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Visfatin concentrations in obese patients in relation to the presence of newly diagnosed glucose metabolism disorders

Stężenie wisfatyny u osób z otyłością w zależności od obecności świeżo wykrytych zaburzeń gospodarki węglowodanowej

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Abstract

Introduction: Visfatin, protein secreted by visceral adipose tissue, exerts insulin-mimetic actions. Visfatin concentration increases in patients with longer-standing diabetes type 2 with progressive β-cell dysfunction. Data about the role of visfatin in newly diagnosed glucose metabolism abnormalities are limited.
Evaluation of visfatin concentration in patients with obesity, in relation to the presence of newly diagnosed glucose metabolism disorders.
Material and methods: The study included 68 subjects with obesity, without a previous diagnosis of abnormal glucose metabolism. In all subjects we performed an oral glucose tolerance test, and according to the results the group was divided into the subgroups: A (n = 31), with glucose metabolism disorders (impaired fasting glucose, impaired glucose tolerance and type 2 diabetes); and B (n = 37), without abnormalities. In all subjects serum lipids, uric acid, C-peptide, glycated haemoglobin (HbA_{1c}), creatinine, and serum visfatin concentrations were measured. The control group comprised 30 lean, healthy individuals with normal glucose tolerance.
Results: We found elevated visfatin levels in obese individuals versus the control group (50.0 ± 48 *vs.* 26.7 ± 22.1 ng/mL; p = 0.01). Visfatin concentrations in both subgroups, A and B, did not differ (40.86 ± 27.84 *vs.* 57.7 ± 59.79 ng/mL; p = 0.19). In subgroup A visfatin concentration correlated significantly with triglycerides (r = 0.37, p = 0.038), HbA_{1c} (r = –0.43, p = 0.02), C-peptide (r = –0.38,p = 0.048), and waist-hip ratio (r = –0.41, p = 0.036).
Conclusions: The presence of newly diagnosed glucose metabolism abnormalities in obese subjects had no influence on the visfatin level, probably due to preserved endogenous insulin secretion and relatively short exposure to hyperglycaemia in patients with prediabetes or at early stage of type 2 diabetes. **(Endokrynol Pol 2015; 66 (2): 108–113)**

Key words: *visfatin; obesity; diabetes; prediabetes*

Streszczenie

Wstęp: Wisfatyna, białko wydzielane przez trzewną tkankę tłuszczową, wykazuje działanie insulinomimetyczne polegające między innymi na zwiększeniu wychwytu glukozy przez komórki insulinowrażliwe. Stężenie wisfatyny wzrasta u osób z przewlekłą cukrzycą typu 2 wraz z postępującą dysfunkcją komórki β trzustki. Dane na temat roli wisfatyny w przypadku świeżo rozpoznanych zaburzeń gospodarki węglowodanowej są ograniczone.
Celem pracy była ocena stężenia wisfatyny u chorych z otyłością prostą w zależności od współistnienia świeżo rozpoznanych zaburzeń gospodarki węglowodanowej.
Materiał i metody: Przebadano 68 osób z otyłością prostą, bez rozpoznanych wcześniej zaburzeń gospodarki węglowodanowej. U wszystkich wykonano doustny test obciążenia glukozą, na podstawie którego wyodrębniono podgrupę A (n = 31) — z zaburzeniami gospodarki węglowodanowej (nieprawidłową glikemią na czczo, upośledzoną tolerancją glukozy i cukrzycą typu 2) oraz podgrupę B (n = 37) — bez zaburzeń. U wszystkich oznaczono stężenie cholesterolu całkowitego, HDL, LDL, triglicerydów, kwasu moczowego, peptydu-C, kreatyniny i wisfatyny. Grupę kontrolną stanowiło 30 szczupłych ochotników bez zaburzeń gospodarki węglowodanowej.
Wyniki: Stężenie wisfatyny u osób otyłych było istotnie wyższe w porównaniu z grupą kontrolną (50.0 ± 48 *vs.* 26.7 ± 22.1 ng/mL; p = 0.01). Stężenie wisfatyny w obu podgrupach, A i B, nie różniło się (odpowiednio 40.86 ± 27.84 *vs.* 57.7 ± 59.79 ng/mL; p = 0.19). W podgrupie A stężenie wisfatyny korelowało istotnie ze stężeniem triglicerydów (r = 0.37, p = 0.038), HbA_{1c} (r = –0.43, p = 0.02), peptydem-C (r = –0.38, p = 0.048) i wskaźnikiem talia-biodra (r = –0.41, p = 0.036).
Wnioski: Obecność świeżo rozpoznanych zaburzeń gospodarki węglowodanowej u osób otyłych nie wpływała na stężenie wisfatyny, prawdopodobnie ze względu na zachowane endogenne wydzielanie insuliny i stosunkowo krótki okres narażenia na hiperglikemię u osób ze stanem przedcukrzycowym i świeżo wykrytą cukrzycą typu 2. **(Endokrynol Pol 2015; 66 (2): 108–113)**

