Metabolic Syndrome in Older Patients

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Abstract

This paper presents an overview of the definitions of metabolic syndrome and the criteria used to determine this diagnosis. It discusses the pathological-physiological aspects of the syndrome´s individual components – insulin resistance and type 2 diabetes mellitus, hypertension, atherogenic hyperlipidemia, as well as the mutual relationship between hyperuricemia and metabolic syndrome. The paper also includes the authors´ original results- a study of the incidence of metabolic syndrome among community dwelling seniors. In South Moravia, 147 seniors were examined in cooperation with general practitioners and the Geriatrics Outpatient Clinic of the Department of Internal Medicine, Geriatrics and General Practice, Medical Faculty of Masaryk University and Faculty Hospital Brno. The criteria of metabolic syndrome diagnosis as per the International Diabetes Federation definition were met by 23 clients i.e. 15.7% of the sample studied. A considerable section of the sample, though, met three of the criteria- 18 clients, 12.1%. It was determined that the incidence of metabolic syndrome did not correlate significantly with age – r = - 0.10, p>0.05 – i.e. there was rather a trend towards lower incidence with advancing age. The incidence of metabolic syndrome appeared to have a significantly negative correlation with cognitive performance tested by Mini Mental State Examination – r= -0.44 and self-sufficiency tested by ADL (activities of daily living) – r=-0.44. Conclusions: Metabolic syndrome occurs in approx. 20-40% of older patients depending on the clinical criteria applied. The incidence of metabolic syndrome in the older population has a significantly negative effect on cognitive functions and the self-sufficiency of older patients as well as on the incidence of depression.

Keywords: Metabolic syndrome; Hypertension; Insulin resistance; Diabetes mellitus; Obesity; Hyperlipidemia; Cognitive disorder; Self-sufficiency; Depression

Introduction

Already decades ago, clinicians noticed the unfavourable influence of a combination of high blood pressure, lipid metabolism disorders, excess weight, obesity and gout on further progression of a patient´s state of health, especially in the sense of accelerated atherosclerosis and incrreased cardiovascular morbidity as well as mortality. Reaven´s syndrome or syndrome X or Kaplan´s deadly quartet have been mentioned in literature since the 1950s [1-3]. Other synonyms used include atherothrombogenic syndrome, metabolic cardiovascular syndrome, and insulin resistance syndrome [4]. As life expectancy increases and new therapeutic methods that help overcome certain serious vascular disorders are developed, finding a solution for the metabolic syndrome is gaining in importance, especially from the aspect of preventing such types of disorders that medicine today is unable to resolve as yet and that have a fundamental negative effect on the self-sufficiency and overall quality of life of seniors.

The definition of metabolic syndrome developed gradually with the implementation of the results of individual studies that evaluated the significance of the syndrome´s individual components from a grouping of individual components (dyslipidemia, obesity) to the completely exact and numerically expressed criteria used today.

Two definitions are used most frequently today – the first according to the IDF – International Diabetes Federation (IDF) and the second according to The National Cholesterol Education Program (NCEP) – Adult Treatment Panel III – ATP III.

Thus, according to current definitions an individual attaining pathological values for at least three of the criteria listed in Table 1 [5] suffers from metabolic syndrome. The IDF definition considers abdominal obesity to be the principal criterion and adds the other criteria to it –Table 2.

Every component of the metabolic syndrome represents a certain damage inducing mechanism, whereby the individual types of damage predominantly mutually combine or potentiate their effects. Recently,

Parameter	Value
waist circumference	men > 102 cm, women > 88 cm
serum triglyceride concentration	≥ 1,7 mmol/l
serum HDL cholesterol concentration	men < 1.0 mmol/l, women < 1.3 mmol/l
arterial blood pressure	≥ 130/ ≥ 85 mmHg
plasma glucose	≥ 5.6 mmol/l

Table 1: NCEP – ATIIImetabolic syndrome criteria.

principal criterion
central obesity (waist circumference > 94cm men, > 80cm women)
atleast two of the following parameters
serum triglyceride concentration ≥ 1.7 mmol/l
serum HDL cholesterol < 1.03 mmol/l in men, < 1.29 mmol/l in women or specific therapy
arterial BP ≥ 130/ ≥ 85 mmHg or treated hypertension
fasting plasma glucose ≥ 5.6 mmol/l or already diagnosed type 2 diabetes mellitus

Table 2: IDFmetabolic syndrome criteria.

it has been proposed that leptin levels could also be included as another component of metabolic syndrome– a significant correlation between this protein hormone and the intensity of metabolic syndrome has been demonstrated [6].

