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Visceral fat measurement by ultrasound as a non-invasive method — can it be useful in evaluating subclinical atherosclerosis in male patients with hypopituitarism and growth hormone deficiency?

Nieinwazyjny pomiar ilości tkanki tłuszczowej trzewnej metodą ultrasonograficzną — potencjalne zastosowanie w ocenie zaawansowania subklinicznej miażdżycy u mężczyzn z niedoczynnością przysadki i niedoborem hormonu wzrostu

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Abstract

Introduction: Growth hormone (GH) deficiency, either isolated or combined with other pituitary hormone deficiencies, is associated with increased mortality and abnormal body composition, particularly visceral adiposity. We aimed to investigate the effects of GH deficiency with or without sex steroid deficiencies on ultrasonographic visceral fat (VF) and cardiovascular risk markers in patients with hypopituitarism on conventional hormone replacement therapy.

Material and methods: Forty hypopituitarism patients (24 women, 16 men; mean age 48 ± 16.1 years) with GH deficiency and 15 age- and sex-matched healthy controls were included in this cross-sectional study. The patients were stable on conventional hormone replacement but they were not on GH therapy. Patients who had sex steroid replacement were classified as Group 1 (n = 19), and patients who did not use sex steroids were classified as Group 2 (n = 21). Anthropometric measurements were performed. VF in three regions, subcutaneous fat, and carotid intima-media thickness (CIMT) were measured. VF volume was calculated by using a formula.

Results: Visceral fat volume and mean CIMT were significantly higher in patients than healthy controls (p = 0.001 and 0.019 respectively). Homocysteine and hs-CRP were higher in patients (p < 0.05). In males, VF volume and VF thickness measured between abdominal muscle and splenic vein were significantly correlated with CIMT (r = 0.54, p = 0.047 and r = 0.66, p = 0.010 respectively). Furthermore, there was a strong positive correlation between VF thickness in pararenal region and homocysteine (r = 0.74, p = 0.001) in males.

Conclusions: VF volume evaluated by ultrasound can be accepted as a cause of subclinical atherosclerosis in GH deficient hypopituitary patients, particularly males. **(Endokrynol Pol 2014; 65 (3): 195–202)**

Key words: *hypopituitarism; visceral fat; ultrasound; atherosclerosis*

Streszczenie

Wstęp: Niedobór hormonu wzrostu (GH, *growth hormone*) może występować jako zaburzenie izolowane lub współistnieć z niedoborami innych hormonów przysadki. Wszyscy pacjenci z niedoborem GH są jednak obarczeni większym ryzykiem zgonu i mają nieprawidłowy skład tkanek ciała, z tendencją do otyłości brzusznej. Celem pracy była ocena zależności pomiędzy niedoborem GH, niezależnie od ewentualnego współistnienia niedoborów hormonów płciowych a grubością tkanki tłuszczowej trzewnej (VF, *visceral fat*) mierzoną metodą ultrasonograficzną oraz czynnikami ryzyka sercowo-naczyniowego u pacjentów z niedoczynnością przysadki, leczonych konwencjonalnymi preparatami hormonalnymi.

Materiał i metody: Badanie miało charakter przekrojowy i zakwalifikowano do niego 40 pacjentów z niedoczynnością przysadki i niedoborem GH, w tym 24 kobiety, 16 mężczyzn; średni wiek badanych wynosił 48 ± 16,1 lat. Do badania włączono też 15 osób w grupie kontrolnej, dobranych pod względem płci i wieku do osób z grupy badanej. Pacjenci w grupie badanej leczeni byli konwencjonalnie preparatami hormonalnymi, ale nie otrzymywali hormonu wzrostu. Pacjenci leczeni hormonami płciowymi zostali włączeni do grupy 1 (n = 19), a pacjenci nie otrzymujący takich preparatów do grupy 2 (n = 21). U wszystkich wykonano badania antropometryczne. Wykonywano pomiar grubości VF w trzech miejscach, badano grubość podskórnej tkanki tłuszczowej oraz grubość warstwy wewnętrznej i środkowej ściany tętnicy szyjnej (CIMT, *carotid intima-media thickness*). Objętość VF wyliczano według wzoru.

