



Ultrasound measurement of visceral fat in patients with primary biliary cirrhosis

Ultrasonografsko merenje visceralne masti kod bolesnika sa primarnom bilijarnom cirozom

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Abstract

Background/Aim. Primary biliary cirrhosis (PBC) is a progressive, chronic liver disease with elevated serum lipids, but it is unclear whether hyperlipidemia in PBC patients is associated with atherosclerosis. Metabolic syndrome promotes development of atherosclerotic cardiovascular disease related to abdominal type obesity and insulin resistance. The aim of our study was to assess abdominal adiposity in patients with PBC. **Methods.** The study included 40 patients with PBC and 50 healthy controls. Age, sex and anthropometric measurements (weight, height, body mass index and waist circumference) were registered for all patients and controls. We used ultrasonography to measure subcutaneous (SF) and visceral fat (VF) diameter, subcutaneous area (SA) and visceral area (VA), as well as perirenal fat diameter (PF). **Results.** Values of SF, VF and PF thicknesses in PBC patients were 19.23 ± 5.85 mm, 10.92 ± 3.63 mm, and 7.03 ± 1.82 mm, respectively. In controls these measurements were 22.73 ± 6.70 mm, 16.84 ± 5.51 mm and 10.50 ± 2.70 mm respectively. In PBC patients SA and VA were calculated to 983.64 ± 322.68 mm² and 403.64 ± 166.97 mm² and in controls 1124.89 ± 366.01 mm² and 720.57 ± 272.50 mm² respectively. Significant difference was found for VF, VA and RF values. **Conclusions.** Considering that the amount of visceral fat plays an important role in development of metabolic syndrome and cardiovascular diseases, we concluded that the lower amount of visceral fat in PBC patients could be related to lower incidence of cardiovascular events, despite hyperlipidemia.

Key words:

liver cirrhosis, biliary; subcutaneous fat, abdominal; obesity; cardiovascular diseases; risk factors; ultrasonography.

Apstrakt

Uvod/Cilj. Primarna bilijarna ciroza (PBC) je progresivno hronično oboljenje jetre sa elevacijom lipida, ali nije sa sigurnošću potvrđeno da je ova hiperlipidemija udružena sa aterosklerozom. Metabološki sindrom dovodi do razvoja ateroskleroze i kardiovaskularnih oboljenja preko abdominalne gojaznosti i insulinske rezistencije. Cilj ovog istraživanja bio je da se proceni abdominalna gojaznost kod bolesnika sa PBC. **Metode.** Studija je obuhvatala 40 bolesnika sa PBC i 50 kontrolnih zdravih osoba. Analizirali smo uzrast, pol i antropometrijska merenja koja su uključivala telesnu masu, telesnu visinu, *body mass index* (BMI) i obim struka. Ultrasonografski, mereni su supkutana i visceralna mast i to njihova širina (SF – *subcutaneous fat*, VF – *visceral fat*) i površina (SA – *subcutaneous fat area*, VA – *visceral fat area*). Takođe, određivan je promer perirenalne masti (PF – *perirenal fat*). **Rezultati.** Vrednosti SF, VF i PF promera u ispitivanoj grupi sa PBC iznosile su $19,23 \pm 5,85$ mm, $10,92 \pm 3,63$ mm i $7,03 \pm 1,82$ mm redom. U kontrolnoj grupi ove vrednosti iznosile su $22,73 \pm 6,70$ mm, $16,84 \pm 5,51$ mm i $10,50 \pm 2,70$ mm redom. Izmerene vrednosti SA i VA bile su $983,64 \pm 322,68$ mm² i $403,64 \pm 166,97$ mm² kod bolesnika sa PBC, dok su u kontrolnoj grupi te vrednosti iznosile $1124,89 \pm 366,01$ mm² i $720,57 \pm 272,50$ mm² redom. Statistički značajna razlika u vrednostima utvrđena je za VF, VA i RF. **Zaključak.** Kako količina visceralne masti ima značajnu ulogu u razvoju metaboličkog sindroma i kardiovaskularnih oboljenja, zaključili smo da je manja količina visceralne masti kod bolesnika sa PBC moguć razlog za manju učestalost kardiovaskularnih oboljenja u ovoj populaciji i pored hiperlipidemije.

