipose tissue and its growth is independently correlated with cardiovascular and cerebrovascular risk. The medical world tried to identify an easy way to assess cardiovascular risk, so the visceral adiposity index was introduced, whose formula includes a number of cardiovascular risk factors.

Keywords: visceral adiposity index, cardiovascular risk, diabetes mellitus.

RÉSUMÉ

L'indice d'adiposité viscérale (IAV) – marqueur potentiel du risque cardio-métabolique

L'importance du risque cardiovasculaire/cardio-métabolique est particulière car le contrôle de ses composantes peut affecter l'athérogenèse et ses conséquences cliniques: la cardiopathie ischémique, la maladie cérébrovasculaire, l'artériopathie périphérique et le diabète sucré (DS). Pour évaluer le risque cardio-métabolique associé à l'obésité viscérale, on a essayé d'identifier un indicateur utile dans la pratique clinique. L'indice d'adiposité viscérale (IAV) pourrait devenir un outil facile à utiliser dans la pratique quotidienne qui met en évidence le risque cardio-métabolique. IAV indique la fonction du tissu adipeux viscéral et sa croissance est indépendamment corrélée aux risques cardiovasculaire et cérébrovasculaire. Le monde médical a essayé d'identifier un moyen facile d'évaluer le risque cardiovasculaire, de sorte que l'indice d'adiposité viscérale, dont la formule inclut un certain nombre de facteurs de risque cardiovasculaires, ait été introduit.

Mots-clés: indice d'adiposité viscérale, risque cardiovasculaire, diabète sucré.

✉ Address for correspondence:

Ionela Mihaela VLADU
University of Medicine and Pharmacy, 20 Petru Rares Street,
Craiova, Romania
Phone : +40763670811,
E-mail: mihmitzu@yahoo.com

INTRODUCTION

The importance of cardiovascular/cardiometabolic risk is a special one, because it may affect atherogenesis and its clinical consequences: ischemic heart disease, cerebrovascular disease, peripheral artery disease and diabetes mellitus (DM)¹.

To evaluate the cardiometabolic risk associated with visceral obesity, a useful indicator for the clinical practice was searched². Amato et al³, in a study made on a European Caucasian population, validated a visceral obesity index defined as the „Visceral Adiposity Index“ (VAI).

VAI could become an easy-to-use tool to evaluate the cardiometabolic risk in everyday practice. VAI

indicates the function of visceral adipose tissue and its elevation is independently correlated with cardiovascular and cerebrovascular risk⁴.

Elements of visceral adiposity index

The VAI formula takes into account:

- sex (M/F)
- anthropometric measurements (abdominal circumference, body mass index)
- biochemical tests (triglycerides, LDL - cholesterol)

The visceral adiposity index (VAI) can be calculated differently by gender, according to the following formulas:

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

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

where: VAI = visceral adiposity index, WC = waist circumference, BMI = body mass index, TG = triglycerides, HDL = high density lipoproteins.

The elements of the visceral adiposity index are:

- **Abdominal obesity and insulin resistance**

Obesity, defined by a body mass index (BMI) above 30 Kg/m², is a risk factor independent of other cardiometabolic risk factors such as high blood pressure, diabetes mellitus, dyslipidemia, metabolic syndrome⁵⁻⁷. The BMI is a true indicator of the total amount of adipose tissue, but it does not provide information about its distribution in the body. The distribution of the total amount of body fat is important, because different locations of adipose tissue are associated with different levels of cardiovascular risk factors⁸. Visceral adipose tissue is not an inert tissue, on the contrary, it manifests as a true endocrine organ with an important secretion of adipokine and vasoactive substances that influence the risk of developing or exacerbating metabolic diseases⁹.

The relationship between insulin resistance and abdominal distribution of adipose tissue was described half a century ago, when the French researcher Jean Vague reported the link between android obesity and the presence of atherosclerosis and type 2 DM¹⁰. Following this finding, other studies have demonstrated the intimate relationship between abdominal obesity and insulin resistance, type 2 DM and other metabolic risk factors for cardiovascular diseases¹¹. Subsequent research has shown that the association between increased abdominal circumference and cardiovascular risk is due to excessive accumulation of visceral adipose tissue¹²⁻¹⁴.