Other disorders combine secondarily with the basic clinical and

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biochemical picture- endothelial dysfunction, hyperhomocysteinemia, steroid metabolism impairment.

Insulin resistance syndrome

Insulin is active in a number of tissues via several mechanisms, central to which is a complicated signalling cellular mechanism consisting of the auto-phosphorylation of the insulin receptor tyrosine kinase beta-subunit. A series of reactions specific for the given cell and eventually tissue ensues. Insulin resistance signifies the inability of the cell or tissue to react with an appropriate metabolic response to standard serum insulin concentrations either at the level of the receptor itself or at the post-receptor level. Compensatory hyperinsulinemia ensues as part of maintaining homeostasis, characterised especially by the late onset of secretion following glucose loading and the subsequent persistent increased secretion [7].

Polygenic inheritance is presumed to be the possible cause of this state – primary insulin resistance. In the general population, though, the undoubtedly most frequent secondary insulin resistance is caused by excessive energy intake, low energy output, unsuitable diet, stress, smoking and certain medications.

Insulin resistance leads to specific changes in lipid metabolism – hypertriglyceridemia, decreased serum HDL cholesterol concentrations, higher post-prandial increments of lipids, water and sodium retention, decreased ability to synthesise nitric oxide, activation of the sympathetic nervous system by insulin. This complex leads to the development of the typical clinical symptoms of metabolic syndrome. Recently, even GM Reaven himself, after whom the metabolic syndrome is also named, stresses insulin resistance as the cause of a further chain of events and wonders whether we still need the diagnosis of metabolic syndrome.

Hypertension

In the search for the aetiology of hypertension, endothelial dysfunction with decreased NO production and subsequent predominance of vasoconstrictive mechanisms is considered to be one of the main factors. In older age, atherosclerosis enters into the picture, with sterile inflammation of the vascular wall as a reaction to the presence of a noxious element contributing among others to its development. CRP as a mediator of inflammation further contributes to endothelial dysfunction by inhibiting NO production [8].

Another fundamental factor is the gradual dominance of vasoconstrictive stimuli in the form of endothelin, thromboxane A2 and angiotensin II over vasodilating stimuli– prostacyclin, endothelial hyperpolarising factor and nitric oxide. Low activity of NO as an anti-inflammatory, vasodilating and anti-thrombotic factor is today considered to be one of the other important stimuli of pro-atherogenic processes [9].

More recently, there has been mention of the synergistic or antagonistic effect of other substances on the arterial system– activation of arginase leads to decreased availability of L-arginine as an accessory factor of NO synthase with the subsequent fall in its production and decrease in its vasodilating effect [10].

From the aspects mentioned above, the question may logically ensue whether in older patients increase in blood pressure truly represents a primary effect and vascular damage is secondary to it, or whether the increase in blood pressure is a secondary phenomenon combining with the undergoing changes in the vascular wall. The different characteristics of hypertension in older age rather points to the second possibility. This opinion is also supported by the significantly weaker predictive value

of hypertension for the development of metabolic syndrome compared to abdominal obesity or higher triglyceride serum levels [11]. Clinical experience shows that many individuals with lifelong excess weight do not have any problems with high blood pressure at a younger age. Nonetheless, as soon as they reach old age, they develop hypertension, usually systolic. The complications of long-term poorly treated hypertension are subsequently one of the principal causes of disability [12]. The aforementioned mechanism is also supported by the results of studies conducted on kidneys removed from persons suffering from Grawitz tumour. The renal vascular system of patients suffering from metabolic syndrome according to the ATP III panel demonstrated significantly more advanced changes in the sense of atherosclerosis compared to patients without metabolic syndrome [13].