Słowa kluczowe: *wisfatyna; otyłość; cukrzyca; stan przedcukrzycowy*

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Introduction

In 2005 visfatin mRNA was identified from visceral adipose tissue [1]. This protein had been previously known as a pre-B-cell colony-enhancing factor, acting on lymphocyte maturation and inflammatory regulation [2]. It was also recognised as nicotinamide phosphoribosyltransferase (Nampt), the limiting enzyme in nicotinamide adenine dinucleotide (NAD) biosynthesis [3].

Increased circulating visfatin levels in obese subjects were confirmed in clinical studies [4–6].

In original work by Fukuhara et al. insulin-mimetic properties of visfatin were shown. This adipocytokine, by binding to the insulin receptor at a site distinct from insulin, increases glucose uptake in muscles and adipose tissue and inhibits hepatic gluconeogenesis [1]. Although the insulin-mimetic effect of visfatin was questioned, resulting in retraction of the article by an author in 2007 [7], numerous subsequent studies focused on the interaction between visfatin, insulin secretion, insulin resistance, and glucose homeostasis were published [6].

Recent studies suggest that visfatin may also act as a proinflammatory cytokine and in this way may indirectly participate in the development of insulin resistance and type 2 diabetes [8].

Visfatin has been widely studied as a potential factor linking obesity and diabetes type 2. Although results of these studies are often conflicting, there is evidence that visfatin concentration increases with progressive β-cell dysfunction in patients with longer-standing diabetes type 2 [6]. Data about visfatin concentration in newly diagnosed glucose metabolism abnormalities are limited.

The aim of our study was to evaluate visfatin concentrations in patients with obesity, in relation to the presence of newly diagnosed glucose metabolism abnormalities, and to find the relationship between visfatin and anthropometric and metabolic parameters in patients with and without glucose metabolism abnormalities.

Material and methods

This is a sub-analysis of the results of an already published study [9], performed on a group of 68 obese patients — 53 females and 15 males (age 37.8 ± 13.2 years, body mass index (BMI) 39.4 ± 6.4 kg/m^2) without previous diagnosis of abnormal glucose metabolism. The control group consisted of 30 healthy, lean individuals - 24 females and 6 males (age 38.2 ± 14.9 years, BMI 22.8 ± 3.0 kg/m^2), with normal glucose tolerance.

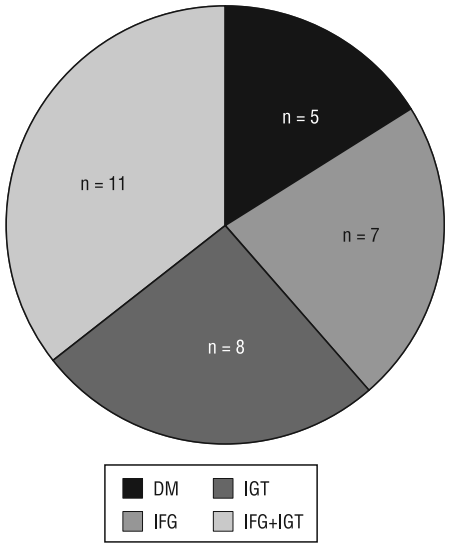

Figure 1. *The distribution of different glucose metabolism disorders in group A (n = 31)*

(DM — diabetes mellitus, IFG — impaired fasting glucose, IGT — impaired glucose tolerance)

Rycina 1. *Rozpowszechnienie różnych zaburzeń gospodarki węglowodanowej w grupie A (n = 31) (DM — cukrzyca, IFG — nieprawidłowa glikemia na czczo, IGT — nieprawidłowa tolerancja glukozy)*

In the examined and control subjects, body weight, height, and waist and hip circumference were measured, then body mass index (BMI) and waist-hip ratio (WHR) were calculated. Oral glucose tolerance test (OGTT) was performed.

