RELATIONSHIP BETWEEN OBESITY AND QUALITY OF GLYCEMIC CONTROL IN POSTMENOPAUSAL WOMEN WITH TYPE 2 DIABETES

Vojislav Ciric[1] and Boris Djindjic[2]

The aim of this paper was to study the relationship between the category of obesity and type of obesity with the quality of glucoregulation in postmenopausal women with type 2 diabetes (T2DM). Glycemic control was assessed according to ADA recommendations (2008). Subsequently, all the patients were divided into two groups - I group included 10 patients with T2DM and satisfactory glycemic control (HbA1c<7%) and II group included 20 patients with T2DM and unsatisfactory glycemic control (HbA1c>7%). All the patients were diagnosed with T2DM at least one year prior to examination and duration of postmenopausal period was at least one year. All the subjects used medical nutrition therapy and oral antidiabetics. Glycemic control was evaluated with fasting plasma glucose and HbA1c, category of obesity was assessed with body mass index (BMI) and type of obesity was evaluated with waist circumference and waist-to-hip ratio. It was shown that age of patients, duration of T2DM and duration of postmenopausal period did not influence the quality of glycemic control. Category of obesity and type of obesity did not show important correlation with glycemic control parameters. The waist circumference relationship with glycemic control parameters was found to be the best, and that was particularly expressed through moderate correlation with fasting plasma glucose. *Acta Medica Medianae 2008;47(2):20-24.*

Clinic for Endocrinology, Diabetes and Metabolic Diseases, Clinical Center in Nis [1]
Pathopsysiology Institute of the Faculty of Medicine in Nis [2]

Contact: Vojislav Ciric
Clinic for Endocrinology, Diabetes and Metabolic Diseases, Clinical Center
48 Dr Zoran Djindjic Blvd.
18000 Nis
Phone: 018233142
E-mail: ciricv@yahoo.com

Introduction

Diabetes mellitus type 2 (DM type 2, T2DM) is one of the most common health problems worldwide. It accounts for 80-90% of all DM patients. DM type 2 incidence has risen considerably over the last three decades (1). World Health Organization recons that by 2025, the number of patients will have surpassed 300 million (2).

DM type 2 incidence increases with age, and it is higher in women than in men; in city than in country population (3).

Patients diagnosed with T2DM are more likely to develop a wide range of complications, leading to premature inability and death. The mortality rate among diabetics is 2-3 times higher than in the general population.

As a consequence of the general and accelerated atherosclerosis in large blood vessels, macroangiopatic complications appear (4). Therefore, the risk of developing coronary disease, cerebrovascular insult, intermittent claudication, and ischemic gangrene increases (5).

Even though the exact ethiopatogenetic mechanisms in the development of atherosclerosis are still unknown, number of epidemiological studies have defined risk factors associated with the subsequent onset of the clinical manifestations of atherosclerosis. The most important risk factors are: hypercaloric nutrition rich in fat and cholesterol; smoking, physical inactivity, hypercholesterolemia, dislipidemia, hypertension, hyperglycemia, diabetes, obesity, age, sex, positive family and personal history for cardiovascular diseases (CVD), etc (6,7).

Risk for CVD is rather high, even at the moment of diagnosing T2DM, due to long-lasting preclinical diabetes (impaired glucose tolerance), which may exist for 10-12 years before a patient is diagnosed with DM (8,9). The duration of diabetes, indirectly, contributes to the increased risk of CVD, due to disorders in the lipid metabolism, especially to the progressive increase of the triglyceride level (10).

Metabolic syndrome is a condition of increased risk to the onset of CVD morbidity and mortality (11). Back in 1988, Reaven found connection among obesity, DM, hypertension, hyperlipidaemia, and clinically manifested athero-sclerosis in some subjects (9). Based on this observation, he came up with the definition of the syndrome of insulin resistance or metabolic syndrome, also known as "syndrome X"; which – along with the above mentioned indicators – also points to an insulin resistance, hyperinsulina-emia, lowered values of HDL-C, protrombotic condition with the increased values of fibrinogen and PAI-1, proinflammatory state with the incre-ased values of CRP and polycystic ovary syndro-me (11,12). All of the components of metabolic syndrome have a joint impact on accelerated processes of aterogenesis and onset of T2DM.

Obesity is, along with hypertension, the most common component of metabolic syndrome and reperesents one out of six major factors responsible for the occurrence of CVD, with the global influence of 15% (13).