Wyniki: U pacjentów w grupie badanej stwierdzono znamiennie większą objętość trzewnej tkanki tłuszczowej i średnią wartość CIMT w porównaniu z osobami zdrowymi (odpowiednio p = 0,001 i p = 0,019). Stężenie homocysteiny i hs-CRP były również większe w grupie badanej (p < 0,05). U mężczyzn stwierdzono istotną korelację pomiędzy objętością VF i grubością VF mierzoną pomiędzy mięśniami brzucha a żyłą śledzionową a wartością CIMT (odpowiednio r = 0,54 i p = 0,047 oraz r = 0,66 i p = 0,010). Ponadto, u mężczyzn stwierdzono wyraźną zależność pomiędzy grubością VF w okolicy nerek a stężeniem homocysteiny (r = 0,74 i p = 0,001).

Wnioski: Objętość VF mierzona ultrasonograficznie może być wykładnikiem subklinicznie toczącej się miażdżycy u pacjentów z niedoborem hormonu wzrostu na skutek niedoczynności przysadki, w szczególności u mężczyzn. **(Endokrynol Pol 2014; 65 (3): 195–202)**

Słowa kluczowe: *niedoczynność przysadki; tkanka tłuszczowa trzewna; ultrasonografia; miażdżyca*

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Introduction

Hypopituitarism is characterised by the loss of function of the anterior pituitary gland. It is a rare condition that can present at any age and is caused by pathology of the hypothalamic-pituitary axis or by genetic mutations [1]. The symptoms and signs of the disease may be non-specific or related to the underlying disease or to the hormone deficiencies [1]. Cardiovascular mortality is increased in adults with hypopituitarism [2, 3]. A number of aetiologies for the excess mortality associated with hypopituitarism have been determined as growth hormone (GH) deficiency [4] and untreated gonadotropin deficiency [3].

GH deficiency is associated with a cluster of cardiovascular risk factors, including central adiposity [5], increased visceral fat [6], and dyslipidaemia [7]. An unfavourable lipid profile is important in the pathogenesis of atherosclerosis, and changes in lipids as in GH deficient patients may help to explain the increased cardiovascular risk in these patients [8].

High sensitivity C-reactive protein (hs-CRP), a serum marker of inflammation, has been considered to play an important role in chronic low grade inflammation and atherosclerotic process [9]. There has been data concerning the relationship between elevated homocysteine levels and cardiovascular risk [10].

Carotid intima–media thickness (CIMT) is an effective and non-invasive procedure for the evaluation of cardiovascular risk. Increased carotid arterial IMT has been reported in hypopituitarism patients with GH deficiency [11, 12].

Visceral fat thickness can be evaluated accurately with computerised tomography (CT) and magnetic resonance imaging (MRI) [13]. Both techniques have some limitations such as radiation exposure for CT and cost-effectiveness for MRI. Abdominal ultrasound (US) is an accurate, non-invasive and cost-effective method for VF evaluation. But it has been found that visceral fat volume measured by US has a similar accuracy compared to the CT [14]. So, ultrasonographic VF evaluation has been determined as a useful method for the assessment of cardiovascular and metabolic risk [15].

The aim of this study was to investigate the effects of GH deficiency with or without sex steroid deficiencies on ultrasonographic visceral fat (VF) and cardiovascular risk markers such as hs-CRP, CIMT, serum lipids and homocysteine in patients with hypopituitarism who are on conventional hormone replacement. To the best of our knowledge, there is limited data about VF measurement by US in patients with hypopituitarism.

Material and method

Subjects

This prospective cross-sectional study was carried out between February 2009 and March 2011. The study group consisted of 40 patients (24 females, 16 males, mean aged 48 ± 16.1 years) who were admitted to Ankara Numune Training and Research Hospital, Endocrinology and Metabolism Department. Also, 15 age- and sex-matched healthy subjects constituted our control group. The patient group had panhypopituitarism due to pituitary and/or hypothalamic disease such as pituitary surgery, empty sellae, Sheehan syndrome and were on conventional hormone replacement therapy such as glucocorticoids, thyroid hormones and gonadotropins.

