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2 ARTIGO DE REVISÃO - *CARDIOVASCULAR DYSFUNCTION IN OBESITY AND NEW DIAGNOSTIC IMAGING TECHNIQUES-THE ROLE OF THE NON-INVASIVE IMAGE METHODS*

(artigo aceito para publicação na revista *Vascular Health Risk and Management* - ANEXO C)

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Abstract

Obesity is a major public health problem affecting adults and children in both developed and developing countries. This condition often leads to metabolic syndrome, which increases the risk of cardiovascular disease. A large number of studies have been carried out to understand the pathogenesis of cardiovascular dysfunction in obese patients. Endothelial dysfunction plays a key role in the progression of atherosclerosis and the development of coronary artery disease, hypertension and congestive heart failure. Non-invasive methods in the field of cardiovascular imaging, such as measuring intima-media thickness, flow-mediated dilatation, tissue Doppler, strain and strain rate, constitute new tools for the early detection of cardiac and vascular dysfunction. These techniques will certainly enable a better evaluation of initial cardiovascular injury and allow the correct, timely management of obese patients. The present review summarizes the main aspects of cardiovascular dysfunction in obesity and discusses the application of recent non-invasive imaging methods for the early detection of cardiovascular alterations.

Keywords: cardiovascular risk, endothelium dysfunction, obesity, strain and strain rate, tissue Doppler.

Introduction

The prevalence of overweight and obesity is increasing at a very high rate, affecting an estimated 300 million individuals worldwide. A number of studies carried out in developing countries report an approximate 20% prevalence of obesity.[1-3] The prevalence is even higher in developed countries. In 2007-2008, obesity in the United States was reported to affect 32.21% of male adults and 35.5% of female adults.[4,5] Considering the standard definition for overweight and obesity in the pediatric population (2 to 19 years of age), 11.9% were at or above the 97th percentile of the body mass index (BMI), 16.9% were at or above the 95th percentile and 31.7% were at or above the 85th percentile.[6-8] Childhood obesity increases the risk of obesity in adulthood tenfold and pediatric patients that persistently remain at the 99th BMI percentile are at very high risk for severe adult obesity.[9,10]

Obesity is commonly associated with a combination of co-morbidities, which collectively comprise metabolic syndrome. In 1998, the World Health Organization published a definition for metabolic syndrome that includes insulin resistance, raised plasma triglycerides, low high-density lipoprotein, central obesity or a BMI greater than 30 Kg/m^2 for adults and above the 95th percentile for children and adolescents, microalbuminuria (> 20 µg/min) or elevated albumin-to-creatinine ratio (≥ 30 mg/g) and hypertension.[11,12] Recently, a number of other clinical and laboratorial features have been associated with metabolic syndrome, such as nonalcoholic fatty liver disease, polycystic ovarian syndrome, atherosclerosis, pro-inflammatory state and oxidative stress. Moreover, body measurements, such as the waist-to-hip ratio and waist circumference, seem to predict the risk of mortality better than the BMI.[12,13]

Cardiovascular complications associated with obesity contribute to high rates of morbidity and mortality. Hypertension is three to five times more common in obese subjects in comparison to individuals within the ideal weight range.[14] All components of metabolic syndrome are independent predictors of cardiovascular events, such as stroke, cardiomyopathy, coronary artery disease, myocardial infarction, congestive heart failure and sudden cardiac death.[15] Central (mesenteric and omental) obesity is highly correlated to the risk of cardiovascular disease.[16-18] The risk of death among obese individuals (BMI > 30 Kg/m^2) is two to three times higher than non-obese individuals and the severely obese individuals

(BMI > 35 Kg/m^2) have a 5-to-20-year decrease in life expectancy in comparison to non-obese individuals matched for age and gender.[14,16]

The present review summarizes the main aspects of cardiovascular dysfunction in obesity and discusses the application of recent non-invasive imaging methods in this context.

Endothelial dysfunction in obesity

Endothelial dysfunction is associated with a large number of clinical conditions and laboratorial alterations, including diabetes mellitus, hypercholesterolemia, hypertension, insulin resistance, advanced age and obesity.[19] Adipose tissue plays a key role in the development of endothelial dysfunction in obese patients.[20] An increase in fat mass increases the size and number of adipocytes. Changes associated with adipocyte hypertrophy seem to produce cell dysfunction. An excessive amount of lipid stored in adipocytes leads to functional abnormalities of the endoplasmic reticulum and mitochondria, which, in turn, contribute to intracellular and systemic disorders, such as the stimulation of a pro-inflammatory state, insulin resistance and high production of free fatty acids (FFAs).[21] FFAs accumulate in non-adipose tissue and cause an overproduction of metabolic toxins. Both effects impair insulin signaling and glucose tolerance.[22] Nonalcoholic fatty liver disease also plays a very important role in this process[23].

In addition, chronic subclinical inflammation associated with visceral and central adiposity often occurs in patients with metabolic syndrome. The major mediators responsible for the balance between pro-inflammatory and anti-inflammatory pathways are C-reactive protein (CRP), leptin, tumor necrosis factor α (TNF-α), interleukin-6 (IL-6), serum retinol binding protein 4 (sRBP-4), plasminogen activator inhibitor 1 (PAI-1), nitric oxide (NO) and adiponectin.[21,24-27] Fat in the liver also represents a site beyond adipose tissue that independently contributes to the synthesis of inflammatory mediators such as CRP, IL-6 and PAI-1, which are increased in nonalcoholic fatty liver disease.[23,28] The predominance of inflammatory mediators in obese patients also contributes to endothelial dysfunction, as next summarized.