Obesity

Obesity as a clinical symptom on the overall evaluation of a patient is a sign of an imbalance between energy intake and output, which given the currently predominant lifestyle in most cases signifies overeating. Visceral- abdominal-omental obesity is an especially important risk factor, signifying as it does the over-production of dipeptidyl peptidase, increased activation of the incretin system, insulin over-production and the subsequent development of insulin resistance. This is why positivity of anthropometric factors such as the parameter evaluating visceral obesity is currently seen as a more significant risk factor. Studies focusing on the significance of individual anthropometric parameters for the evaluation of metabolic syndrome arranged their sensitivity in descending order. The most sensitive appeared to be the patient´s waist: height ratio (WHtr),second came the value of BMI and waist circumference (WC), and the previously frequently used waist: hip ratio (W:HpR) and hip circumference (HC) ranked only third [14].

On the other hand, there also exists a group of patients who do not meet the criteria of either overall or visceral-abdominal obesity but who nonetheless are metabolically significantly at risk from the aspect of developing cardiovascular disorders [15]. This discrepancy leads to discussions regarding the possible causes yet the presumed genetic influence has not been demonstrated thus far [16]. The attempt to influence obesity by the administration of anti-obesity medication with the aim of changing dietary habits thus far also appears not to have been successful- studies that aimed to induce a change in dietary habits in obese patients with metabolic syndrome by the administration of orlistat did demonstrate after two years a decreased intake of fats, nonetheless energy intake was supplemented by an increased proportion of carbohydrates in the diet [17].

More encouraging results were achieved in a study that included for one year patients- women with an average age of 69 years- suffering from metabolic syndrome in a training program. Compared to the control group, there was a significant decrease in total body fat, hip circumference, total cholesterol and triglyceride levels and an increase in HDL cholesterol levels. In contrast to the study´s expectations, plasma glucose levels, serum CRP concentration, waist circumference nor blood pressure were affected. [18]. The decrease in weight induced by a hypo-caloric diet also led to an adjustment of the suppressed reactivity of the sympathetic-adrenal system to glucose intake in insulin-resistant patients with metabolic syndrome- this phenomenon is considered by the authors as a manifestation of a more effective post-prandial processing of energy [19].

Abdominal obesity has been shown to be a very strong predictive factor for the development of metabolic syndrome during long-term follow-up by the Baltimore study [11].

Atherogenic hyperlipidemia

Currently, increased triglyceride levels together with decreased HDL-cholesterol levels appear to be the most serious combination for accelerating vascular damage. This combination represents a continuous higher stress on the endothelium and the whole vascular wall due to flawed transport [20]. The fall in HDL-cholesterol levels as part of insulin resistance is explained by the increase in triglyceride levels, which are rapidly exchanged for cholesterol esters. Insufficient blockage of lipolysis in fatty tissue leads to an increase in free fatty acid levels. Free fatty acids inhibit at the level of all insulin sensitive tissues the insulin stimulated uptake of glucose and thus the vicious circle closes [20].

It is interesting that most probably the principal cause of increasing triglyceride levels in metabolic syndrome is insulin resistance itself, as the measures leading to decreased insulin resistance lead to a decrease in triglyceride levels but on the contrary pharmacological decrease of triglyceridemia does not lead to a decrease in insulin resistance [4].

Decrease of HDL cholesterol serum concentrations and increase of triglyceridemia were previously revealed as independent risk factors for the development of coronary artery disease [21].

Hyperuricaemia

Increased uric acid levels were long considered to be one of the standard components of metabolic syndrome. Recently though, this has become the subject of much discussion. Currently, hyperuricemia is considered to be rather a secondary manifestation of metabolic syndrome caused by decreased renal excretion of uric acid. On the other hand, the effect of hyperuricemia on increasing insulin resistance remains acknowledged [2]. Uric acid itself has demonstrated antioxidant effects and thus its protective role is also being considered. Another intriguing aspect is the observed normalisation of uric acid levels upon the onset of type 2 diabetes, while during the period of impaired glucose tolerance its levels were higher.

Metabolic Syndrome in Community Dwelling Seniors- Original Results

Patients and methods

The aim of our study was to determine the representation of metabolic syndrome in a population of community dwelling seniors aged over 65 and cared for by general practitioners and geriatrics specialists. The whole sample of seniors was examined in cooperation with general practitioners from Hodonín, Uherské Hradiště, Zlín and the Geriatrics Outpatient Clinic of the Department of Internal Medicine, Geriatrics and General Practice, Medical Faculty of Masaryk University and Faculty Hospital Brno (KIGPL).