Since L-Arginine was not found in Turkey, GH deficiency was diagnosed based on GH response to insulin tolerance test (ITT) (n = 20) if a patient had no contraindication such as age over 65 years, history of cardiovascular disease or epilepsy, or an IGF-1 level more than 5 percentiles below the age-specific normal range in a patient with at least two documented anterior pituitary hormone deficiencies (n = 20). After overnight fasting, ITT was performed using regular insulin (*i.v.*) at doses of 0.1 U/kg, and serum glucose and GH levels were measured before and after 30, 45, 60, 90 and 120 min. Serum glucose was measured < 2.2 mmol/L at the moment of hypoglycaemia. GH deficiency was defined as a GH peak of less than 3 ng/mL on stimulation.

Height of hypophysis equal to or less than 3 mm on MRI was accepted as empty sellae syndrome. Subjects on thyroid hormone, gonadotropins, and/or glucocorticoid replacement therapy were required to receive stable replacement doses for at least three months before entry into the study.

Exclusion criteria included history of acromegaly, active Cushing's disease, unstable coronary artery or cerebrovascular disease within one year of entry into the study, GH therapy, pregnancy, breast-feeding, surgery or radiotherapy to the pituitary gland due to acromegaly, congestive heart failure, and uncontrolled diabetes mellitus.

Height and weight were measured in light clothing wearing no shoes, and body mass index (BMI) was calculated as weight (kg)/height $(m)^2$. Waist circumference (WC) was measured at the umbilicus level in the standing position.

The underlying causes of panhypopituitarism were as follows: 20 patients (50%) with surgery for pituitary adenoma, 14 patients (35%) with empty sellae, one patient (2.5%) with compression due to pituitary tumour, two patients (5%) with no cause named as idiopathic, and three patients (7.5%) with Sheehan's syndrome. In all patients, hormone deficiencies were replaced

with levothyroxine, glucocorticoids, and desmopressin acetate. All sex hormone-deficient males were receiving testosterone. Female patients ≤ 40 years of age were currently receiving sex steroids. In order to exclude sex steroid deficiency on VF and cardiovascular risk markers, patients were divided into two groups. Patients who had sex steroid replacement were classified as Group 1, and patients who did not use sex steroids were classified as Group 2. Statistical analyses were performed between the three groups, i.e. controls, Group 1 and Group 2.

This study was approved by the ethics committee and the institutional review board of Ankara Numune Training and Research Hospital, and written informed consent was obtained from each subject.

Biochemical analyses

Serum insulin like growth factor 1 (IGF-1) levels were measured by the auto analyser method (Immulite 2000 XPI), anterior hypophyseal hormones like GH, thyroid stimulating hormone (TSH), follicular stimulating hormone (FSH), luteinising hormone (LH), prolactin, adreno corticotrophic hormone (ACTH) and the target tissue hormone (fT4, fT3, oestradiol, total testosterone, free testosterone, cortisol) concentrations were evaluated by the auto analyser method (Adriacentaur). Fasting venous blood samples were collected, promptly centrifuged, and analysed within hours. Lipid parameters i.e. total cholesterol (TC), high-density lipoprotein cholesterol (HDL-C), triglyceride (TG), low-density lipoprotein cholesterol (LDL-C), uric acid, and high-sensitive CRP were measured by the photometric method (Unicel DxC 800, Beckman Coulter auto analyser). Fasting glucose was measured with a spectrophotometric analyser (Unicel DxC 800, Beckman). Serum homocysteine was measured with chemi-luminescence immunometric assay (Immulite 1000) and fibrinogen was evaluated with the coagulametric method (SYSMEX CA 7000).