Most studies show that obesity is an independent risk factor for the onset of athero-sclerosis. Though pathogenetic mechanisms are highly complex, the presence of visceral obesity is nowadays considered to be the major cause of the increased level of circulating inflammatory factors, called adipokines. Adipokines include: tumor necrosis type α (TNF-α), leptin, adiponectin, PAI-I, interleukin-6 (IL-6) (14). TNFα is one of the main causes for the onset of insulin resistency. Circulating level of leptin correlates to the onset of manifested atherosclerosis in humans.

The main risk factors for the occurrence of CVD in women and men are alike; but their quantitative importance for the prediction of CVD is different. As far as women going through regular menopause are concerned, coronary risk gradually grows with aging and represents the culmination of a long-lasting period of decreased ovarian function. Postmenopausal status is connected to accelerated atherogenesis and the onset of clinical CVD, which appear to be 2-3 times more common in this group of patients, than in the premenopausal patients; even though the role of the hormonal status and other risk factors is still not very clear (15).

Aim

The aim of this paper was to study the relationship between the category of obesity and type of obesity with the quality of glucoregulation in postmenopausal women with type 2 diabetes (T2DM).

Patients and Methodology

Total number of 30 postmenopausal women suffering from diabetes mellitus type 2 were observed, diagnosed and treated in the Daily Hospital of the Clinic for Endocrinology, Clinical Center in Nis; between January and March 2008. All the patients suffered from T2DM at least one year before evaluation, while at the same time, their postmenopausal periods did not last shorter than one year. All the patients had already started medical nutrition treatment and treated with oral antidiabetics.

For all patients history was taken, glucoregulation was evaluated with fasting glycemia (FG), the percentage of glycolized hemoglobin (HbA1c), category of obesity was assessed with body mass index BMI, type of obesity with waist circumference (WC) and waist to hip ratio (WHR).

Fasting glycemia was determined using standard laboratory method enzyme UV tests with hexokinase.

The value of glycolized hemoglobin was determined by the use of immune-inhibitory test.

The quality of glucoregulation was assessed according to ADA recommendations (2008) (16), whereby all the patients were divided into two groups:

Group I – including 10 patients with T2DM and satisfactory glycemic control (HbA1c <7%).

Group II – including 20 patients with T2DM and unsatisfactory glycemic control (HbA1c>7%).

The quality of glucoregulation was assessed according to WHO recommendations (1998) (17). Central obesity, ethnically different type of obesity, was assessed with waist circumference, according to IDF recommendations (International Diabetes Foundation) (18), and the W/H ratio according to WHO recommendations (1999) (19).

Obesity was defined according to WHO recommendation as BMI>30 kg/m² (17). Ethnically specific criterion for central obesity in people from Europe means that the WC in men is 94 cm and more; and WC in women is 80cm or more (18). According to WHO, the definition of visceral obesity means the W/H ratio of >0,9 for men and >0,85 for women (19).

Results

Table 1. Characterisics of investigated groups

	Age	Duration of postmenopausal period	Duration of obesity	Duration of T2DM
HbA1c≤7%	56.16±2.6	6.6±2.8	4.71±1.2	4.18±1.4
HbA1c>7%	56.41±2.5	7.37±2.9	4.7±1.9	5.05±1.7
average	56.36±2.5	7.21±1.7	4.75±1.7	4.87±1.6

NS for all parameters

The statistic analysis shows that age, duration of postmenopausal period, obesity and T2DM do not have high impact on the quality of glucoregulation in women subjected to this study (Table 1). Obesity defined as BMI>30 kg/m² was found in 5(50%) subjects with satisfactory glucoregulation, while 12 (60%) of the patients with unsatisfactory glucoregulation were considered obese. Abdominal obesity defined as waist circumference of over 80 cm was found in 4 (40%) patients with satisfactory glucoregulation, and in 10 (50%) patients with unsatisfactory glucoregulation. Fisher's test of the exact proba-bility did not confirm the significance of these differences.

Table 2. Evaluation of obesity and glucoregulation in investigated groups

	BMI	WC	WHR	FG
HbA1c$\leq$7%	29.2±1.0	81.33±4.5	0.82±0.07	8.23±1.1
HbA1c>7%	29.56±1.9	83±4.4	0.83±0.06	8.45±0.8
average	29.5±1.8	82.1±4.4	0.83±0.07	8.41±0.88

NS for all parameters

The category of obesity assessed with BMI and the type of obesity evaluated with WHR, did not differ significantly in relation to the quality of achieved glycemic control. Values of the fasting glycemia were rather similar among the groups of subjects with satisfactory and unsatisfactory glucoregulation (Table 2).