The examination of the sample included a basic medical history and physical exam, basic laboratory tests, basic geriatric tests – MMSE (Mini Mental State Examination), ADL (Activities of Daily Living), IADL (Instrumental Activities of Daily Living) and the geriatric depression scale, determination of all diagnoses for which the senior was being treated and all medication taken regularly by the senior.

All seniors were examined according to a unified protocol. General practitioners and physicians from the Geriatrics Outpatient Clinic and their nurses were instructed as to the unified system of filling out questionnaires and examination protocols.

In our sample, we evaluated the incidence of the individual components of metabolic syndrome, as well as the number of clients meeting the criteria for the diagnosis of metabolic syndrome and the effect of the presence of metabolic syndrome on the overall state of health and performance of the seniors studied. The IDF criteria were used to determine the diagnosis of metabolic syndrome in view of the already ongoing treatment of dyslipidemia, diabetes and hypertension.

Basic statistical methods for sample characterisation as well as Student´s T test, χ – chi square test and correlation analysis were used to evaluate the collected data.

Results

The sample included a total of 147 clients, of which 55 were men and 92 women. The average age of the clients was 72.8±6.29 years, range65-98 years. The clients studied were being treated on average for 5.8±2.73 diagnoses, range 0-11 diagnoses and they were regularly taking on average 4.9±2.70 types of medication, range 0-11 types of medication.

Impaired glucose tolerance or type 2 diabetes mellitus occurred in 45 clients i.e. 30.3%, of which 25 were receiving pharmacological treatment and 5 had an actual plasma glucose level exceeding 10 mmol/l.

Hypertension occurred in 131 of the clients from the studied sample i.e. 88.5%, and in 10 the measured values indicated unsatisfactory control.

Dyslipidemia was uncovered in 116 clients from the studied sample i.e. 78%, of which 64 were receiving pharmacological treatment: 6 patients were on fibrates and 58 on statins.

Excess weight occurred in 71 clients i.e. 48% and obesity in 37 clients – 25.3%. The average value of BMI for the whole sample was 27.5±4.09, range 17.9-43.9.

Hyperuricemia or gout was diagnosed in 46 clients i.e. 31.5%, of which 23 were receiving pharmacological treatment. For an overview see Figure 1.

Incidence of the components of metabolic syndrome among the clients from the studied sample

Criteria of metabolic syndrome according to IDF (obesity together with at least another 2 signs) were met by a total of 23 clients i.e. 15.7%

Figure 1: Incidence of the components of metabolic syndrome among the clients from the studied sample.
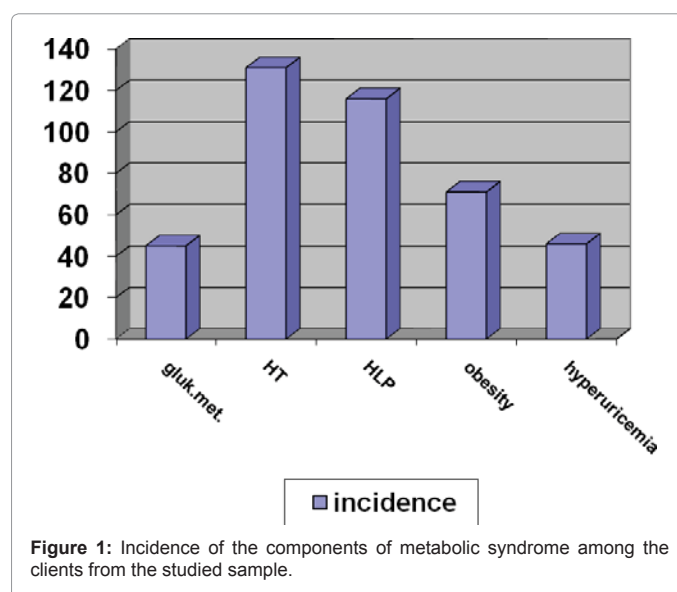
of the sample. A relatively considerable section of the studied sample though met three criteria – 18 clients, 12.1%. Nonetheless, in view of the absence of abdominal obesity they could not be diagnosed as suffering from metabolic syndrome according to IDF criteria. Absence of any of the components of metabolic syndrome was noted in the same number of clients. Figure 2 illustrates the representation of the individual components of metabolic syndrome in the patients from the studied sample expressed in percent.