Measurement of visceral and subcutaneous fat

Ultrasonography (Toshiba Aplio Ultrasound Imaging System, Japan) was performed after overnight fasting and visceral fat was measured at the end of a normal exhalation in the supine position. For each patient, a total of four measurements was obtained, as follows: i) the distance between the internal surface of the splenic vein and the abdominal muscle; ii) thickness of the fat layer of the posterior right renal wall in the right posterior perinephric space; iii) distance between the internal surface of the abdominal muscle and the posterior wall of the aorta on the umbilicus; and iv) the thickness of preperitoneal and subcutaneous fat layers in the xiphoid process [14]. The visceral fat volume was calculated by using an equation as follows: [visceral fat volume] = –9.008+1.191 × [distance between the internal surface of the abdominal muscle and the splenic vein (mm)] + 0.987 × [distance between the internal surface of the abdominal muscle and the posterior wall of the aorta on the umbilicus (mm)] + 3.644 × [thickness of the fat layer of the posterior right renal wall (mm)] [14]. A 3.75-MHz convex-array probe was used to measure each parameter except the thickness of both the subcutaneous and the preperitoneal fat layers, which was measured using a 7.5 MHz linear-array probe by performing a longitudinal scan. The procedures were performed by the same experienced radiologist (S.S.K). The intra-examination coefficient of variation (within-subject variation from measurement to measurement) for US was 1%. To assess the reliability and reproducibility of US, five participants were selected and these measurements were repeated at the same time after one day by the same investigator. Within 95% confidence limits, intra class correlation coefficient was 97.6 for US. This assessment showed reliability and reproducibility of our measurements.

Measurement of carotid artery intima media thickness

Intima-media thickness (IMT) of the carotid arteries was measured by ultrasound in the supine position by the same experienced investigator. High resolution B-mode ultrasound images (Loqic 3, General Electric, USA) with a 11 MHz linear array transducer were applied for IMT measurement. Three arterial wall segments in each carotid artery were imaged from a fixed lateral transducer angle at the far wall. The mean IMT over the three segments of both carotid arteries was calculated and designated as mean IMT.

Statistical analyses

Normal distributions of the quantitative variables were analysed by Kolmogorov-Smirnov test. Parametric tests were applied when variables distributed normally and non-parametric tests were applied when variables did not distribute normally. Parametric test results were given as means ± standard deviations (SD). Non-parametric test results were given as means, minimum-maximum. Qualitative variables were presented as counts and proportions. For normally distributed variables, ANOVA was applied to evaluate the differences among groups and the Bonferoni test was as used for post hoc analysis. Comparison of variables which did not distribute normally was performed by using the Kruskal-Wallis test. To evaluate the correlation between the visceral fat measurements and the cardiovascular risk variables, Pearson/Spearman correlation analysis

Table I. *Baseline characteristics of GH deficient patients and controls*

Tabela I. *Ogólna charakterystyka pacjentów z niedoborem hormonu wzrostu i osób w grupie kontrolnej*

Characteristic	Patients (n = 40)	Controls (n = 15)	p
Age (year)	48 ± 16.2	39.9 ± 5.0	0.092
BMI [kg/m^2]	28.6 ± 5.1	31.5 ± 5.9	0.094
Waist circumference [cm]	97.2 ± 13.5	103.2 ± 13.3	0.121
Fasting glucose [mg/dL]	78.3 ± 8.8	80.5 ± 11.3	0.563
Total cholesterol [mg/dL]	237.3 ± 67.3	169.1 ± 23.2	< 0.001*
Triglyceride [mg/dL]	220.5 ± 185.7	107.8 ± 60.7	0.001*
HDL-cholesterol [mg/dL]	44.1 ± 13.2	42.2 ± 10.6	0.692
LDL-cholesterol [mg/dL]	149.3 ± 47.5	105.2 ± 16.9	< 0.001*
Homocysteine [μmol/L]	13.8 ± 7.0	7.7 ± 2.9	< 0.001*
Hs-CRP [mg/dL]	2.3 ± 2.9	0.2 ± 0.3	< 0.001*

Variables are expressed as means ± SD. HDL — high-density lipoprotein; LDL — low-density lipoprotein; hs-CRP — high-sensitivity C-reactive protein; *p < 0.05

Table II. *Comparison of the characteristics of GH deficient patients in Group 1 (patients with sex steroid replacement), and Group 2 (patients without sex steroid replacement), and controls*

Tabela II. *Zestawienie danych pacjentów z niedoborem hormonu wzrostu w grupie 1 (pacjenci leczeni hormonami płciowymi), grupie 2 (pacjenci nieleczeni hormonami płciowymi) i osób w grupie kontrolnej*