Ključne reči:

jetra, bilijarna ciroza; masno tkivo, potkožno, merenje; gojaznost; kardiovaskularne bolesti; faktori rizika; ultrasonografija.

Introduction

Primary biliary cirrhosis (PBC) is a progressive, chronic liver disease ultimately leading to hepatic failure and death if not treated by hepatic transplantation¹. Serum lipids are often markedly elevated in PBC², but it is not clear if this hyperlipidemia is associated with accelerated atherosclerosis.

The risk of cardiovascular disease in PBC has been investigated in a few studies^{2,3} but an increase in related mortality was not demonstrated. There are few reports on the use of lipid lowering agents in PBC suggesting that lipid treatment could reduce LDL cholesterol and triglycerides leading to improved serum measures of hepatic function⁴.

Metabolic syndrome (MS), that has received increased attention in the past few years, consists of multiple, interrelated risk factors of metabolic origin that appear to directly promote the development of atherosclerotic cardiovascular disease (ASCVD). Most important of these underlying risk factors are abdominal obesity and insulin resistance. Other associated conditions include physical inactivity, aging, hormonal imbalance, and genetic or ethnic predisposition⁵.

The measurement of abdominal obesity through waist circumference (WC) has been established as a simple, inexpensive and useful method for the diagnosis of abdominal obesity. Thus, WC has been proposed as a key element for the diagnosis of MS and its use suggested as a part of the routine general physical examination in clinical practice⁶. Moreover, WC correlates with visceral obesity, and in clinical studies, it has been associated with increased cardiovascular risk⁷. Ultrasonography (US) is a simple and reliable method for measuring both subcutaneous and visceral fat showing a strong correlation with both adiposities measured with computed tomography scan⁸.

The aim of this study was to determine the amount of abdominal adipose tissue in PBC patients by anthropometry and ultrasonography measurements and to correlate these values with healthy control subject.

Methods

Study included 40 patients with PBC (4 males and 36 females), who underwent medical examination. The diagnosis was based on clinical features, laboratory tests, imaging diagnostics, and, whenever possible, on liver histology. All subjects gave written informed consent for participation in the study.

Anthropometric measurements included age, sex, weight, height, body mass index (BMI), and WC. Weight was measured to the nearest 0.1 kg with a calibrated physician's office scale, and the height to the nearest 1 mm with a wall-mounted height meter. Waist circumference was measured with a heavy-duty inelastic plastic fibre tape measure placed directly on the skin while the subject stood balanced on both feet, with the feet touching each other and both arms hanging freely. The measurement was taken immediately above the iliac crest and at the end expiration⁹. Sonography measurements were performed as described by Meriño-

Ibarra et al.¹⁰ using a linear-array probe (Toshiba Core Vision, Tokyo, Japan, 8 MHz PLF-805ST) in the supine position. It was kept perpendicular to the skin on the upper median abdomen, and longitudinal scan was done in the mid-point between the xyphoid and the navel along the alba line with regard to the surface of the liver, to be almost parallel to the skin. Subcutaneous fat thickness (SF) and area (SA) were measured on the xyphoumbilical line in both longitudinal and transverse views. Measurements were taken 3 times directly from the screen using electronic callipers at the inner edge of the skin and at the outer edge of the alba line and the fat muscle interfaces for area. Preperitoneal fat thickness or visceral fat thickness (VF) and area (VA) were measured in the same sites and views (Figures 1 and 2).



Fig. 1 – Subcutaneous and visceral fat thickness measurement



Fig. 2 – Subcutaneous and visceral fat area measurement

In this case, measurements were taken at the inner edge of the alba line and at the peritoneal line for thickness and area. Then mean values were calculated. All the subjects were asked to hold their breath during the examination. Special care was taken to keep the probe just touching the skin to prevent compression of the fat layers. A 3.75 MHz convex probe (PVF-375MT) was used to perform measurement of perirenal fat layer of the posterior right renal wall in the right posterior perinephric space¹¹. All measurements were performed by a single physician.