Examined individuals were divided, according to the results of OGTT, into subjects with glucose tolerance abnormalities (group A) and subjects with normal glucose tolerance (group B). Impaired glucose tolerance (IGT), impaired fasting glucose (IFG), and diabetes mellitus (DM) were defined according to WHO criteria [10]. Figure 1 shows the distribution of different glucose metabolism abnormalities in group A. All patients with glucose metabolism disorders were treatment-naïve. Characteristics of groups A and B are shown in Table I.

In both groups, A and B, total cholesterol, low density lipoprotein cholesterol (LDL-cholesterol), high density cholesterol (HDL-cholesterol), triglycerides (TG), uric acid, C-peptide, glycated haemoglobin (HbA_{1c}), creatinine, and thyroid stimulating hormone (TSH) were estimated. Mean values of examined parameters in both groups are shown in Table II.

Serum visfatin concentration was assessed in groups A and B and in control subjects by ELISA method (Visfatin C-terminal [Human], Phoenix Pharmaceuticals).

Table I. *The characteristics of group A (with glucose metabolism disorders) and group B (with normal glucose tolerance)*

Tabela I. *Charakterystyka grupy A (z zaburzeniami gospodarki węglowodanowej) i grupy B (z prawidłową tolerancją glukozy)*

Parameter (unit)	Group A	Group B	p
	Mean ± SD	Mean ± SD	
Age [years]	41.3 ± 14.1	33.6 ± 10.7	< 0.05
BMI [kg/m^2]	40.8 ± 6.9	37.3 ± 4.5	< 0.05
Waist circumference [cm]	121.11 ± 15.9	110.4 ± 10.8	< 0.05
Hip circumference [cm]	129.6 ± 14.3	123 ± 11	< 0.05
WHR	0.94 ± 0.1	0.9 ± 0.1	0.27 (NS)

SD — standard deviation; BMI — body mass index; WHR — waist to hip ratio

All subject participating in the study signed an informed consent form. The study was approved by the Bioethics Committee of the Ludwik Rydygier Collegium Medicum in Bydgoszcz, Nicolaus Copernicus University.

Statistical analysis

Statistical analysis of the results was performed. Results are presented as mean ± standard deviation (SD). We used the Shapiro-Wilk test to assess the normality of the distribution of the study variables. In the case of samples characterised by a normal distribution, the means were compared with the use of Student's *t*-test for independent variables. Where the distribution significantly differed from the normal distribution, the significance of between-group comparisons was verified using the non-parametric Mann-Whitney U test. The relationship between two variables was assessed with Pearson's linear correlation coefficient (r). A p value of less than 0.05 was considered statistically significant. All the calculations were performed using the Statistica software.

Results

Serum visfatin concentration was significantly higher in obese subjects than in the control group (50.0 ± 48 *vs.* 26.7 ± ± 22.1 ng/mL; p = 0.01). No difference in visfatin concentration between groups A and B was found (40.86 ± ± 27.84 *vs.* 57.7 ± 59.79 ng/mL; p = 0.19).

In group A with glucose tolerance abnormalities, visfatin concentration correlated significantly with TG (r = 0.37, p = 0.038), C-peptide (r = –0.49, p = 0.009), HbA_{1c} (r = –0.43, p = 0.02) and WHR (r = –0.41, p = 0.036). In group B and in the control group, visfatin did not correlate with any anthropometric or biochemical parameters. Figures 2, 3, and 4 show correlations in group A between visfatin and C-peptide, visfatin and HbA_{1c}, visfatin and WHR, respectively.

Discussion

The pathogenic relationship between obesity and diabetes exists. Obese or overweight subjects are at higher risk for development of type 2 diabetes [11]. Abdominal fat accumulation is associated with insulin resistance and is an independent risk factor for developing diabetes. Visceral fat is a source of free fatty acids (FFA). Elevated FFA and their conversion to long chain acyl

Table II. *Mean values of examined parameters in group A (with glucose metabolism disorders) and B (with normal glucose tolerance)*

Tabela II. *Średnie wartości badanych parametrów w grupie A (z zaburzeniami gospodarki węglowodanowej) i grupie B (z prawidłową tolerancją glukozy)*