Characteristic	Group 1 (n = 19)	Group 2 (n = 21)	Controls (n = 15)	p
Fasting glucose [mg/dL]	77.5 ± 7.0	78.9 ± 10.4	80.5 ± 11.3	0.688
Total cholesterol [mg/dL]	222.7 ± 43.3	251.1 ± 83.0	169.1 ± 23.2	0.001*
Triglyceride [mg/dL]	170.9 ± 76.2	267.6 ± 242.2	107.8 ± 60.7	0.015*
HDL-cholesterol [mg/dL]	40.3 ± 14.8	47.7 ± 10.6	42.2 ± 10.6	0.161
LDL-cholesterol [mg/dL]	147.3 ± 35.4	151.0 ± 57.6	105.2 ± 16.9	0.004*
Homocysteine [μmol/L]	13.7 ± 4.6	13.9 ± 8.8	7.7 ± 2.9	0.009*
Hs-CRP [mg/dL]	2.4 ± 3.0	2.3 ± 3.0	0.2 ± 0.3	0.027*

Variables are expressed as means ± SD. HDL — high-density lipoprotein; LDL — low-density lipoprotein; hs-CRP — high-sensitivity C-reactive protein; *p < 0.05

was used. A p value < 0.05 was considered as statistically significant. Statistical analysis was performed using the SPSS version 18.0 software (SPSS Inc., Chicago, IL, USA).

Results

Baseline characteristics of patients and controls are summarised in Table I. Mean serum IGF-1 concentration in the patient group was 101.9 ± 90.0 ng/mL. Median disease time was 4 (range: 1–22) years. Mean disease duration was 3.7 ± 2.7 years for Group 1 and 5.9 ± 5.7 years for Group 2 (p = 0.35). Mean peak level of GH response to ITT in all patients was < 3 ng/mL, which is accepted as GH deficiency.

Baseline laboratory characteristics according to the three groups are summarised in Table II. There was no significant difference for BMI in the three groups. The glucose and HDL-C were similar in Group 1, Group 2 and controls. Mean TG, Total-C, LDL-C, homocysteine and hs-CRP levels were significantly higher in the patients than in the controls (p < 0.05). Moreover, total-C levels were significantly higher in group 2 than either the patients in group 1 or the controls. TG and LDL-C levels were similar in the two patient groups. Hs-CRP and homocsyteine levels were significantly lower in controls than the patients. However, there was no statistically significant difference in hs-CRP and homocsyteine levels between the two patient groups (Table II).

Subcutaneous fat thickness was similar in the three groups. Visceral fat thickness of three areas, VF volume, and CIMT were significantly lower in the controls that the patients (Table III). However, there was no significant difference in these parameters between Groups 1 and 2 (p > 0.05).

Table III. *Distribution of subcutaneous fat, visceral fat, and carotid artery IMT (CIMT) in Group 1, Group 2 and controls*

Tabela III. *Rozkład grubości podskórnej tkanki tłuszczowej, tkanki tłuszczowej trzewnej i grubości błony wewnętrznej i środkowej (IMT) tętnicy szyjnej (CIMT) w grupach 1 i 2 oraz grupie kontrolnej*

Variable	Group 1 (n = 19)	Group 2 (n = 21)	Controls (n = 15)	p
Subcutaneous fat thickness [mm]	31.9 ± 9.2	27.5 ± 9.5	29.3 ± 9.2	0.347
Abdominal muscle-splenic vein distance [mm]	60.7 ± 14.6	56.6 ± 12.7	42.7 ± 9.4	0.001*
Abdominal muscle-aorta distance [mm]	77.7 ± 21.6	83.1 ± 14.6	45.7 ± 16.7	0.001*
Pararenal fat thickness [mm]	17.4 ± 8.3	14.5 ± 5.0	11.7 ± 4.7	0.040*
Visceral fat volume [mm^2]	204.2 ± 63.5	192.6 ± 39.0	129.5 ± 38.2	0.001*
Carotid intima media thickness [mm]	0.8 ± 0.1	0.8 ± 0.2	0.6 ± 0.1	0.019*

Variables are expressed as means ± SD; *p < 0.05

Table IV. *Comparison of basal characteristics in hypopituitary patients according to gender*