Table 3. Correlation coefficients between obesity and glucoregulation parameters

	HbA1c	Morning glycemia
WC	0.25	0.30
WHR	0.03	0.04
BMI	0.025	0.023

The category of obesity assessed with BMI and the type of obesity evaluated with WHR did not show a significant relation to the parameters of glucoregulation, WC showed the best relationship to quality of glucoregulation, which can particularly be seen in correlation of the moderate intensity and the values of the fasting glycemia.

Discussion

In patients suffering from T2DM, the changes in hormonal status, abdominal obesity and the quantity of visceral fat, as well as the changes in the fat metabolism accompanying menopause – represent extra factors which interfere with the glucoregulation, whereby these disorders are more important than the classic factors, such as aging and duration of T2DM (20). All this is in accordance with the research data, showing that age, length of menopause and diabetes mellitus are not vital for the quality of glucoregulation (Table 1).

Obesity, defined as BMI>30 kg/m², was found in the large percentage of subjects. It is worth mentioning that it was less present in patients with satisfactory glucoregulation. These results agree with the findings of EUROSPIRE I and II studies, where the incidence of obesity was 33% (21). Average value of BMI and WHR (Table 2) are similar to those found in patients suffering from diabetes type 2, dealt with in the studies of primary and secondary prevention of coronary diseases (22,23,24) (BMI: CARDS study 28.8±3.52; HPS 28.6±5.0 kg/m²). In the DAIS study, the WHR in female patients was 0.88±0.06 and even higher in 13.8% of patients, which is a bit higher than the average values found in this research.

Average WC of 89.44± in postmenopausal women in the Hernandez-Ono and associates study (25) is a bit higher than the values registered in this study (Table 2).

Experimental studies have shown that 25-30% of circulating IL-6 come from the subcutaneous fat. Moreover, adypocites of visceral fat of omentum secrete 2-3 times more IL-6 than the subcutaneous fat and there lies significant connection between the abdominal obesity and the insulin resistance (26). This implies that the rise of inflammatory activity can be an early phase in the development of insulin resistance. Keeping that in mind, we can understand that BMI and CRP show significant connection with the fasting insulinemy in nondiabetic women (27). As far as women with T2DM are concerned, there is also a rise in the quantity of abdominal fat and higher cardiovascular risk (25). This research did not show any significant correlation of BMI values with the fasting glycemia (Table 3), which implies that in postmenopausal women suffering from T2DM, the category of obesity and the quantity of subcutaneous fat are not crucial indicators of the level of insulin resistance; while the quantity of visceral fat most probably is. When the decreased metabolism of fat in peripheral tissues in postmenopausal women is taken into consideration, it can be concluded that visceral fat is the main source of their IL-6, and that it determines the level of insulin resistance and glucoregulation.

Slight correlation between BMI and the values of glycolized hemoglobin (Table 3) agrees with the findings of other authors. In the research study done by Ferrera et al., the weak correlation between BMI and the values of HbA1c was found in postmenopausal women suffering from T2DM (28).

Higher values of glycemia seem to be connected to hyperinslinaemia in postmenopausal women; while the values of HbA1c do not. This indicates that menopause leads to insulin resistance characterized by heavy disorder of the fasting glycemia and milder disturbance of postprandial glycemia and HbA1c (29). Keeping in mind that the hyperpoduction of IL-6 accompanied by the visceral obesity lead to the onset of insulin resistance in menopausal women, the finding of moderate positive correlation of WC with the values of fasting glycemia (Table 3) can be explained. According to Berger et al. (29), moderate connection between abdominal obesity and the values of HbA1c (Table 3) can be explained. In the study conducted by Hernandez-Ono et al., (25), it was shown that in postmenopausal women suffering from T2DM, WC sets a benchmark for abdominal obesity and correlates moderately with the values of fasting glycemia of C=0,20; while WHRo shows somewhat better relation of C=0,30, which indicates how important it is to determine these parameters in evaluation of abdominal obesity in postmenopausal women (25). Our study shows that the only significant relation is the one between WC and the quality of glucoregulation; while W/H ratio did not show any such tendency.

Conclusion

- Quality of glucoregulation is not determined by the age of the patient, duration of type 2 diabetes and postme-

nopausal period, category and type of obesity.
- Visceral type of obesity has a higher impact on the quality of glucoregulation comparing to the category of obesity.