Representation of the components of metabolic syndrome in the patients from the studied sample expressed in percent

From the aspect of any influence on the overall state of health and performance of the seniors, no significant correlation between the incidence of metabolic syndrome and age was found in the studied sample – $r = -0.10$, $p>0.05$ – i.e. there was rather a trend towards a lower incidence with advancing age. Clients suffering from metabolic syndrome were statistically significantly younger than those who did not meet the criteria of metabolic syndrome – 69.8 ± 3.58 vs. 73.2 ± 6.65, $p<0.01$. Impairment of cognitive functions expressed as the results of the MMSE test showed a significant correlation with the incidence of metabolic syndrome– $r = -0.44$, $p<0.05$ see Figure 3. A similar correlation was also found between the incidence of metabolic syndrome and the results of the ADL test - $r = -0.44$, $p<0.05$. Another significant correlation was revealed on evaluating the results of the geriatric depression scale and the incidence of metabolic syndrome components – an increasing number of components represented led to more inferior results on the depression scale – $r = 0.21$, $p<0.05$.

Correlation between the MMSE test results and the incidence of metabolic syndrome

A more significant correlation was uncovered when studying the influence on self-sufficiency and body weight or BMI. Here a surprisingly positive correlation was found between BMI and IADL – $r = 0.18$, $p < 0.05$ – see Figure 4. Correlation between age alone and weight or BMI was shown to be significantly reciprocal – $r = -0.35$, $p<0.01$, resp. $r = -0.24$, $p<0.01$.

Correlation between IADL and BMI values

When evaluating the laboratory findings, a clear correlation was
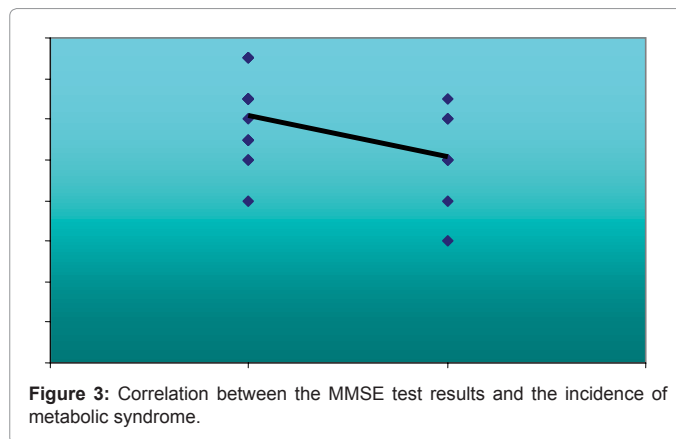
Figure 3: Correlation between the MMSE test results and the incidence of metabolic syndrome.
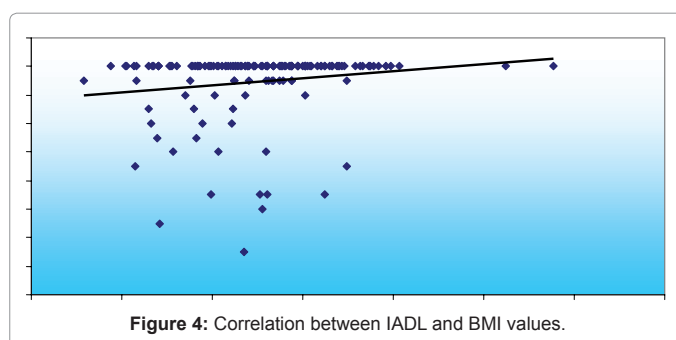
Figure 4: Correlation between IADL and BMI values.

found as expected between serum triglyceride values and body weight or BMI – $r = 0.31$, $p<0.01$, resp. $r = 0.22$, $p<0.01$. The correlation between serum triglyceride levels and plasma glucose levels was even more significant– $r = 0.35$, $p<0.01$. Evaluation of the relationship between serum uric acid levels and the components of metabolic syndrome clearly demonstrated that hyperuricemia is significantly associated with the incidence of metabolic syndrome, both in relation to increased triglyceride levels, body weight or BMI– $r = 0.24$, $p<0.01$, $r = 0.41$, $p<0.01$, $r = 0.25$, $p<0.01$, and to a lesser degree to plasma glucose levels – $r = 0.20$, $p<0.05$.

