Japanese Journal of Gastroenterology and Hepatology

Research Article

ISSN: 2435-1210 | Volume 9

Ultrasonography to Measure Abdominal Fat – A Future Marker of Cardiovascular Risk?

Cursino-Andrade K*, dos Santos PNS, Bahamondes L, and Fernandes A

Department of Obstetrics and Gynecology, Faculty of Medical Sciences, University of Campinas (UNICAMP), Brazil

***Corresponding author:**

Kleber Cursino-Andrade,
Department of Obstetrics and Gynecology, Faculty of Medical Sciences, University of Campinas (UNICAMP), Rua Maria José Ferreira 432, Barão Geraldo, Campinas, SP, 13085-085, Brazil, Tel: +55-19-3289-4884;
E-mail: ciencia@volutamedical.com.br

Received: 01 Jan 2023
Accepted: 13 Feb 2023
Published: 20 Feb 2023
J Short Name: JJGH

Citation:

Cursino-Andrade K. Ultrasonography to Measure Abdominal Fat – A Future Marker of Cardiovascular Risk?. J Gastro Hepato. 2023; V9(16): 1-7

Keywords:

Body composition; Abdominal fat; Diagnostic imaging; Female; Ultrasound

Abbreviations:

CV: Cardiovascular Disease; VF: Visceral Abdominal Fat; BC: Body Composition; DXA: Dual-Energy X-Ray Absorptiometry; ScF: Abdominal Wall Subcutaneous Fat Tissue; VF: Visceral Fat Tissue; PPF: Preperitoneal Fat in the Epigastric Regions; LLL: Caudate Liver Lobe; HEC: Hyperinsulinemic Euglycemic Clamp; PPF: Preperitoneal Fat; WC: Waist Circumference

A Summary Statement

Ultrasonography for measurement of abdominal fat: our results suggest being a promising technique for cardiovascular risk assessment, it may show early warning signs for this very prevalent disease. Ultrasound evaluation of abdominal fat in non-obese women showed a strong correlation between body composition and anthropometric measures related to cardiovascular diseases.

Key Points

• Abdominal wall subcutaneous fat tissue measurement was significantly correlated with BMI (r= 0.85), total mass (r= 0.78), fat mass percentage (r= 0.82), total fat tissue (r= 0.87), waist circumference (r= 0.84) and hip circumference (r= 0.75) at the beginning of the study and after 12 months.

• Abdominal wall subcutaneous fat tissue measurement had a significant correlation with total cholesterol concentrations at baseline and at 12 months (r= 0.51 and r= 0.54, respectively), LDL cholesterol (r= 0.42 and r= 0.53, respectively) and Apo B-100 (r=0.44).

• preperitoneal fat had a positive correlation with CRP in both time periods (r=0.44 and r=0.41), while VF had a positive correlation with LDL-chol at baseline (r=0.34).

1. Abstract

1.1. Objectives: To evaluate ultrasound measurements of abdominal fat and correlation with body composition and Cardiovascular (CV) disease markers.

1.2. Methods: A pilot study with 37 females aged 18-40 years, body mass index <30 (BMI; kg/m2) and no history of illness or use of medication. All patients were assessed for insulin resistance using the Hyperinsulinemic Euglycemic Clamp (HEC) at baseline and at 12 months. Ultrasound measurements of abdominal fat, anthropometry, Body Composition (BC) obtained by densitometry (DXA) and serum parameters related to CV health were made by the same observer during two time periods, at baseline and after 12 months. Measurements of liver volume, abdominal wall Subcutaneous Fat tissue (ScF), Preperitoneal Fat (PPF) and Visceral Fat tissue (VF) were taken. Lipid and liver profile, apolipoprotein levels and biomarkers of CV health were analyzed. Spearman coefficient was used for correlation analysis. The significance level was set at 5%.

1.3. Results: A slight elevation of the mean weight, BMI and ultrasound measurements was observed at12 months. In both time periods, there was a significant correlation between ScF and total serum cholesterol levels (r=0.54), LDL-chol (r=0.53) and Apo B-100 (r=0.44), BMI (r=0.85), waist circumference (WC; r=0.84) and hip circumference (r=0.75), total mass (r=0.78), fat mass percentage and total fat mass (r=0.82and r=0.87, respectively). PPF measurements showed a significant correlation with CRP in both time periods (r=0.44) and WC (r=0.51), while VF correlated with the waist/hip ratio (r=0.60).