References

1. Burke PJ, Williams K, Gaskill PS, Hazuda PH. Rapid Rise in the Incidence of Type 2 Diabetes From 1987 to 1996. Results From the San Antonio Heart Study. Archives of Internal Medicine 1999; 159:1450-6.
2. American Diabetes Association: Evidence-based nutrition principles and recommendations for the treatment and prevention of diabetes and related complications (Position Statement). Diabetes Care 2003;26(Suppl.1):S51-S61.
3. Djordjevic BP. Etiopatogeneza Diabetes Mellitus-a. U Endokrinologija, III izmenjeno i dopunjeno izdanje. Kovac T, Lepsanovic L. (ur.). Beograd: Savremena Administracija dd, 1996. pp. 201-12.
4. Wattanakita K, Folsoma AR, Selvinb E, Weatherleyc B, Pankowa J, Brancatib FL, et al. Risk factors for peripheral arterial disease incidence in persons with diabetes: the Atherosclerosis Risk in Communities (ARIC) Study. Atherosclerosis 2005; 180: 389-97.
5. Coen DA, Stehouwer A, Lambert J, Donker M, VanHinsbergh V. Endothelial Dysfunction and Pathogenesis of Diabetic Angiopathy. Cardiovascular Research 2003;37(1):55-68.
6. Gotto AM, Pownall HJ. Manual of lipid disorders. Reducing the risk for coronary heart disease. Philadelphia: Lippincott Williams and Wilkins, 2003.
7. Ross R. The Pathogenesis of Atherosclerosis. In: Braunnwald E., (Ed.) Heart Disease. A Text Book of Cardiovascular Medicine. London: W.B. Saunders Company 2000. pp.1105-1124.
8. Alexander CM, Landsman PB, Teutsch SM, Haffner SM, Third National Health and Nutrition Examination Survey (NHANES III); National Cholesterol Education Program (NCEP), NCEP-defined metabolic syndrome, diabetes, and prevalence of coronary heart disease among NHANES III participants age 50 years and older. Diabetes 2003;52:1210–14.
9. Reaven GM, Metabolic syndrome: pathophysiology and implications for management of cardiovascular disease. Circulation 2002;106:286-8.
10. Đinđić B, Radić S, Antić S, Sokolović D. Značaj glikoregulacije u patogenezi koronarne bolesti srca u dijabetes melitusu. Acta Medica Medianae 2000;4:12-8.
11. Ford ES, Giles WH, Dietz WH et al. Prevalence of the metabolic syndrome in US adults: findings from the third national health and nutrition examination survey. JAMA 2002;287:356-9.
12. Meigs JB. Epidemiology of metabolic Syndrome. Am J Manag Care 2002;8(Suppl 11):S283-S292.
13. WHO Technical Raport Series, Diet, Nutrition and Prevention of Chronic Disease Report of a Joint WHO/FAO Expert Consultation. WHO Geneva, 2003.
14. Caglayan E, Blaschke F, Takata Y, Hsueh W. Metabolic syndrome-interdependence of the cardiovascular and metabolic pathways. Current Opinion in Pharmacology 2005, 5:135–42.
15. Stangl V, Baumann G, Stangl K. Coronary Atherogenic Risk Factors In Women. Eur Heart J 2002; 23:1738-52.
16. Executive Summary: Standards of Medical Care in Diabetes—2008. Diabetes Care 2008, 31(Suppl1): DOI: 10.2337/dc08 –S005.