Parameter (unit)	Group A	Group B	p
	Mean ± SD	Mean ± SD	
Fasting glucose [mg/dL]	106.1 ± 14.0	87.6 ± 6.3	< 0.00001
2-hour glucose (OGTT) [mg/dL]	158.7 ± 40.5	103.2 ± 19.9	< 0.00001
HbA_{1c} (%)	6.05 ± 0.8	5.4 ± 0.28	< 0.001
C-peptide [ng/dL]	3.52 ± 2.13	2.59 ± 1.8	< 0.001
Total cholesterol [mg/dL]	190.8 ± 25.14	187.9 ± 32.9	0.69 (NS)
LDL cholesterol [mg/dL]	115.3 ± 21.17	112.9 ± 30.5	0.71 (NS)
HDL cholesterol [mg/dL]	45.4 ± 7.16	48.7 ± 8.9	0.09 (NS)
Triglycerides [mg/dL]	152.5 ± 70.8	129.9 ± 61.7	< 0.05
Uric acid [mg/dL]	5.69 ± 1.51	4.77 ± 1.5	< 0.05
TSH [μIU/mL]	1.91 ± 1.43	1.92 ± 1.28	0.98 (NS)

SD — standard deviation; OGTT — oral glucose tolerance test; HbA_{1c} — glycated haemoglobin; TSH — thyroid stimulating hormone

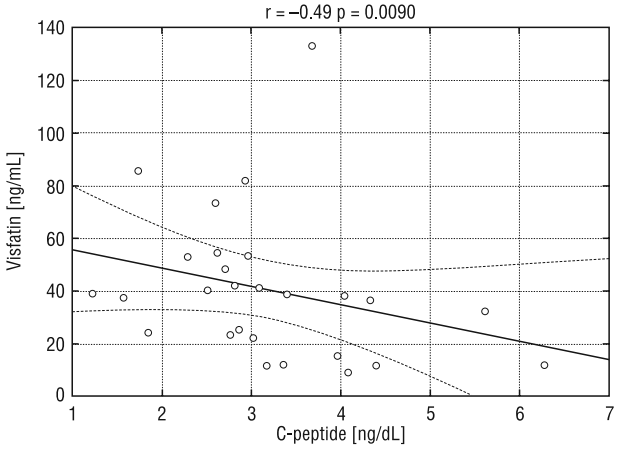

Figure 2. *Correlation between visfatin and C-peptide in group A. r — Pearson's linear correlation coefficient*

Rycina 2. *Korelacja pomiędzy wisfatyną a peptydem-C w grupie A. r — współczynnik korelacji Pearsona*

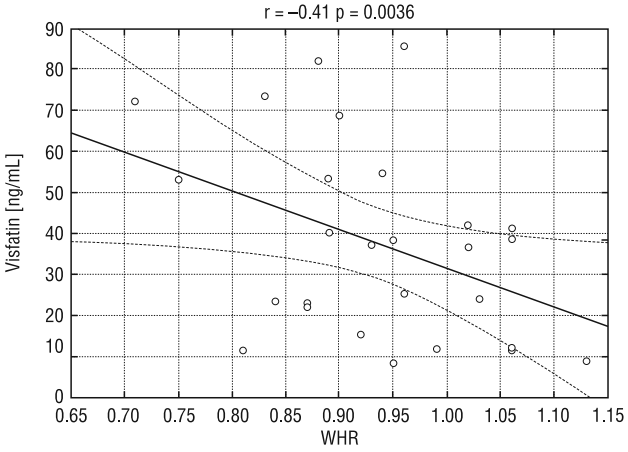

Figure 4. *Correlation between visfatin and WHR in group A. WHR — waist to hip ratio; r — Pearson's linear correlation coefficient*

Rycina 4. *Korelacja pomiędzy wisfatyną a WHR w grupie A. WHR — wskaźnik talia–biodra; r – współczynnik korelacji Pearsona*