1.4. Conclusions: Ultrasound measurement of abdominal fat

showed a good correlation with anthropometric and BC measurements, and CV markers in this non-obese female sample. It is a promising technique that should be tested in the largest number of individuals in other populations to determine the cutoff parameter as a potential early marker of CV risk.

2. Introduction

Social, demographic and behavioral changes have directly influenced health, in addition to the causes of morbidity and mortality in individuals [1]. Transmissible and Cardiovascular (CV) diseases have been the major global causes of death [2, 3]. One-third of the female mortality rates have been attributed to CVD and the number of deaths in the age groups younger than 55 years have not shown a decrease, despite all existing US protocols for the prevention and treatment of CV diseases [4-6] .

The majority of CV events occur during people's normal routine, often outside a hospital or healthcare unit. Therefore, it becomes clear that primary prevention should be top priority. Changes in feeding habits [7], physical activity [8], postmenopausal hormone therapy [9] and preventive surgeries for the obese [6, 10] have been described as factors that may reduce morbidity and mortality from CV diseases. On the other hand, the proposal for more effective preventive measures focused on predisposed individuals, requires screening methods for CV disease risk factors.

The probable cause of the increasing prevalence of CVD is the number of people with excessive weight in fat, particularly those with Visceral abdominal Fat (VF) [11-13]. VF is a known risk factor for CVD, metabolic diseases and some types of tumors [14-19]. It has been described that dysfunctional and hypertrophic adipocytes located in VF precede the predisposing inflammatory processes of CVD and thromboembolism [20].

Although abdominal fat is estimated by anthropometric and Body Composition (BC) measurements using total body Densitometry (DXA), Computed Tomography (CT) scan has been the gold standard of VF assessment. CT is an expensive technique that emits some level of radiation [21]. Regional fat compartments were measured with the aid of new software (iDXA) for BC assessment. A study of females and males aged 18-70 years compared abdominal fat compartments by iDXA and ultrasound measurements. It was concluded that ultrasound is reliable for visceral fat estimation [22].

Ultrasonography (US) is a widely available and safe exam, with a high reproducibility. The aim of this study was to assess fat measurements by ultrasound and its correlation with anthropometry, BC data and laboratory parameters related to CV health in young non-obese females, without a known history of illness.

3. Methods

A pilot study that used secondary data from a study conducted from February 2011 to February 2013 in the Ultrasonography Unit of the Department of Obstetrics and Gynecology, State University of Campinas (UNICAMP) School of Medicine, Campinas, Brazil. The project was approved by the Ethics Committee. All female participants signed a consent term prior to the beginning of the study.

Thirty-seven female participants received follow-up during 12 months for the assessment of insulin resistance. The study project was registered in ClinicalTrials.gov, under number NCT01527526. All had undergone the Hyperinsulinemic Euglycemic Clamp at baseline and at12 months. The M-value was calculated which corresponded to glucose consumption at steady-state. M values<4mg/kg/min were defined as diagnostic for insulin resistance.

Inclusion criteria were age, ranging from 18-40 years; Body Mass Index <30 (BMI, kg/m2); fasting blood glucose <100 mg/dL and OGTT (75 g oral glucose) at 120 minutes <140 mg/dL. Exclusion criteria were breastfeeding; first-degree family history of Diabetes Mellitus (DM); history of DM 1 or 2; Systemic Arterial Hypertension (SAH); hyperthyroidism or hypothyroidism; chronic kidney failure; and any organ transplantation; use of corticosteroids, antipsychotics, thiazidics or statins; females with hirsutism and/or hyperandrogenism, Polycystic Ovarian Syndrome (PCOS) and a previous history of bariatric surgery or omentectomy.

The variables evaluated were anthropometry (weight, body mass index (BMI; kg/m2), waist/hip circumference and waist/hip ratio], Body Composition (BC) assessed by the Dual-energy X-ray Absorptiometry (DXA) technique using the Lunar DPX bone densitometer device (GE Healthcare Lunar Corporation, WI, USA). All measurements were taken at baseline and at 12 months. Anthropometric measurements were always made by the same observer; for BC the inter-observer coefficient of variation for fat mass measurement was 0.7%

