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METABOLIC SYNDROME IN PATIENTS WITH DEPRESSIVE DISORDER - FEATURES OF COMORBIDITY

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SUMMARY

Background: *Depression is associated with increased physical morbidity and overall mortality. The results of a previous investigation on the relationship of the metabolic syndrome and its single components with coronary heart disease, cardiovascular disease (CVD), and all-cause mortality suggested that the metabolic syndrome is a marker of CVD risk, but not above and beyond the risk associated with its individual components. The aim of this article is to review literature regarding prevalence of metabolic syndrome in patients with depressive disorder, and association between metabolic syndrome and depression.*

Content analysis of literature: *Literature research included structured searches of Medline and other publications on the subject of metabolic syndrome, particularly prevalence of metabolic syndrome in patients with depressive disorder, and association between metabolic syndrome and depression.*

Conclusion: *Prevalence of the metabolic syndrome in patients with depression is high and varies among the analysed studies. Some investigations showed association between metabolic syndrome and depression. Further investigations are necessary in order to clarify the association between metabolic syndrome and depression.*

Key words: *depressive disorder - metabolic syndrome - antidepressants - side effects*

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INTRODUCTION

Depression is associated with increased physical morbidity and overall mortality (Koponen et al. 2010). Patients with such psychiatric disorders as depression, anxiety and psychosis are at higher risk for cardiac mortality compared with the general population (Choka et al. 2006). The results of a recently published investigation suggested that screening and effective treatment of depression are important in the primary and secondary prevention of cardiovascular events, especially in males (Koponen et al. 2010). The results of a previous investigation on the relationship of the metabolic syndrome and its single components, defined by six different criteria, with coronary heart disease (CHD), cardiovascular disease (CVD), and all-cause mortality in a prospective population-based study suggested that the metabolic syndrome is a marker of CVD risk, but not above and beyond the risk associated with its individual components (Wang et al. 2007).

The aim of this article is to review literature regarding prevalence of metabolic syndrome in patients with depressive disorder, and association between metabolic syndrome and depression.

CONTENT ANALYSIS OF LITERATURE

Literature research included structured searches of Medline and other publications on the subject of metabolic syndrome, particularly prevalence of metabolic syndrome in patients with depressive disorder and association between metabolic syndrome and depression.

RESULTS

Prevalence of metabolic syndrome in patients with depressive disorder & association between metabolic syndrome and depression

Prevalence of metabolic syndrome in patients with depressive disorder, as well as association between metabolic syndrome (and components of metabolic syndrome) and depression was investigated in different studies. In the study that aimed to examine the prevalence of the metabolic syndrome (according to the modified criteria of the National Cholesterol Education Program (NCEP)) in depressive outpatients and to identify its correlates in depression, at 6-year follow-up, the prevalence of metabolic syndrome in the study group of depressive outpatients was 36%. The syndrome was associated with a current diagnosis of major depression and overeating, but not with age or sex (Heiskanen et al. 2006). The results of another study that aimed to assess the prevalence of metabolic syndrome (according to the NCEP criteria) among inpatients of a psychiatric ward of a general hospital in Brazil and correlate it with their respective psychiatric diagnoses and with the antipsychotics and mood stabilizers used showed that the prevalence stratified by psychiatric diagnostic was 48.1% for depression, 38.3% for bipolar disorder, 31.8% for schizophrenia and schizoaffective disorder, 5.1% for alcoholism, and 23.1% for "other mental disorders" (Teixeira & Rocha 2007). In the study that evaluated the occurrence of the metabolic syndrome (according to the modified criteria of the American NCEP Treatment Panel III (ATP III)) in depressive inpatients, to analyze the association

between the severity of depression and the metabolic syndrome and to screen specific laboratory values in the course of depressive illness showed that 25% of the depressive patients fulfilled the criteria of metabolic syndrome. Also, an association between metabolic parameters and the course of depression could only be detected in the group of patients with metabolic syndrome (Richter et al. 2010). Furthermore, the study that aimed to assess the prevalence of metabolic syndrome and its association with sociodemographic, clinical and lifestyle variables in a sample of patients with a variety of major mental illnesses attending a public mental health service in Australia showed that the prevalence of IDF-defined metabolic syndrome by psychiatric diagnosis was 67% (bipolar disorder), 67% (schizoaffective disorder), 51% (schizophrenia), 46% (major depression with psychotic symptoms), 46% (drug-induced psychosis), and 41% (borderline personality disorder) (John et al. 2009). In the study that aimed to evaluate the prevalence of metabolic syndrome (according to the NCEP ATP III guidelines) and depression among Sopot inhabitants aged 50 or 60 years, the results showed that in the studied group of middle-aged subjects, especially among women, a high prevalence of depression symptoms was noted. Statistically significant correlations between the prevalence of depressive symptoms and visceral obesity in men and an elevated glucose level in women were shown (Gil et al. 2006).