Tabela IV. *Zestawienie badanych parametrów u pacjentów z niedoczynnością przysadki w zależności od wieku*

Characteristic	Female (n = 24)	Male (n = 16)	p
Age (year)	51.3 ± 15.9	43.1 ± 15.7	0.122
BMI [kg/m^2]	29.0 ± 4.6	28.0 ± 5.8	0.456
Waist circumference [cm]	98.9 ± 10.7	94.6 ± 17.0	0.189
Fasting glucose [mg/dL]	79.1 ± 10.0	77.0 ± 6.9	0.692
Total cholesterol [mg/dL]	343.9 ± 77.9	227.8 ± 49.3	0.539
Triglyceride [mg/dL]	250.9 ± 230.0	176.8 ± 79.3	0.648
HDL-cholesterol [mg/dL]	47.0 ± 11.9	40.1 ± 14.3	0.067
LDL-cholesterol [mg/dL]	145.5 ± 53.5	154.6 ± 36.3	0.416
Homocysteine [μmol/L]	13.6 ± 6.8	14.3 ± 7.7	0.783
Hs-CRP [mg/dL]	2.4 ± 3.1	2.3 ± 2.8	0.851

Variables are expressed as means ± SD. HDL — high-density lipoprotein; LDL — low-density lipoprotein; hs-CRP — high-sensitivity C-reactive protein; *p < 0.05

Table V. *Distribution of subcutaneous fat, visceral fat, and carotid artery IMT (CIMT) in hypopituitary patients according to gender*

Tabela V. *Rozkład grubości podskórnej tkanki tłuszczowej, tkanki tłuszczowej trzewnej i grubości błony wewnętrznej i środkowej (IMT) tętnicy szyjnej (CIMT) u pacjentów z niedoczynnością przysadki w zależności od płci*

Variable	Female (n = 24)	Male (n = 16)	p
Subcutaneous fat thickness [mm]	28.9 ± 8.9	31.0 ± 10.6	0.638
Abdominal muscle-splenic vein distance [mm]	56.0 ± 12.8	63.1 ± 14.4	0.044*
Abdominal muscle-aorta distance [mm]	79.0 ± 16.8	82.9 ± 21.4	0.555
Pararenal fat thickness [mm]	14.5 ± 6.3	18.3 ± 7.6	0.064
Visceral fat volume [mm^2]	188.2 ± 46.3	215.9 ± 58.9	0.215
Carotid intima media thickness [mm]	0.8 ± 0.2	0.7 ± 0.1	0.848

Variables are expressed as means ± SD; *p < 0.05

The patients' characteristics according to gender are summarised in Table IV. There was no significant difference between the two genders. Distribution of subcutaneous fat, visceral fat, and CIMT was also investigated in female and male hypopituitarism patients. VF thickness measured between abdominal muscle-splenic vein distance was significantly increased in males but not in females (p = 0.044) (Table V).

Correlation analyses were performed in females and males. There were significant positive correlations between CIMT and visceral fat thickness of abdominal muscle-splenic vein distance (r = 0.66,

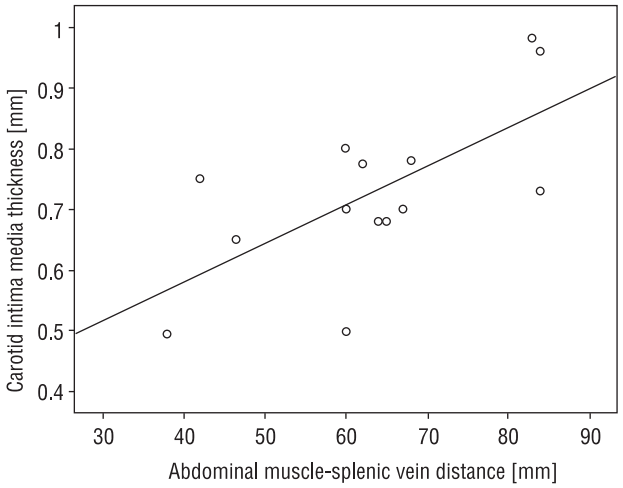

Figure 1. *Relation between carotid intima media thickness and distance between abdominal muscle and splenic vein (r = 0.66, p = 0.010)*