Blood samples following a 12-hour fast were collected at baseline and at 12 months. Total cholesterol, HDL-chol and triglycerides were measured by the colorimetric method (CHOD-PAP and GPO-PAP; Roche Diagnostics, Mannheim, Germany). LDL-chol concentration was calculated by the Friedewald equation [LDL cholesterol mg/dL = total cholesterol – HDL cholesterol – (triglycerides/5)]. Leptin and adiponectin measurements were performed by commercial immunoassay kits (Human Leptin "Dual Range and Human Adiponectin ELISA; Merck Millipore, Darmstadt, Germany), apolipoprotein measurements were performed by turbidimetry using PowerWave XS (BioTek, Winooski, USA) and Tina-quant APO A-I and Tina-quant APO B reagents (Roche, Indianapolis, USA). Free fatty acids were measured using the WAKO enzymatic colorimetric kit (Dusseldorf, Germany); interleukin-6 and TNF-alpha (Human IL-6 Quantikine E and TNF-alpha Quantikine HS; R&D Systems, Minneapolis, USA), and RCP was evaluated by the Nephelometry method, using the BN ProSpec System (Dade Behring, Liederbach, Germany) and Siemens CardioPhase hs CRP kit (Erlangen, Germany). Liver enzymes Alanine Aminotransferase (ALT), Aspartate Aminotransferase (AST) and Gamma-Glutamyl Transferase (GGT) were measured by automated assays (COBAS- Roche, USA).

3.1. Procedures for Ultrasound Fat Assessment

Participants were in the supine position and all measurements were taken in triplicate from frozen screen images. Cards were used for image occlusion. After the end of the exam, measurements were retrieved from the file and the arithmetic mean was calculated. All measurements were performed by the same observer and the average coefficient of interobserver variation was always lower than 5%.

A Toshiba Xario machine and multifrequency probes were used. Convex probes ranged from 3.0 to 6.0 MHz and linear probes ranged from 6.6 to 9.0 MHz. A convex probe was used to measure the liver, and visceral fat when the use of a linear probe was not feasible and to compare echogenicity of the liver with kidney/spleen echogenicity. A linear probe was used to measure abdominal wall fat above the umbilicus (ScF), Visceral Fat in the mesogastric (VF) and preperitoneal fat in the epigastric regions (PPF).

ScF was measured in centimeters (cm) in the region immediately above the umbilical scar, in the xiphoid umbilical line. Its measurement was considered from the skin to the linea alba, in the region between the rectus abdominus muscles, during expiration [15, 23] (Figure 1). PPF and VF were measured in two regions of the xiphoid umbilical line. VF was measured in the region immediately above the umbilical scar and was considered the extension in cm from the linea alba to the anterior wall of the aorta, during diastole and at the end of expiration. PPF was measured in the epigastric region, from the linea alba to the surface of the left liver lobe, at the end of expiration. Measurements were determined from frozen amplified images that occupied 2/3 of the screen (Figures 2 and 3).

Measurement of the Right Liver Lobe (RLL) was calculated by the mean of three longitudinal distances, from the lower border of the right liver lobe to the upper border proximal to the diaphragm, in the right hemi clavicular line. Measurement of the caudate Liver Lobe (LLL) was obtained by the anteroposterior distance placing the transducer in the right paramedian epigastric region [24]. To evaluate liver echotexture, the cortical regions of the kidneys or spleen were used for comparison [25, 26].

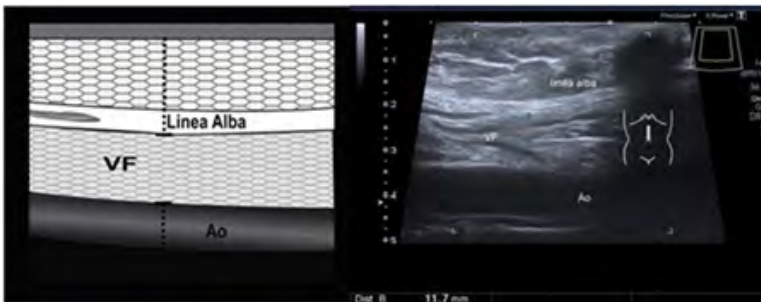

Figure 1: measurement of subcutaneous fat (ScF) obtained with a multifrequency linear probe in the midline, 1.5 cm above the umbilicus. Amplified screen image, with placement of the calipers between the skin and the linea alba.