In the study that aimed to establish an association between depression and the metabolic syndrome (as defined by the Third Report of the NCEP Expert Panel on Detection, Evaluation, and Treatment of High Cholesterol in Adults) in a nationally representative sample, women with a history of a major depressive episode were twice as likely to have the metabolic syndrome compared with those with no history of depression. Men with a history of depression were not significantly more likely to have the metabolic syndrome (Kinder et al. 2004). Another study showed that even in a generally healthy population with access to health care, the presence of depressive symptoms was associated with increased metabolic syndrome; individuals with depressive symptoms had an increased frequency of higher waist circumference, higher triglycerides, and lower high-density lipoprotein, while women with depressive symptoms also had marginally higher fasting blood glucose levels (East et al. 2010). The study that aimed to examine in a sample representative of the general population whether depression, anxiety, and psychological distress are associated with metabolic syndrome (according to the NCEP ATP III and International Diabetes Federation (IDF) criteria) and its components, showed that metabolic syndrome was associated with depression but not psychological distress or anxiety. Large waist circumference and low HDL cholesterol showed significant and independent associations with depression (Dunbar et al. 2008).

The results of a study that aimed to evaluate the risk for developing metabolic syndrome (using the modified NCEP-ATP III criteria) when having depressive symptoms, showed that there was a 2.5-fold risk for the females with depressive symptoms at baseline to have metabolic syndrome at the end of the follow-up (the prevalence of depressive symptoms and metabolic syndrome at baseline, and after a 7-year follow-up were studied in a middle-aged population-based sample). In men, there was no risk difference. It was concluded that the higher risks for metabolic syndrome in females with depressive symptoms at baseline suggested that depression may be an important predisposing factor for the development of metabolic syndrome (Vanhala et al. 2009). Also, in another study that aimed to prospectively examine the association of major depression with incidence of the metabolic syndrome (according to NCEP criteria) in women, major depression was a significant predictor of the onset of the metabolic syndrome (Goldbacher et al. 2009).

On the other hand, not all investigation showed association between metabolic syndrome and depression. In the investigation that aimed to estimate the association between metabolic syndrome (according to IDF, NCEP/ATP-III and ATP-IIIa criteria) and depressive symptoms among the employees of a medical school, no association was observed between metabolic syndrome and depression (Díaz-Martínez et al. 2007). Furthermore, the study that aimed to characterize the relationship between major depression and the metabolic syndrome in a large community based sample of Australian men and women aged 26-90 years (according to NCEP AP-III guidelines) showed that there was no association between a lifetime history of major depression and the presence of the metabolic syndrome. There was a weak association between depression and low high-density lipoprotein cholesterol but not with other component criteria of the metabolic syndrome (Foley et al. 2010). In the study that aimed to examine gender effects and the role of cortisol in the association between depressive symptoms and metabolic risk, depressive symptoms were not associated with the metabolic syndrome as entity in the total sample or in men and women separately. In men, an association between depressive symptoms and variables of the metabolic syndrome was not found. In women, depressive symptoms were associated with several variables of the metabolic syndrome. Elevated afternoon and evening cortisol appear to partially mediate this association (Muhtz et al. 2009).

In the investigation that aimed to determine the extent to which depressive symptoms are associated with metabolic risk factors and whether genetic or environmental factors account for this association twin structural equation modeling indicated that the associations were attributable to environmental (nongenetic) factors (McCaffery et al. 2003). The results of the study that aimed to examine the

association between depression and multiple unhealthy behaviors in hypertensive patients with the metabolic syndrome showed that the prevalence of depression was greater in women than in men. Presence of depression was significantly associated in both men and women with unhealthy diet (in particular, excessive cholesterol and total caloric intake) but also with decreased physical activity in men and with smoking habits in women (Bonnet et al. 2005). The results of a study that investigated in each gender whether the metabolic syndrome is associated with anxiety or depression and whether these relationships are independent of age, obesity, smoking status, socioeconomic factors, and lifestyle (metabolic syndrome (American Heart Association/National Heart, Lung, and Blood Institute criteria), depression, and anxiety were assessed in 1598 subjects at risk of cardiovascular disease) showed that in both men and women, the metabolic syndrome was associated with an increased prevalence of depression but not anxiety, and that the association between the metabolic syndrome and depressive symptoms was independent of age, smoking status, socioeconomic factors, and lifestyle (Skilton et al. 2007). The results of another study that aimed to examine the association between leisure-time physical activity (LTPA) and simultaneous presence of metabolic syndrome and depressive symptoms (4500 randomly selected Finnish men and women aged 45-74 years were initially enrolled; metabolic syndrome was based on the NCEP criteria) showed that the prevalence of simultaneous metabolic syndrome and depressive symptoms was higher in participants with low LTPA compared with participants with high LTPA. Furthermore, LTPA level was associated with socioeconomic status and other health related outcomes, outlining the importance of LTPA as part of the general health promotion (Katariina et al. 2010). In a study of 1024 outpatients with stable coronary heart disease, it was found that participants with greater levels of depressive symptoms, anger expression, hostility, and pessimism had a significantly higher prevalence of the metabolic syndrome. This association appeared to be explained by differences in socioeconomic status and health behaviors (physical inactivity, smoking, alcohol use, and body mass index (BMI)) (Cohen et al. 2010). The results of the study that examined the associations of depression and anxiety with BMI after taking into consideration the obesity-related comorbidities and other psychosocial or lifestyle factors (the data collected from 177,047 participants were analyzed) demonstrated that disparities in the prevalence of depression and anxiety exist among people with different BMI levels independent of their disease status or other psychosocial or lifestyle factors (Zhao et al. 2009). The results of the study that aimed to evaluate the association between obesity and depression among middle-aged women showed that depression was strongly and consistently associated with obesity, lower physical activity and (among the obese) higher caloric intake (Simon et al. 2008).