The metabolic consequences of this dysfunctional energy balance are visceral obesity, insulin resistance, atherogenic dyslipidemia, proinflammatory status and prothrombotic status, all of which are characteristics of metabolic syndrome¹⁵.

The factors that determine the preferential accumulation of visceral fat and the consequent occurrence of insulin resistance are genetic susceptibility, smoking and a neuroendocrine profile that is not performing as to stress adaptation¹⁶.

The pro-inflammatory status of obesity is a well-known phenomenon. The release of proinflammatory cytokines by visceral adipose tissue was demonstrated by numerous cytokine studies, that found high levels of TNF α in obese patients. Further cytokines and chemokines, such as IL-6, IL-8 and MCP-1, have been described to alter the physiological action of insulin, with decreased insulin sensitivity¹⁷.

Prothrombotic status is mainly related to the release of the PAI-1 protein, with strong prothrombotic properties by the adipose tissue.

The combination of obesity, especially central obesity, dyslipidemia, high blood pressure, insulin resistance, hyperinsulinemia, glucose intolerance has been called „metabolic syndrome“ (MS). This syndrome is a powerful determinant of cardiovascular disease and DM¹⁸⁻²⁰. A recent report from the National Health and Nutrition Survey (NHANES-III) database^{21,22} evaluated the increasing prevalence of metabolic syndrome in the United States population, by using the ATP- III guidelines. Thus, based on these criteria, age-adjusted metabolism prevalence among adults in the United States was estimated at

34%²³. Rates were similar in males and females and increased with age. In specific population groups, Americans-Mexicans had the highest prevalence of age (31.9%)²⁴. An estimated percentage of 47 million people probably have MS in the United States²³.

The increased body mass index (BMI) is the risk factor for the MS. Obesity increases insulin resistance and increases circulating insulin levels. Obesity is due to increased deposits of visceral and subcutaneous fat. The particularly problematic weight gain model is visceral or central obesity^{25,26}. MS may be present also in weak subjects with central weight gain²⁷.

Fat deposits were considered to be storage areas for energy. However, fat cells have been shown to secrete a number of different substances and it is now thought that fat creates an active metabolic organ. The adipose cells have central nervous system relevant pathways. Abdominal adipocytes exert effects on beta cell function, hepatic glucose production, muscle glucose uptake, appetite regulation and arterial inflammation, through various adipocytokines such as leptin, resistin, TNF- α , and adiponectin^{28,29}. Visceral adipose tissue has a higher lipolysis rate, and increased flow of free fatty acids into the liver increases insulin resistance and abnormal production of lipid particles, especially triglycerides. Visceral adipose cells are more resistant to the suppressing effects of insulin on lipolysis than on subcutaneous fat tissue.

Visceral fat can be measured by computed tomography (CT) and magnetic resonance imaging (MRI). Central obesity is measured clinically with a measuring tape or by observation.

• **Abnormalities of lipid metabolism**

Insulin resistance causes abnormalities of lipid metabolism that are not well understood by practitioners who are trained to recognize cholesterol level as a risk factor for cardiovascular disease³⁰. Dyslipidemia is characterized by high levels of plasma triglycerides (> 150 mg/dL) and low HDL-cholesterol level (<40 mg/dL in males and <50 mg/dL in females)²⁹. Although HDL-cholesterol may be increased in this syndrome, effective levels of LDL-cholesterol are often not significantly elevated. However, when measuring the size of LDL particles, it is found that they tend to be smaller and denser³¹, which increases their atherogenic potential.