Rycina 1. *Zależność pomiędzy grubością blaszki wewnętrznej i środkowej tętnicy szyjnej a odległością pomiędzy mięśniami brzucha i żyłą śledzionową (r = 0,66, p = 0,010)*

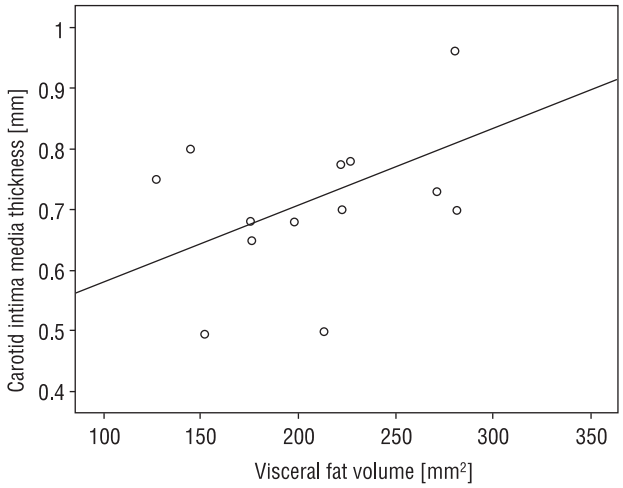

Figure 2. *Relation between carotid intima media thickness and visceral fat volume (r = 0.54, p = 0.047)*

Rycina 2. *Zależność pomiędzy grubością blaszki wewnętrznej i środkowej tętnicy szyjnej a objętością tkanki tłuszczowej trzewnej (r = 0,54, p = 0,047)*

p = 0.010) (Fig. 1) and also CIMT and visceral fat volume (r = 0.54, p = 0.047) (Fig. 2) in males. Homocysteine levels were significantly correlated with pararenal fat thickness (r = 0.79, p = 0.001) (Fig. 3) and visceral fat volume (r = 0.66, p = 0.015) in males. However, there was no significant correlation between these parameters in females.

Discussion

The present study revealed that GH deficient hypopituitary patients who are under conventional hormone replacement therapy with or without sex-steroids have significantly increased visceral fat thickness and volume evaluated by ultrasound in three different abdominal regions compared to healthy controls, despite similar body mass indexes. Furthermore, this study found that male hypopituitary patients with GH deficiency showed a significant association between VF thickness and well-known indicators of subclinical atherosclerosis such as CIMT and homocysteine.

Epidemiological studies have demonstrated that hypopituitarism is associated with an increased risk of cardiovascular events, and GH deficiency has been hypothesised to be a contributory factor [4, 16]. The mechanisms underlying the effects of GH deficiency on the cardiovascular system may include effects on inflammatory pathways. Although atherosclerosis is a multifactorial disease, inflammation plays a central role in the pathophysiology of atherosclerosis [17]. Accordingly, as an inflammatory marker, hs-CRP was found to be higher in patients with GH deficiency than healthy controls in our study. In addition, moderate

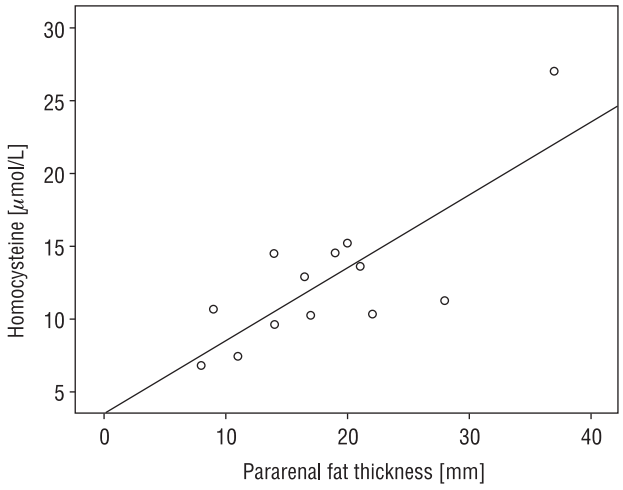

Figure 3. *Relation between homocysteine and pararenal fat thickness (r = 0.79, p = 0.001)*

Rycina 3. *Zależność pomiędzy stężeniem homocysteiny a grubością torebki tłuszczowej nerki (r = 0,79, p = 0,001)*

elevations in homocysteine levels are assumed to play a role in the risk of cardiovascular events [10]. As expected, we found elevated homocysteine levels in the patients with GH deficiency.