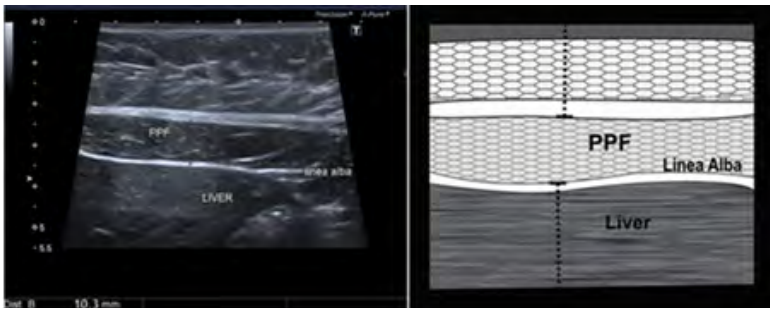

Figure 2: measurement of visceral fat in the mesogastric region (VF) obtained with a multifrequency linear probe or sector transducer in the midline, near and above the umbilicus, placing the calipers between the linea alba and the anterior wall of the abdominal aorta.

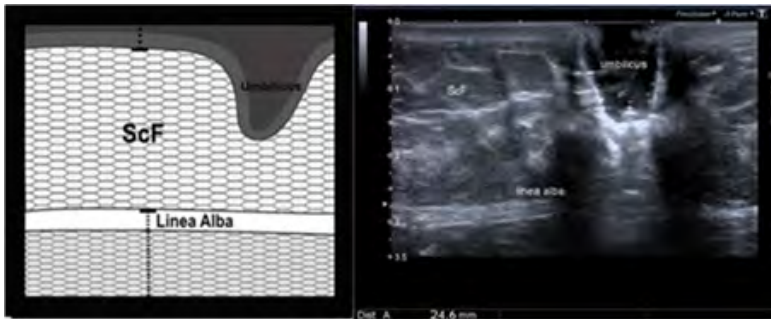

Figure 3: measurement of preperitoneal fat in the epigastrium (PPF) obtained with a multifrequency linear probe in the midline, placing the calipers between the linea alba and the anterior surface of the left lobe of the liver

3.2. Statistical Analysis

The mean, standard deviation and median of all measurements and Spearman's correlation coefficient were used to correlate ultrasound measurements with anthropometric/body composition measurements and laboratory test results. Measurements taken at baseline and at 12 months in the same female sample were analyzed. The significance level of 5% was adopted.

4. Results

The mean age of the female patients was 28.8 (±5.7) years, a little more than half of these females were self-reported as non-white (59.4%) and had >8 years of school education (54.0%) (data not shown). Mean weight, BMI and abdominal measurements increased slightly at 12 months and there was no variation in the mean M-value measured by HEC (Table 1).

Table 2 shows the statistically significant correlations between variables measured by ultrasonography and body composition/anthropometric measurements. ScF measurement was significantly correlated with body weight (r= 0.78), BMI (r= 0.85), total mass (r= 0.78), fat mass percentage (r= 0.82), total fat tissue (r= 0.87), waist circumference (r= 0.84) and hip circumference (r= 0.75) at the beginning of the study. After 12 months, the same correlations remained significant. BMI and waist measurements had the highest values, emerging a correlation with a new variable--the waist/hip ratio (r= 0.66) (Table 2).

VF measurement had a significant correlation with waist/hip ratio in both time periods (r= 0.60 and r= 0.50 at baseline and at 12 months, respectively) (Table 2). PPF measurements had a significant correlation with anthropometric and body composition variables at baseline. In both time periods, correlation was only mantained for waist circumference (r= 0.51 and r= 0.34 at baseline and at 12 months, respectively) (Table 2).

Concerning serum markers, the ScF measurement had a significant correlation with total cholesterol concentrations at baseline and at 12 months (r= 0.51 and r= 0.54, respectively), LDL cholesterol (r= 0.42 and r= 0.53, respectively) and Apo B-100 (r=0.44) (Table 3). PPF had a positive correlation with CRP in both time periods (r=0.44 and r=0.41), while VF had a positive correlation with LDL-chol at baseline (r=0.34). Measurements of LLL showed a negative correlation with HDL-chol (r= -0.37) and free fatty acids (r= -0.39) only at baseline. Measurements of LHD and echotexture had no correlation with the variables studied (data not shown).