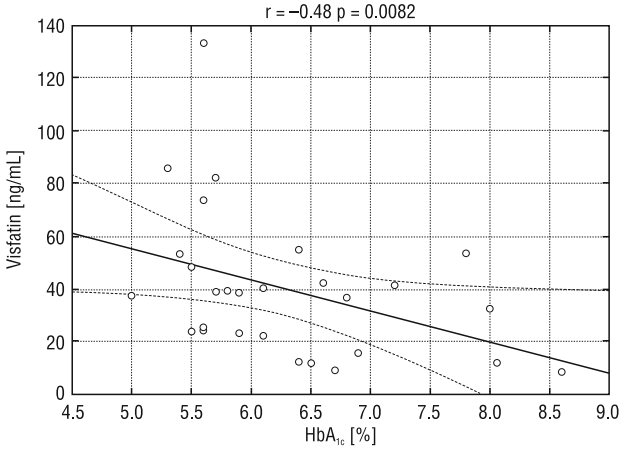

Figure 3. *Correlation between visfatin and HbA_{1c} in group A. HbA_{1c} — glycated haemoglobin; r — Pearson's linear correlation coefficient*

Rycina 3. *Korelacja pomiędzy wisfatyną a HbA_{1c} w grupie A. HbA_{1c} — hemoglobina glikowana; r — współczynnik korelacji Pearsona*

CoA derivatives result in reduced insulin signalling and glucose transport. "Lipotoxicity" and the resulting oxidative stress may contribute to the decline in β-cell mass and diminished insulin secretion [12]. Obesity-associated changes in circulating adipocytokines may contribute to both B-cell destruction and increased insulin resistance [12,13]. Visfatin, an adipocytokine with insulin-mimetic activity [1] and proinflammatory actions [8], is considered as a potential factor that may contribute to the development of diabetes in obese individuals.

The mechanisms of visfatin secretion and action are not fully understood. Haider at al. showed that visfatin is upregulated in a glucose-dependent manner. Hyperglycaemia induced an increase in visfatin concentration, and the release of visfatin was dependent on the duration and the magnitude of glucose elevation. Glucose-induced increase of visfatin was prevented by hyperinsulinaemia [14]. Recently, Kowalska et al. found decreased visfatin levels after insulin infusion and an increase of visfatin after FFA infusion that induced insulin resistance [15]. Thus, the increase of visfatin, observed in patients with type 2 diabetes, may be a result of β-cell dysfunction [16] or insulin inability to suppress visfatin production in insulin-resistant conditions [15]. On the other hand, a recent experimental study by Cheng demonstrates that visfatin protects pancreatic β-cells from FFA-induced apoptosis, via the mitogen-activated protein kinase/phosphoinositide 3-kinase pathway. One might suggest that the increase of visfatin seen in obesity and obesity-associated diseases may be a compensatory mechanism of the body to protect β-cells against metabolic dysfunction induced by cellular exposure to FFAs [17].

We found higher plasma visfatin levels in obese subjects than in lean individuals, but no difference in visfatin concentration was found between two subgroups of obese patients: with impaired glucose metabolism and with normal glucose tolerance. In the subgroup with glucose metabolism disorders visfatin correlated significantly negatively with C-peptide, HbA_{1c} and WHR and positively with triglycerides con-

centration. In contrast, in the subgroup with normal glucose tolerance visfatin did not correlate with any of examined parameters.

Most of our patients with glucose metabolism abnormalities had prediabetes — IFG, IGT, or both. The lack of difference in visfatin concentration between two subgroups is consistent with the findings obtained by other authors who evaluated visfatin levels in individuals with prediabetes [18–20]. Dogru found no difference in the plasma levels of visfatin between non-obese patients with newly diagnosed diabetes and newly diagnosed impaired glucose tolerance, as well as between patients with impaired glucose tolerance and healthy controls. In this study visfatin levels were higher in the diabetic group than in controls [20]. Elevated visfatin concentration in patients with type 2 diabetes was shown by other authors [16, 21–24]. In patients with longer-standing diabetes type 2 and with endogenous insulin deficiency (more than one third of patients were treated with insulin), visfatin concentration increased with progression of β-cell dysfunction and with worsening of glycaemia control [16]. In our study, patients with glucose metabolism abnormalities had higher C-peptide levels than did subjects with normal glucose tolerance. This may reflect a compensatory (to probable insulin resistance) increase of insulin secretion and confirms preserved β-cell function in our patients with prediabetes or at early stage of type 2 diabetes.

Similarly to the Lopez-Bermejo study [16], in our patients visfatin concentration increased with decreased endogenous insulin secretion. However, in contrast to the above-mentioned study, in our group of patients visfatin declined with increasing HbA_{1c}. This is consistent with the results presented by Li et al. [25]. We can suppose that in our subjects insulin secretion was sufficient to inhibit visfatin release, and glucose levels were too low (mean HbA_{1c} level 6.05 ± 0.8%) to stimulate visfatin increase. This may also explain the lack of differences in visfatin concentration between the two study subgroups.