Collected data were compared to 50 healthy subjects matched by sex and age.

Statistical analysis was performed using the SPSS software package (version 11.0). Mean values, SD, and ranges of the anthropometric and sonographic measurements were calculated. The Student's *t*-test was applied to assess the association of sonographic measures and the rest of studied variables. A *p*-value less than 0.05 was regarded as significant.

Results

We have studied 40 patients known to have PBC (36 females, and 4 males) whose mean age was 55.65 ± 10.88 years. In the control group we studied 50 patients (46 females, and 4 males); mean age of the controls was 48.68 ± 7.87 years. Pearson's χ^2 test failed to prove a significant difference in subject's gender between the studied group and the controls ($\chi^2 = 0.055, p > 0.05$). No significant difference regarding sex was found, i.e. the *t*-test failed to prove a significant differences between studied subjects and the controls (*t* = 2.492, *p* > 0.05).

Anthropometric and US measurements are shown in Table 1. Student's *t*-test did not reveal a significant differ-

Discussion

Primary biliary cirrhosis produces a marked increase in total cholesterol levels, primarily due to increased Lp-X¹². Despite a marked hypercholesterolemia, excess mortality from cardiovascular diseases was not found in our PBC population¹³. This finding is in the agreement with other studies. It has made some investigators to conclude that PBC patients might even be protected from cardiovascular diseases^{2, 14, 15}. Close patient follow-up in the same center, with immediate recording of any clinically relevant event, allowed us to reliably estimate for the first time the incidence of non-fatal cardiovascular events in PBC. The present data suggests that despite of high prevalence of hypercholesterolemia, patients with PBC are not exposed to a higher risk of cardiovascular events than the general population. Attentive PBC patient follow-up could explain differences in detection rates of clinical events between PBC patients and general population and account for slightly higher incidence of coronary events that appear to be of borderline significance in PBC¹³.

It is shown that mesenteric fat thickness is an independent determinant of metabolic syndrome in apparently healthy Chinese subjects, with an odds ratio of 1.35 for every 1 mm

Table 1
Anthropometric and ultrasound measurements of patients with primary biliary cirrhosis (PBC) and controls

Parameters	$\bar{x} \pm SD$		<i>t</i>	<i>p</i>
	The patients with PBC (n = 40)	The control subject (n = 50)		
Body mass index (kg/m ²)	25.386 ± 2.753	26.540 ± 3.543	-1.195	0.239
Waist circumference (mm)	90.08 ± 9.08	90.76 ± 12.74	-0.203	0.840
Perirenal fat (mm)	7.03 ± 1.82	10.4960 ± 2.7053	-4.902	0.000
Subcutaneous fat (mm)	19.23 ± 5.85	22.73 ± 6.70	-1.841	0.072
Subcutaneous fat (mm ²)	983.64 ± 322.68	1124.89 ± 366.01	-1.355	0.183
Visceral fat (mm)	10.92 ± 3.63	16.84 ± 5.51	-4.137	0.000
Visceral fat (mm ²)	403.64 ± 166.97	720.57 ± 272.50	-4.556	0.000

ence in BMI, nor in diameter and subcutaneous fat area, i.e. a highly significant difference was found in correlation of perirenal fat thickens and parameters for visceral fat (diameter and visceral fat area) (Figures 3 and 4).

increase, at least within the observed range of mesenteric fat thickness. The discriminating cut-off point of 10 mm indicates the presence of metabolic syndrome and identifies subjects with increased intima-media thickness. Hypotheses