Table 1: Mean and standard deviation of some sample variables at baseline and at 12 months

Variables	Baseline	12 months
Weight *Kg, mean (SD)*	61.8 (8.4)	63.0 (8.4)
BMI *kg/m², mean (SD)*	24.2 (3.2)	24.7 (3.1)
ScFl *cm, mean (SD)*	24.3 (10.3) *	26.3 (9.7)
PPF *cm, mean (SD)*	12.6 (4.1) *	14.5 (8.6)
VF *cm, mean (SD)*	32.2 (10.8) *	34.0 (11.5)
M-value *mg/kg/m², mean (SD)*	5.6 (1.5)	5.5 (1.7)

SD: Standard deviation. *Missing = 1 (abdominal fat measurements calculated at baseline with 36 females). BMI: body mass index; ScF: subcutaneous abdominal fat; PPF: preperitoneal epigastric fat; VF: visceral mesogastric fat. M-value: measured by Hyperinsulinemic Euglycemic Clamp (M<4= insulin resistance).

Table 2: Significant correlations between ultrasound measurements and DXA anthropometric and body composition measurements, at baseline and after 12 months

Variables	Baseline				12 Months			
	ScF*	PPF*	VF*	LLL*	ScF	PPF	VF	LLL
Weight	0.7807	0.4672			0.6499			
p value	<.0001	0.004			<.0001			
BMI	0.8517	0.4599			0.747		0.3937	
p value	<.0001	0.004			<.0001		0.0159	
Total mass	0.7899	0.4271			0.6284			
p value	<.0001	0.009			<.0001			
% Fat mass	0.8244	0.4263			0.6334			
p value	<.0001	0.009			<.0001			
Total fat tissue	0.8723	0.4977			0.6794			
p value	<.0001	0.002			<.0001			
Waist circunference	0.8455	0.5184			0.7931	0.3473	0.444	
p value	<.0001	0.001			<.0001	0.035	0.005	
Hip circunference	0.752	0.4274			0.5306			
p value	<.0001	0.009			0.0007			
Waist/hip ratio			0.6066	0.3465	0.6654		0.5083	
p value			<.0001	0.0384	<.0001		0.0013	

Spearman's correlation coefficient. BMI: Body Mass Index. ScF: Subcutaneous abdominal fat. PPF: Preperitoneal epigastric fat. VF: visceral mesogastric fat. LLL: Left liver lobe. *Missing = 1 (abdominal fat measurements of 36 females calculated at baseline).

Table 3: Significant correlations between ultrasound measurements and serum markers at baseline and at 12 months

Variables	ScF*	PPF*	VF*	LLL*	ScF	PPF	VF	LLL
Total Cholesterol	0.513	-	-	-	0.5423	-	-	-
p value	0.001				0			
HDL-chol	-	-	-	-0.378	-	-	-	-
p value				0.002				
LDL-chol	0.4222	-	0.3449		0.532	-	-	-
p value	0.001		0.003		0			
Triglycerides	0.3595	-	-	-	-	-	0.3632	-
p value	0.003						0.027	
ALT	-	-	-	-	-	-	0.3824	-
p value							0.019	
Gama GT	-	-	-	0.3753	-	0.4016	0.4408	-
p value				0.024		0.013	0.006	
CRP	0.4951	0.4427	-	-	-	0.4122	-	-
p value	0.002	0.006				0.011		
APO-A	-	-	-	-	-	0.3681	-	-
p value						0.025		
APO-B	0.4479	-	-	-	0.4446	-	-	-
p value	0.006				0.005			
Interleukin-6	-	-	-	-	-	-	-	-
p value								
Free fatty acids	-	-	-	-0.3947	-	-	-	-
p value				0.018				

Spearman's coefficient correlation. BMI: Body Mass Index. ScF: Subcutaneous Abdominal Fat. PPF: Visceral Epigastric Fat.VF: Visceral Mesogastric Fat. LLL: Left Liver Lobe. *Measurements of 36 females taken at baseline.

5. Discussion

This study of non-obese females showed that ultrasound measurements of ScF was strongly correlated with body composition and anthropometric measurements. Study participants had a negative history of known diseases and laboratory parameters assessed at the beginning of the study were within the normal range. This result allows us to affirm that ultrasonography may be used to assess ScF and offered advantages over anthropometric measurements.

Previous studies that described anthropometric measurements had the highest interobserver error, did not reflect the location of fat deposition in a reliable manner and did not correlate with variations in body weight [15, 27-29] while BMI in non-obese females may not reflect VF deposition, decreasing the perception of CV risk [30] DXA assessment of BC is expensive and the method is not available in the majority of health services. In general, it is most frequently indicated for females older than 60 years to measure bone mass. Furthermore, even when available the device may not always distinguish between different abdominal fat deposits [31].