17. World Health Organization, Report of a WHO consultation on obesity. Obesity: preventing and managing the global epidemic, World Health Organization, Geneva; 1998.
18. Zimmet P, Alberti G, Shaw J. A New IDF worldwide definition of the metabolic syndrome: the rationale and the results. Diabetes Voice 2005;50:31-3
19. World Health Organisation. Definition, diagnosis and classification of diabetes mellitus and its complications: report of a WHO consultation. Part 1: diagnosis and clasiffication of diabetes mellitus. Geneva: World Health Organisation, 1999.
20. Poehlman ET, Toth MJ, Gardner AW: Changes in energy balance and body composition at menopause: a controlled longitudinal study. Ann Intern Med 1995; 123:673– 5).
21. Clinical reality of coronary prevention guidelines: a comparison of EUROASPIRE I and II in nine countries. EUROASPIRE I and II Group. European Action on Secondary Prevention by Intervention to Reduce Events. Lancet 2001;357:995-1001.
22. Steiner G, Stewart D, Donald Hosking J, and The DAIS Project Group and the World Health Organization Collaborating Centre for the Study of Atherosclerosis in Diabetes. Baseline Characteristics of the Study Population in the Diabetes Atherosclerosis Intervention Study (DAIS). Am J Cardiol 1999;84:1004–10.
23. Heart Protection Study Collaborative Group. MRC/BHF Heart Protection study of cholesterol lowering with simvastatin in 20,536 high-risk individuals: a randomised placebo-controlled trial. Lancet 2002;360:7–22.
24. Colhoun HM, et al. Collaborative AtoRvastatin Diabetes Study (CARDS), Design of the collaborative AtoRvastatin Diabetes Study (CARDS) in patients with type 2 diabetes. Diabet Med 2002;19:201–11.
25. Hernández-Ono A, Monter-Carreola G, Zamora-González J, Cardoso-Saldaña G, Posadas-Sánchez R, Torres-Tamayo M, Posadas-Romero C. Association of visceral fat with coronary risk factors in a population-based sample of postmenopausal women. Int J Obes Relat Metab Disord 2002;26(1):33-9.
26. Mohamed-Ali V, Goodrick S, Rawesh A, Katz DR, Miles JM, Yudkin JS, Klein S, Coppack SW. Subcutaneous adipose tissue releases interleukin-6, but not tumor necrosis factor-alpha, in vivo. J Clin Endocrinol Metab. 1997;82:4196–4200.
27. Pradhan AD, Cook NR, Buring JE, Manson JE, Ridker PM. C-reactive protein is independently associated with fasting insulin in nondiabetic women.Arterioscler Thromb Vasc Biol. 2003;23:650-5.
28. Ferrara A, Karter AJ, Ackerson LM, Liu JY, Selby JV. Northern California Kaiser Permanente Diabetes Registry. Hormone replacement therapy is associated with better glycemic control in women with type 2 diabetes: The Northern California Kaiser, 2005.
29. Berger GM, Naidoo J, Gounden N, Gouws E. Marked hyperinsulinaemia in postmenopausal, healthy Indian (Asian) women. Diabet Med 1995; 12(9):788-95.

POVEZANOST GOJAZNOSTI SA KVALITETOM GLIKOREGULACIJE KOD ŽENA SA DIJABETESOM TIPA 2 U POSTMENOPAUZALNOM PERIODU

Vojislav Ćirić i Boris Đinđić

Cilj rada bio je da se ispita povezanost stepena i tipa gojaznosti sa kvalitetom glikoregulacije kod žena u postmenopauzi obolelih od dijabetes melitusa tipa 2. Procena kvaliteta glikoregulacije vršena je na osnovu ADA preporuka iz 2008. godine, pri čemu su sve bolesnice podeljene u dve grupe: I grupa- obuhvata 10 bolesnica sa dijabetes melitusom tip 2 i zadovoljavajućom glikoregulacijom (sa vrednostima HbA1c<7%) i II grupa- obuhvata 20 bolesnica sa dijabetes melitusom tip 2 i nezadovoljavajućom glikoregulacijom (sa vrednostima HbA1c>7%). Sve bolesnice imaju dokazan dijabetes melitus tipa 2 u trajanju od najmanje jedne godine, ujedno, postmenopauzalni period nije trajao kraće od jedne godine. Sve bolesnice su imale otpočeti higijensko dijetetski tretman i terapiju oralnim hipoglikemicima. Kod svih bolesnica, pored anamnestičkog ispitivanja, primenjene su metode za procenu glikoregulacije (vrednosti glikemije našte i određivanje procenta glikoziliranog hemoglobina), metode za procenu stepena gojaznosti (indeks mase tela-BMI) i metode za procenu tipa gojaznosti (merenje obima struka i odnosa struk/kuk). Pokazano je da starost bolesnika, trajanje DM tip 2, trajanje postmenopauzalnog perioda ne utiču na kvalitet glikoregulacije. Stepen gojaznosti i tip gojaznosti nisu pokazali značajniju povezanost sa parametrima glikoregulacije. Obim struka je pokazao najbolju povezanost sa kvalitetom glikoregulacije, što je posebno vidljivo u korelaciji umereno jakog intenziteta sa vrednostima jutarnje glikemije. *Acta Medica Medianae 2008;47(2):20-24.*

Ključne reči: *gojaznost, glikoregulacija, menopauza, dijabetes melitus*