Discussion

In the studied sample, women were represented in a higher number as expected. Neither the average number of diagnoses nor the average number of medication used differed from our previous data [22]. Some components of metabolic syndrome occurred in the studied sample in a clearly higher percentage than that cited for the general population– hypertension in almost 90%, lipid metabolism disorders in nearly 80%. Nonetheless, the incidence of metabolic syndrome according to the appropriate criteria in 18% of the clients from the studied sample was rather lower compared to various studies evaluating the incidence of metabolic syndrome, whereby references regarding its incidence range from 15 to 40%. However, the group of patients with 3 components of metabolic syndrome but without central obesity, i.e. not meeting the criteria of metabolic syndrome, yet who are at risk according to data in literature [15] should be discussed further.

The cause may lie in the overall tendency to lose weight with increasing age. As this is a cross-sectional study, this phenomenon may be considered to be indirect proof that clients with a lower incidence of metabolic syndrome live longer.

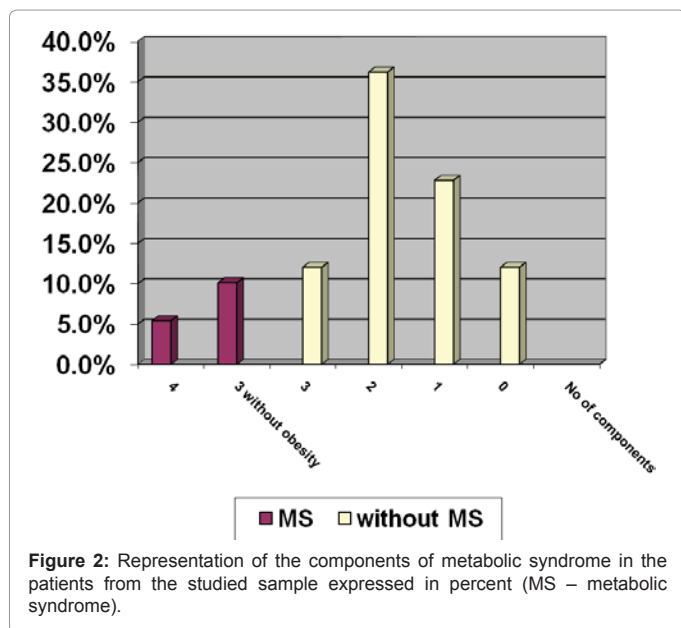In the sample studied, we did not confirm the association between

Figure 2: Representation of the components of metabolic syndrome in the patients from the studied sample expressed in percent (MS – metabolic syndrome).

the presence of metabolic syndrome and positivity of inflammatory parameters as the often cited integral component of endothelial damage development [8,23]. This may be explained on the one hand by advanced age and thus a decreased ability to produce an inflammatory reaction and on the other by the pathophysiological mechanism itself, whereby involvement of the inflammatory component in the development of endothelial damage is presumed to more likely occur at the beginning of the process [24]. Naturally, another cause may be the selection of the relevant marker, as the commonly used CRP may not be a sufficiently sensitive method in this situation.

In concurrence with literary data, we also found a positive correlation between the results of the geriatric depression scale and the increasing number of metabolic syndrome components [25].

Discussions relating to hyperuricemia as a component of metabolic syndrome or a as a secondarily induced phenomenon are also interesting. Our results confirmed the close correlation between serum uric acid levels and the incidence of hypertriglyceridemia, diabetes and BMI. This may be explained as the consequence of increased food intake in general, including foods rich in purines, as well as by the potentiation of tissue insulin resistance by increased uric acid levels [26].

Conclusions for Clinical Practice

Metabolic syndrome occurs in approx. 20-40% of older patients; depending on the clinical criteria used. The incidence of metabolic syndrome in the older population has a significantly negative effect on cognitive functions, the self-sufficiency of older patients and the incidence of depression.

When a certain component of metabolic syndrome is diagnosed, it is necessary to actively look for the presence of other components in order to intervene in time and thus slow down the progression of the whole patho-physiological complex.

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