It is important to be aware of the insulin regulation role of free fatty acid metabolism (AGL) and the production of triglycerides rich in very low density lipoprotein particles (VLDL) in order to understand lipid changes in patients with insulin resistance. Insulin resistance results in increased release of AGL from adipocytes, leading to increased

circulating levels of AGL, which stimulates the synthesis of triglyceride-rich VLDL particles in the liver, all of which result in elevated LDL-rich high density lipoprotein triglycerides (HDL) and LDL particles. Increased triglycerides in lipid particles change the metabolism. HDL particles are hydrolyzed more rapidly and HDL levels decrease. LDL particles are still subject to lipolysis, which results in the formation of small and dense LDL particles. The resulting dyslipidemia is thus extremely atherogenic and represents at least some of the increased risk of cardiovascular disease in insulin-resistant individuals^{32,33}.

High blood pressure occurs in one third of people with MS. Insulin resistance was directly related to the development of high blood pressure and other vascular compartment anomalies³⁴ and may directly affect the function of endothelial cells through mediators such as nitrogen oxide. In addition, elevated insulin levels may increase sympathetic nervous system activity and may cause sodium retention. Treating insulin resistance helps lower the blood pressure. There is evidence that insulin sensitizers, such as glitazones, are causing blood pressure to fall^{35,36}, which does not exclude the standard treatment of hypertension, with angiotensin converting enzyme inhibitors (ACEI), diuretics, beta-blockers, calcium channel blockers^{37,38}.

Insulin resistance is a condition in which increased amounts of insulin are needed to produce a normal biological response. Although insulin resistance is present in almost all cases of type 2 DM, there is an increasing number of people who do not yet have hyperglycemia, but who have a metabolic syndrome and are at risk of developing type 2 DM. Before DM installs, the pancreas secretes excess insulin to maintain normal blood glucose levels^{39,40}. People with type 2 DM will experience beta cell deficiency, with decreased insulin levels and increased blood glucose. Insulin resistance is most often the last component to be diagnosed in the clinical setting of the MS, even if this is the basic condition from which all other abnormalities of MS start.

Studies evaluating the applicability of VAI in the prediction of MS have shown that the presence of VAI is closely related to components of MS⁴¹.

Knowles et al³⁹, in a Peruvian adult study, analyzed the utility of different anthropometric indicators in the assessment of the risk of MS. All evaluated indicators showed a significant relationship with the components of the MS, so hypertriglyceridemia, hypo-HDL-emia, and blood sugar à jeun in both sexes showed a correlation with anthropometric measurements.

In the study of Amato et al⁴² performed in an adult European population, cardiovascular and cerebrovascular risks were analyzed according to the BMI, WC and VAI values. VAI was independently associated with cardiovascular and cerebrovascular disease, whereas WC and BMI did not show a statistically significant correlation.

Another study by Amato et al³⁶, performed on a sample of Caucasian adults, validated VAI as „cut-off point“ for cardiovascular and cerebrovascular events in individuals with MS, corroborating previous data indicating increased cerebrovascular and cardiovascular risk with VAI increase.

VAI itself is an easy-to-use tool in clinical practice to assess the cardiometabolic risk associated with visceral obesity⁴³.

In adults, general obesity is associated with cardiovascular risk, especially adipose tissue located in the upper body. A possible explanation for this risk is represented by the metabolic characteristics of abdominal fat tissue and visceral adipose tissue (VAT)^{44,45}.

Studies in young people with general obesity have highlighted the presence of cardiovascular risk factors that cause early cardiovascular disease^{46,47}.

However, there is little data on visceral adipose tissue compared to general obesity, especially related to cardiovascular risk factors in young people. Studies in obese children and adolescents have shown that visceral obesity, more than the general one, is associated with an altered lipid profile^{48,49}. This suggests that visceral adipose tissue begins to exert adverse effects from childhood⁵⁰.

CONCLUSIONS

Studies over time have identified hypertriglyceridemia, hypo-HDL-emia and fasting glycaemia as a cardiovascular risk factor. The medical world has tried to identify an easy way to assess cardiovascular risk, so the visceral adiposity index, the formula of which includes these cardiovascular risk factors, has been introduced.

In conclusion, the visceral adiposity index can be considered an easy tool for assessing the cardiometabolic risk associated with obesity.

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