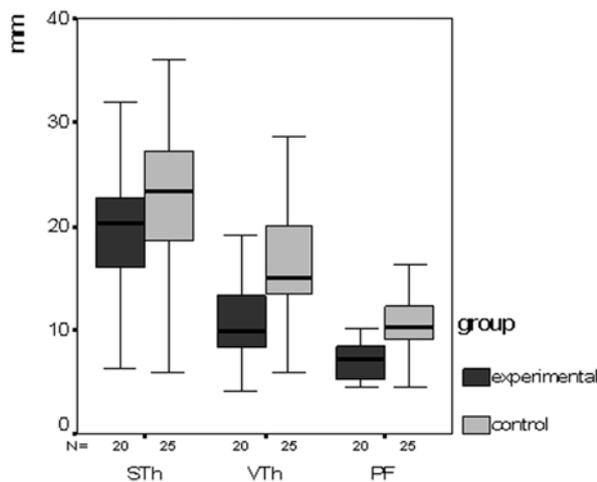


Fig. 3 – Difference in diameter of subcutaneous, visceral and perirenal fat thickness (Sth – subcutaneous fat, VTh – visceral fat, PR – perirenal fat)

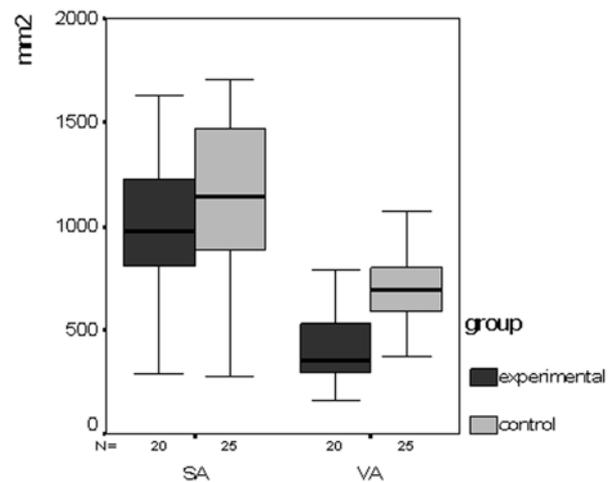


Fig. 4 – Difference between subcutaneous and visceral fat area (SA – subcutaneous fat area, VA – visceral fat area)

relating central adiposity to the metabolic syndrome focus on the newly emerging evidence that adipose tissue (particularly visceral adipose tissue) is a source of various factors, including free fatty acids, and tumor necrosis factor- α (TNF- α) that impair insulin action in skeletal muscle. In addition, adiponectin (adipose specific collagen-like molecule), has been found to have antidiabetic, antiatherosclerotic and antiinflammatory functions¹⁶. Excessive adipose tissue is associated with a decreased production of adiponectin which may impair insulin sensitivity¹⁷. Measurement of mesenteric fat thickness may potentially be developed into an alternative tool to identify subjects at risk for cardiovascular diseases¹⁸.

Several imaging methods have been proposed for estimation of visceral adipose tissue. Recent advances in imaging techniques and an understanding of differences in molecular biology of different adipose tissue depots have been reported. Computed tomography (CT) and especially Magnetic Resonance Imaging (MRI), the gold standard technique, provide methods to non-invasively estimate visceral adipose tissue safely and accurately¹⁹⁻²¹. Unfortunately, both MRI and CT are high-cost technologies, and CT requires radiation exposure. In addition, a great variability in the precise definition of adipose tissue compartments by CT and MRI measure-

ments is found in clinical studies²². The measurement of visceral fat volume using US could be as effective as CT. This method should be used in clinical settings due to its low cost, no side effects and technical suitability^{23,24}.

Analysing the data gathered by US, as non-invasive, inexpensive, and non-ionization method, we found that despite the lack of significant differences of BMI, PBC patients have smaller amount of perirenal and visceral fat, as well as visceral fat area compared to controls. Other measurements of fat tissues (diameter and surface of subcutaneous fat) in the PBC patients are lower compared to the control subjects, but the observed difference was not significant.

Conclusion

Using ultrasonography as a reliable method for measurement visceral fat amount and taking into account importance of visceral fat in development of metabolic syndrome and cardiovascular diseases, we conclude that patients with primary biliary cirrhosis have lower amount of visceral fat, and probably due this phenomenon a lower incidence of cardiovascular diseases, despite a marked hypocholesterolemia.

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