Previous studies have associated VF deposition with increased body weight [15, 28] and increased risk for CVD [32]. In this study, we did not find any correlation between these variables, which may be explained by the characteristics of the non-obese female sample.

Regarding the weak correlation encountered between ultrasound VF measurements and anthropometric measurements and the lack of correlation with fat measured in BC, we could speculate that visceral fat at baseline induced a "safe" deposition, located in the subcutaneous tissue. We can also speculate that inflammatory biomarkers could already have been affected at this stage, which was shown in our study. It has been described that VF has a particular metabolism, limited by the intra-abdominal space. It accumulates by hypertrophy of adipocytes, through mechanisms that are not fully understood, and is capable of shifting excess fat to muscles and subcutaneous tissue deposits. In contrast, subcutaneous fat deposition occurs through adipogenesis and precedes an increase in VF, playing a protective role in the beginning of body weight gain [33].

The study has some strengths and limitations. The strengths were the evaluation of a non-obese female cohort with measurements obtained with ultrasound by only one experienced observer and two measurements taken 12 months apart. These characteristics demonstrated that some results were repeated with strong correlation in both time periods of assessment. It is possible that the results related to CVD markers such as LDL-chol, Apo B-100 and C-RP had weaker correlations with ultrasound measurements due to the sample characteristics (non-obese, apparently healthy females). On the other hand, limitations are those of a pilot study, and results should be tested by other studies using a larger number of individuals in different populations.

There are no studies on the amount of abdominal fat that can be regarded as physiological or normal for an individual. Studies on the values above which it would be considered a higher risk for metabolic diseases or CVD are also lacking. Studies to confirm or refute whether ultrasound measurement of abdominal fat deposition may

occupy a role in the prediction of CVD risks must be conducted. In case of affirmative results, professionals dedicated to imaging diagnostics will become involved in screening for individual indicators of CVD risk.

Since it shows early variation in fat gain, ultrasound measurement of abdominal ScF may be conducted during abdominal ultrasound ordered for other indications, permitting longitudinal comparisons to detect any changes. Ultrasound is a widely available, low-cost method, with a safe application. Therefore, assessment of ScF could be encouraged and included in the standard report, irrespective of test indication.

Future studies need to be conducted with a larger number of females to assess ultrasound use for the measurement of abdominal fat thickness in different populations and age groups, with and without comorbidities and determine measurements of maximum thickness, velocity of increased fat deposition or cut-off value indicating CVD risk. Studies should propose to standardize the best locations for visceral fat measurement. It is most important to specifically study the deposition of subcutaneous fat located above and below the Scarpa's fascial layer, since its relation is modulated by body weight gain [34, 35].

6. Conclusion

On ultrasound assessment of abdominal fat, there was a strong correlation between body composition and anthropometric measurements. Due to the high prevalence of CVD in females and the pronounced effect of well-known CV risk factors on this population, it may be important to carry out studies with practical procedures that are new, easy, inexpensive and available for the detection of alarm signals to prevent these diseases. Ultrasound as a screening method for assessment of fat deposition is quite promising.

7. Declarations

7.1. Ethics Approval and Consent to Participate

We declare that informed consent has been obtained from all subjects and/or their legal guardians and all methods were carried out in accordance with relevant guidelines and regulations.

This was a prospective, non-randomized, comparative study conducted at the family planning clinic of the Department of Obstetrics and Gynecology and at the Metabolic Unit of the Department of Clinical Medicine, School of Medical Sciences, University of Campinas (UNICAMP), Campinas, SP, Brazil between February 2011 and February 2013. The project was registered at Clinical Trials under reference number NCT01527526. The Ethical Committee of the University of Campinas (UNICAMP) approved the study protocol under number 903/2009, and all the volunteers signed an informed consent form prior to admission.

8. Funding

This study was funded by Fundação de Amparo à Pesquisa do Estado de São Paulo (FAPESP), Secretaria de Estado da Saúde de São Paulo (SES-SP) grant PPSUS/2009, #2009/53293-0, and by the Brazilian National Research Council (CNPq), Brazil.