Positive correlation of visfatin and triglycerides, found in our patients with impaired glucose metabolism, was also shown in patients with newly diagnosed type 2 diabetes [24] in obese women with metabolic syndrome [26] and in healthy young men [27]. Hypertriglyceridemia is typical for individuals with visceral obesity and insulin resistance. When insulin resistance develops, increased lipolysis results in FFA elevation and excessive production of glucose and triglycerides [28]. The correlation between visfatin and insulin resistance was shown in a meta-analysis by Chang et al. [6]. We did not evaluate insulin resistance and thus, on the basis of our data, it is not possible to explain the causal relationship between visfatin and triglycerides.

It was demonstrated by Fukuhara that plasma visfatin levels strongly correlate with the quantity of visceral adipose tissue assessed by computed tomography [1]. Although conflicting results were obtained in different studies assessing correlations between visfatin and anthropometric parameters [16, 19, 29], there is evidence that plasma visfatin levels are largely determined by body weight, probably mainly by visceral adipose tissue [6]. A significant decrease in mean serum visfatin concentration was found in girls with anorexia nervosa, the disease that leads to significant reduction of adipose tissue mass [30].

The lack of correlation between visfatin and BMI or waist circumference found in our patients was also confirmed by other authors in patients with diabetes [16], in obese non-diabetic patients [29] and in non-obese patients with newly diagnosed type 2 diabetes and impaired glucose tolerance [20]. We found negative correlation between visfatin and WHR in obese subjects with glucose metabolism disorders. Our results could suggest that higher visfatin levels are associated with the adipose tissue distribution pattern typical for gynoid rather than visceral obesity. It should, however, be taken into account that measuring waist circumference does not reliably distinguish a large waist due to subcutaneous tissue versus visceral fat [28].

Conclusions

Obese subjects had higher visfatin levels in comparison with lean individuals. The presence of newly diagnosed glucose metabolism abnormalities in obese subjects had no influence on the visfatin level, probably due to preserved endogenous insulin secretion and short exposure to hyperglycaemia in patients with prediabetes or at early stage of type 2 diabetes.

References

1. Fukuhara A, Matsuda M, Nishizawa M et al. Visfatin: a protein secreted by visceral fat that mimics the effects of insulin. Science 2005; 21: 426–430.
2. Samal B, Sun Y, Stearns G et al. Cloning and characterization of cDNA encoding a novel human pre-B-cell colony-enhancing factor. Mol Cell Biol 1994; 14: 1431–1437.
3. Rongvaux A, Shea RJ, Mulks MH et al. Pre-B-cell colony — enhancing factor, whose expression is upregulated in activated lymphocytes, is nicotinamide phosphoribosylotransferase, a cytosolic enzyme involved in NAD biosynthesis. Eur J Immunol 2002; 32: 3225–3234.
4. Haider DG, Schindler K, Schaller G et al. Increased plasma visfatin concentrations in morbidly obese subjects are reduced after gastric banding. J Clin Endocrinol Metab 2006; 91: 1578–1581.
5. Zahorska-Markiewicz B, Olszanecka-Glinianowicz M, Janowska J et al. Serum concentration of visfatin in obese women. Metabolism 2007; 56: 1131–1134.
6. Chang YH, Chang DM, Lin KC et al. Visfatin in overweight/obesity, type 2 diabetes mellitus, insulin resistance, metabolic syndrome and cardiovascular diseases: a meta-analysis and systemic review. Diabetes Metab Res Rev 2011; 27: 515–527.
7. Fukuhara A, Matsuda M, Nishizawa M et al. Retraction. Science 2007;318: 565.
8. McGee KC, Harte AL., da Silva NF et al. Visfatin is regulated by rosiglitazone in type 2 diabetes mellitus and influenced by NF$\kappa\beta$ and JNK in Human Abdominal Subcutaneous Adipocytes. PLoS one 2011; 6: e 20287