Fat distribution is important in the assessment of cardiovascular and metabolic risk. The mechanism of increased metabolic risk is assumed to be related to adipose tissue in the visceral region which is metabolically active [18–20]. Anthropometric measurements, such as weight or BMI, are not sufficient to evaluate visceral adiposity. It is known that WC is a traditional method used to measure metabolic risk [21]. WC is an important

risk factor for cardiovascular diseases regardless of the increased weight [22]. WC measurement is a practical, non-invasive, simple, and widely used method but it has a limitation. It evaluates not only visceral fat but also subcutaneous fat. So in order to detect visceral obesity, it is better to perform abdominal images such as CT, MRI, dual energy X-ray absorptiometry (DEXA) or US. Of these methods, CT is the most useful [23, 24]. However, both CT and MRI have some limitations such as high ionising radiation for the first method and less cost-effectiveness for the second. The DEXA method is also able to assess regional fat mass in conditions of minimal exposure to radiation [25]. Therefore, alternative, simple, non-invasive methods of assessing visceral fat accumulation are needed. Ultrasonography is a reliable and simple way for evaluating visceral and subcutaneous fat [14, 26–28]. Hirooka et al. demonstrated a technique for the measurement of visceral fat volume by ultrasonography and compared this with the volume measured by CT [14]. The same authors suggested that the measurement of VF volume using US could be as effective as using CT. We used the same technique in patients with hypopituitarism in order to evaluate VF thickness and volume. It is obvious that growth hormone and oestrogen deficiencies are associated with increased visceral fat in hypopituitarism patients. There have been a few studies concerning VF evaluation in hypopituitarism patients with GH deficiency [29–31]. VF was evaluated by CT in most of the previous studies about GH deficiency. We used ultrasonography for evaluating VF as a non-invasive and accurate method in hypopituitarism. In the present study, VF thickness and volume were found to be increased in three different abdominal regions in patients with GH deficiency and hypopituitarism compared to healthy controls.

Homocysteine and CIMT are well-known markers of subclinical inflammation and atherogenesis. CIMT measured by high resolution B-mode ultrasonography is a non-invasive marker of subclinical atherosclerosis that has been used widely in vascular health assessment both in adults and children [32–34]. It has been suggested that assessment of abdominal visceral fat by US predicts the presence and severity of coronary artery disease in clinical practice [15, 35, 36]. Kim et al. investigated VF thickness measured by US in diabetic patients (240 men and 106 women) and found correlations between VF and HDL-C , hs-CRP concentrations and the intima-media thickness at the common carotid artery [15]. They emphasised that VF thickness might be a reliable index for assessing the amount of visceral fat and for identifying diabetic patients, particularly men, who are at high risk of cardiovascular disease. In the present study, a positive significant correlation between VF thickness, CIMT and homocysteine levels was found in the male patients with GH deficiency.

This study had several limitations. The number of our study patients was not large, since hypopituitarism patients with GH deficiency constitute a small proportion of the general population. Although VF thickness in men reasonably reflected atherosclerotic risk, it did not do so in women. This can be explained by the genetics of males in the Turkish population. Age, gender, genetics, and ethnicity are broad etiological factors contributing to variations in visceral adipose tissue accumulation and also cardiovascular risk. As a result, additional work is needed to validate using ultrasonographic VF thickness with larger groups of subjects in both sexes.

Conclusions

VF evaluation is important in GH deficient patients for the evaluation of atherosclerosis. GH deficient hypopituitary patients, with or without sex steroid deficiencies, have increased visceral fat volume compared to healthy controls. Additionally, the results confirm the usefulness of ultrasonographic VF volume assessment in GH deficient patients. Finally, these results indicate that excessive visceral fat accumulation affects the growth of subclinical atherosclerosis in GH deficient men.

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