References

1. Abma JC, Chandra A, Mosher WD, Peterson LS, Piccinino LJ. Fertility, family planning and women's health: New data from the 1995 National Survey of Family Growth. Vital and Health Statistics, Series. 1997; 23(19): 1-114.
2. Nowbar AN, Howard JP, Finegold JA, Asaria P, Francis DP. Global geographic analysis of mortality from ischaemic heart disease by country, age and income: Statistics from World Health Organisation and United Nations. International Journal of Cardiology. 2014; 2: 293-8.
3. Ministério da Saúde. SIM-Sistema de Informações de Mortalidade [Internet]. DATASUS. 2017.
4. Wang H, Naghavi M, Allen C, Barber RM, Bhutta ZA, Carter A, et al. Global, regional, and national life expectancy, all-cause mortality, and cause-specific mortality for 249 causes of death, 1980-2015: a systematic analysis for the Global Burden of Disease Study 2015. Lancet. 2016; 10053: 1459-544.
5. Wilmot KA, O'Flaherty M, Capewell S, Ford ES, Vaccarino V. Coronary Heart Disease Mortality Declines in the United States From 1979 Through 2011: Evidence for Stagnation in Young Adults, Especially Women. Circulation. 2015; 2015(11): 997-1002.
6. Kasner SE, Swaminathan B, Lavados P, Sharma M, Muir K, Veltkamp R, et al. Rivaroxaban or aspirin for patent foramen ovale and embolic stroke of undetermined source: a prespecified subgroup analysis from the NAVIGATE ESUS trial. The Lancet Neurology. 2018; 12: 1053-60.
7. Fisher G, Hyatt TC, Hunter GR, Oster RA, Desmond RA, Gower BA. Effect of diet with and without exercise training on markers of Inflammation and Fat Distribution in Overweight Women. Obesity, Silver Spring. 2011; 6: 1131-6.
8. Fayh APT, Lopes AL, Fernandes PR, Reischak-Oliveira A, Friedman R. Impact of weight loss with or without exercise on abdominal fat and insulin resistance in obese individuals: A randomised clinical trial. The British Journal of Nutrition. 2013; 3: 486-92
9. Mikkola TS, Tuomikoski P, Lyytinen H, Korhonen P, Hoti F, Vattulainen P, et al. Increased cardiovascular mortality risk in women discontinuing postmenopausal hormone therapy. The Journal of Clinical Endocrinology and Metabolism. 2015; 12: 4588-94
10. Dixon JB, Roux CWL, Rubino F, Zimmet P. Bariatric surgery for type 2 diabetes. Lancet. 2012; 9833: 2300-11.
11. Wang H, Naghavi M, Allen C, Barber RM, Carter A, Casey DC, et al. Global, regional, and national life expectancy, all-cause mortality, and cause-specific mortality for 249 causes of death, 1980–2015: a systematic analysis for the Global Burden of Disease Study 2015. Lancet. 2016; 10053: 1459-544.
12. Dutheil F, Lac G, Lesourd B, Chapier R, Walther G, Vinet A, et al. Different modalities of exercise to reduce visceral fat mass and cardiovascular risk in metabolic syndrome: The RESOLVE* randomized trial. International Journal of Cardiology. 2013; 4: 3634-42.

13. Quintero FS, Ariza AJ, García FB, Molano NCD, Benavides MC, Muñoz SC, et al. Overweight and obesity: review and update]. Acta Gastroenterologica Latinoamericana. 2016; 2: 131-59.

14. Matsuzawa Y. Establishment of a concept of visceral fat syndrome and discovery of adiponectin. Proceedings of the Japan Academy, Series B, Physical and biological sciences. 2010; 2: 131-41.

15. Berker D, Koparal S, Işik S, Paşao lu L, Aydin Y, Erol K, et al. Compatibility of different methods for the measurement of visceral fat in different body mass index strata. Diagnostic and Interventional Radiology. 2010; 2: 99-105.

16. Nazare JA, Smith J, Borel AL, Aschner P, Barter P, Gaal LV, et al. Usefulness of measuring both body mass index and waist circumference for the estimation of visceral adiposity and related cardiometabolic risk profile (from the INSPIRE ME IAA Study). The American Journal of Cardiology. 2015; 3: 307-15.

17. Shulman GI. Ectopic Fat in Insulin Resistance, Dyslipidemia, and Cardiometabolic Disease. The New England Journal of Medicine. 2014; 12: 1131-41.

18. Borel AL, Nazare JA, Smith J, Aschner P, Barter P, Gaal LV, et al. Visceral, subcutaneous abdominal adiposity and liver fat content distribution in normal glucose tolerance, impaired fasting glucose and/or impaired glucose tolerance. International Journal of Obesity. 2015; 3: 495-501.