9. Kamińska A, Kopczyńska E, Bronisz A et al. An evaluation of visfatin levels in obese subjects. Endokrynol Pol 2010; 61: 169–173.
10. The Expert Committee on the Diagnosis and Classification of Diabetes Mellitus: Follow-up report on the diagnosis of diabetes mellitus. Diabetes Care 2003; 26: 3160–3167.
11. Field AE, Coakley EH, Must A et al. Impact of overweight on the risk of developing chronic diseases during a 10-year period. Arch Intern Med 2001; 161: 1581–1586.
12. Colagiuri S. Diabesity: therapeutic options. Diabetes Obesity Metab 2010; 12: 463–473.
13. Wang C, Guan Y, Yang J. Cytokines in the progression of pancreatic β-cell dysfunction. Int J Endocr 2010: 515136 (published online 2010 Nov 14).
14. Haider DG, Schaller G, Kapiotis S et al. The release of the adipocytokine visfatin is regulated by glucose and insulin. Diabetologia 2006; 49: 1909–1914.
15. Kowalska I, Karczewska-Kupczewska M, Adamska A et al. Serum visfatin in differentially regulated by insulin and free fatty acids in healthy men. J Clin Endocrinol Metab 2013; 98: E293–297.
16. Lopez-Bermejo A, Chico-Julia B, Fernandez-Balsells M et al. Serum visfatin increases with progressive β-cell deterioration. Diabetes 2006; 55: 2871–2875.
17. Cheng Q, Dong W, Qian L et al. Visfatin inhibits apoptosis of pancreatic β-cell line, MIN 6, via the mitogen-activated protein kinase/phosphoinositide 3-kinase pathway. J Mol Endocr 2011; 47: 13–21.
18. Hofsr D, Ueland T, Hager H et al. Inflammatory mediators in morbidly obese subjects; associations with glucose abnormalities and changes after oral glucose. Eur J Endocrinol 2009; 161: 451–458.
19. Jian WX, Luo TH, Gu YY et al. The visfatin gene is associated with glucose and lipid metabolism in a Chinese population. Diabet Med 2006; 23: 967–973.
20. Dogru T, Sonmez A, Tasci I et al. Plasma visfatin levels in patients with newly diagnosed and untreated type 2 diabetes mellitus and impaired glucose tolerance. Diab Res Clin Pract 2007; 76: 24–29.
21. Chen MP, Chung FM, Chang DM et al. Elevated plasma level of visfatin/pre-B cell colony-enhancing factor in patients with type 2 diabetes mellitus. J Clin Endocrinol Metab 2006; 91: 295–299.
22. Shaker O, El-Shehaby A, Zakaria A et al. Plasma visfatin and retinol binding protein-4 levels in patients with type 2 diabetes mellitus and their relationship to adiposity and fatty liver. Clin Biochem 2011; 44: 1457–1463.
23. Hajianfar H, Bahonar A, Entezari MH et al. Lipid profiles and serum visfatin concentration in patients with type II diabetes in comparison with healthy controls. Int J Prev Med 2012; 3: 326–331.
24. Esteghamati A, Alamdari A, Zandieh A et al. Serum visfatin is associated with type 2 diabetes mellitus independent of insulin resistance and obesity. Diab Res Clin Pract 2011; 91: 154–158.
25. Li L, Yang G, Li Q et al. Changes and relations of circulating visfatin, apelin and resistin levels in normal, impaired glucose tolerance, and type 2 diabetic subjects. Diabetes 2006; 114: 544–548.
26. Olszanecka-Glinianowicz M, Kocelak P, Janowska J et al. Plasma visfatin and tumor necrosis factor-alpha (TNF-α) levels in metabolic syndrome. Kardiol Pol 2011; 69: 802–807.
27. Sun G, Bishop J, Khalili S et al. Serum visfatin concentrations are positively correlated with triacyloglicerols and down-regulated by overfeeding in healthy young men. Am J Clin Nutr 2007; 85: 399––404.
28. Eckel RH. The metabolic syndrome. In: Jameson JL, ed. Harrison's Endocrinology. Mc Graw Hill Medical, 2nd edition 2010: 261–262.
29. de Luis DA, Sagrado MG, Conde R et al. Effect of a hypocaloric diet on serum visfatin in obese non-diabetic patients. Nutrition 2008; 24: 517–521.
30. Ostrowska Z, Ziora K, Oświęcimska J et al. Bone metabolism, osteoprotegerin, receptor activator of nuclear factor $\kappa\,\beta$ ligand and selected adipose tissue hormones in girls with anorexia nervosa. Endokrynol Pol 2014; 65: 33–39.