Antidepressants and metabolic syndrome

Many psychiatric drugs, such as antidepressants and antipsychotics, are associated with weight gain. Some drugs, such as tricyclic antidepressants, can cause insulin resistance and can increase serum lipids independent of their affect on weight (Choka et al. 2006). The study that investigated whether diagnosis, symptom severity and antidepressant use are associated with the metabolic syndrome showed that symptom severity was positively associated with prevalence of the metabolic syndrome, which could be attributed to abdominal obesity and dyslipidemia. Tricyclic antidepressant (TCA) use also increased odds for the metabolic syndrome, independent of depression severity (van Reedt Dortland et al. 2010). According to an earlier review, TCA's induced weight gain correlated positively with dosage and duration of treatment, more pronounced with amitriptyline, while selective serotonin reuptake inhibitors (SSRI) decrease transiently bodyweight during the first few weeks of treatment and may then increase bodyweight (Ruetsch et al. 2005). The conclusion of an earlier analysis that reviewed recommendations from treatment guidelines and articles about management of antidepressants' side effects during treatment of major depressive disorder was that monitoring of side effects should be undertaken during treatment with antidepressants and that potential side effects should be considered when selecting an antidepressant (Uzun & Kozumplik 2009).

Onset of depressive symptoms in patients with metabolic syndrome

Beside investigations on development of metabolic syndrome in patients with depression, investigations also focused on onset of depressive symptoms in patients with metabolic syndrome. The results of the study that examined whether the metabolic syndrome (according to NCEP criteria) is associated with the onset of depressive symptoms in a cohort of middle-aged British civil servants showed that the presence of the metabolic syndrome was associated with an increased risk of future depressive symptoms. Of the five components, only central obesity, high triglyceride levels, and low HDL cholesterol levels predicted depressive symptoms. These components explained most of the association between the metabolic syndrome and the onset of depressive symptoms. It was concluded that the results suggested that metabolic syndrome, in particular the obesity and dyslipidemia components, is predictive of depressive symptoms (Akbaraly et al. 2008). Furthermore, in the investigation that aimed to evaluate the risk for developing depressive symptoms in patients with metabolic syndrome in a population-based follow-up study, the results showed that nondepressed women and men with metabolic syndrome at baseline were twice as likely to have depressive symptoms at follow-up as compared with the nondepressed cohort members without metabolic syndrome at baseline (the prevalence

of depressive symptoms and metabolic syndrome at baseline and at 7-year follow-up was studied in a large, middle-aged, population-based sample; metabolic syndrome was assessed using the modified NCEP ATP III criteria). It was concluded that the higher rate of depressive symptoms in the subgroup with metabolic syndrome suggested that the metabolic syndrome may be an important predisposing factor for the development of depression (Koponen et al. 2008). The results of a 1-year cohort study that aimed to evaluate the association of metabolic syndrome (according to the IDF criteria) with the development of both depression and anxiety showed a positive relationship between metabolic syndrome at baseline and new-onset depression in the subsequent year. Of the five metabolic syndrome components examined, only waist circumference was significantly related to new-onset depression. It was concluded that the results suggested that metabolic syndrome is a predictive factor for the development of depression, and that waist circumference largely contributes to the association between metabolic syndrome and depression (Takeuchi et al. 2009). The results of the study that evaluated the association between various measures of obesity and incident depression over a 10-year period in a large cohort of community-based older men (the authors recruited 12,216 men aged 65-84 years) indicated that obesity and metabolic syndrome were associated with an increase in the risk of incident depression among older men (Almeida et al. 2009).

CONCLUSION

Prevalence of the metabolic syndrome in patients with depression is high and varies among the analysed studies. The results of some investigations showed association between metabolic syndrome and depression. Further investigations are necessary in order to clarify the association between metabolic syndrome and depression.

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