19. Ciavattini A, Di Giuseppe J, Clemente N, Moriconi L, Carpini GD, Montik N, et al. Thickness of preperitoneal fat as a predictor of malignancy in overweight and obese women with endometrial polyps. Oncology Letters. 2016; 3: 2278-82.

20. Kishida K, Funahashi T, Matsuzawa Y, Shimomura I. Visceral adiposity as a target for the management of the metabolic syndrome. Annals of Medicine. 2012; 3: 233-41.

21. Huh JY, Park YJ, Ham M, Kim JB. Crosstalk between Adipocytes and Immune Cells in Adipose Tissue Inflammation and Metabolic Dysregulation in Obesity. Molecules and Cells. 2014; 5: 365-71.

22. Jeanson AL, Dupej J, Villa C, Brůžek J. Body composition estimation from selected slices: equations computed from a new semi-automatic thresholding method developed on whole-body CT scans. PeerJ. 2017; 3302.

23. DeFronzo RA, Tobin JD, Andres R. Glucose clamp technique: a method for quantifying insulin secretion and resistance. The America Journal of Physiology. 1979; 3: 214-23.

24. Gosink BB, Leymaster CE. Ultrasonic determination of hepatomegaly. Journal of Clinical Ultrasound. 1981; 1: 37-44.

25. Xia MF, Yan HM, He WY, Li XM, Li CL, Yao XZ, et al. Standardized ultrasound hepatic/renal ratio and hepatic attenuation rate to quantify liver fat content: An improvement method. Obesity, Silver Spring. 2012; 2: 444-52.

26. Takahashi Y, Sugimoto K, Inui H, Fukusato T. Current pharmacological therapies for nonalcoholic fatty liver disease/nonalcoholic steatohepatitis. World Journal of Gastroenterology. 2015; 13: 3777-85.

27. Bazzocchi A, Diano D, Ponti F, Salizzoni E, Albisinni U, Marchesini G, et al. A 360-degree overview of body composition in healthy people: Relationships among anthropometry, ultrasonography, and dual-energy x-ray absorptiometry. Nutrition. 2014; 6: 696-701.

28. Ribeiro-Filho FF, Faria AN, Azjen S, Zanella MT, Ferreira SRG. Methods of estimation of visceral fat: Advantages of ultrasonography. Obesity Research. 2003; 12: 1488-94.

29. Armellini F, Zamboni M, Rigo L, Todesco T, Bosello O, Bergamo-Andreis IA, et al. The contribution of sonography to the measurement of intra-abdominal fat. Journal of Clinical Ultrasound. 1990; 7: 563-7.

30. Nazare JA, Smith JD, Borel AL, Haffner SM, Balkau B, Ross R, et al. Ethnic influences on the relations between abdominal subcutaneous and visceral adiposity, liver fat, and cardiometabolic risk profile: The international study of prediction of intra-abdominal adiposity and its relationship with cardiometabolic risk/intra-abdominal adiposity. The American Journal of Clinical Nutrition. 2012; 4: 714-26.

31. Suh YS, Kim DH, Lee IK. Usefulness of lumbar AP spine DXA for measuring the percentage of perilumbar regional fat and predicting visceral fat in obese postmenopausal women. Nutrition. 2002; 1: 84-5.

32. Ng M, Fleming T, Robinson M, Thomson B, Graetz N, Margono C, et al. Global, regional, and national prevalence of overweight and obesity in children and adults during 1980-2013: A systematic analysis for the Global Burden of Disease Study 2013. Lancet. 2014; 9945: 766-81.

33. Obata Y, Maeda N, Yamada Y, Yamamoto K, Nakamura S, Yamaoka M, et al. Impact of visceral fat on gene expression profile in peripheral blood cells in obese Japanese subjects. Cardiovascular Diabetology. 2016; 1: 159.

34. Harley OJH, Pickford MA. CT analysis of fat distribution superficial and deep to the Scarpa's fascial layer in the mid and lower abdomen. Journal of Plastic Reconstructive & Aesthetic Surgery. 2013; 4: 525-30.

35. Bays HE, González-Campoy JM, Bray GA, Kitabchi AE, Bergman DA, Schorr AB, et al. Pathogenic potential of adipose tissue and metabolic consequences of adipocyte hypertrophy and increased visceral adiposity. Expert Review of Cardiovascular Therapy. 2008; 3: 343-68.