CRP is predominantly produced by the liver in response to IL-6 and is chronically elevated in metabolic syndrome. CRP levels are positively correlated with BMI and visceral fat accumulation.[29] CRP inhibits the formation of NO by

endothelial cells. The lack of NO promotes vasoconstriction, leukocyte adherence, platelet activation, oxidation and thrombosis, thereby leading to endothelial dysfunction and arterial hypertension.[21,24] High levels of CRP are also predictive of atherothrombotic events[26].

Leptin is secreted by adipose tissue. This secretion is directly proportional to adipose tissue mass. Leptin receptors are mainly expressed in the hypothalamus and brainstem neuronal circuit and control satiety, energy expenditure and neuroendocrine functions. Obese patients have elevated levels of endogenous leptin that fail to suppress appetite, thus characterizing a leptin-resistant state. High levels of leptin have been linked to vasculopathy via obesity associated to hypertension.[20,25,30] High leptin levels are also associated with insulin resistance and correlated with artherosclerosis and coronary artery calcifications.[31,32]

TNF-α is a pro-inflammatory cytokine whose expression is elevated in obese adipose tissue. This cytokine is mainly produced from macrophages within the adipose tissue as well as adipocytes themselves.[21,33] There is a strong relationship between TNF-α and the effect of the lipoprotein lipase, which is responsible for the breakdown of circulating triglycerides and very low density cholesterol. In metabolic syndrome, there is an increase in macrophage TNF-α expression and a decrease in the effect of lipoprotein lipase, thereby causing hypertriglyceridemia. TNF-α impairs insulin signaling by an increase in circulating FFAs, which induces insulin resistance. TNF-α also plays a role in stimulating the expression of other inflammatory mediators, such as IL-6, and reduces the expression of anti-inflammatory mediators, such as adiponectin.[20,25] Furthermore, TNF-α induces insulin resistance through the down-regulation of the tyrosine kinase activity of insulin receptors and the serine phosphorylation of insulin substrate 1, which converts this protein into an insulin-receptor inhibitor in adipose tissue.[34] TNF-α also activates transcription nuclear factor kappa beta (NF-κβ), which induces inflammatory changes within the vessel wall.[35,36] Summarizing, TNF-α is pro-inflamatory cytokine that plays a very important role on the vascular dysfunction in obese patients.

sRBP-4 is a circulating protein of the lipocalin family associated with visceral adiposity and insulin resistance. sRBP-4 is secreted by the liver and adipocytes, reaching high concentrations in chronic low-state inflammation [35]. In

mouse models, sRB4 induces insulin resistance in the liver and skeletal muscle.[35] In humans, a number of studies report an association between sRB4, insulin resistance and type 2 diabetes.[21]

PAI-1 is a member of the serine protease inhibitor family and is the primary inhibitor of fibrinolysis. It is secreted mainly by platelets and vascular endothelium and is also produced by adipocyte cells. Plasma PAI-1 is elevated in individuals with obesity and plays a key role in promoting thrombus formation following the rupture of atherosclerotic plaque.[25,37]

NO has a large number anti-atherogenesis actions, including induction of potent vasodilatation, capacity to diminish the adhesion of monocytes and the aggregation of platelets to the endothelium, and inhibitory effect on the proliferation of smooth muscle cells.[38] Reduced synthesis of NO is also an early inducer of obesity. Insulin resistance and the chronic rise in plasma glucose enhance the expression of glutamine fructose 6 phosphate transaminase, which, in turn, stimulates the production of glucosamine, thereby favoring oxidative stress in endothelial cells.[39,40] TNF-α also plays a role in this process, as it inhibits endothelium-dependent vasorelaxation by increasing the generation of reactive oxygen species, which activate NF-κβ, a transcription regulator of molecular adhesion important to the control of inflammatory and oxidative states of vascular endothelial cells.[19,41-43]

Adiponectin is a protein with 247 amino acids produced by adipocytes (adipokine) that exerts potent endothelium-protective effects.[44] Adiponectin levels are significantly lower in obese individuals in comparison to non-obese individuals and have been negatively correlated with percentage of body fat, waist-to-hip ratio and abdominal fat.[45] Serum adiponectin circulates in three forms – low, middle and high molecular weight, which is the most active form. Adiponectin receptors are expressed in muscle, liver and fat cells.[46] Low concentrations of adiponectin contribute to a variety of obesity-related diseases, including diabetes, vascular abnormalities and heart disease, and are inversely associated with CRP and TNF-α levels.[45,46] The main effects of adiponectin are the regulation of glucose metabolism, the improvement of sensitivity to insulin, the reduction in atherosclerotic lesions, the inhibition of monocyte adhesion to endothelial cells, the suppression of macrophage transformation into foam cells, and the decrease in the proliferation and migration of smooth muscle cells.[35] It also increases

endothelial NO production, thereby enhancing vasodilatation and inhibiting platelet aggregation. Adiponectin influences cardiac remodeling by suppressing pathological heart growth and is believed to have a protective effect on ischemic/reperfusion cardiac injury.[22,44,45,47-49] Nonalcoholic fatty liver disease has been also associated to low serum levels of adiponectin.[23]

Atherosclerosis and coronary artery disease in obesity

Obesity is an independent predictor of coronary artery disease. Among men under 50 years of age, obese individuals have twice the risk of coronary disease and obese women of a similar age have a 2.4-fold greater risk.[50]

Obesity results in increased deposition of perivascular fat around the heart and its major branches. This increased adipose tissue surrounding the blood vessels causes the overproduction of pro-inflammatory and pro-fibrotic cytokines, leading to inflammation and atherosclerosis, with a consequent increase in intima-media thickness and decrease in arterial distensibility.[17] The activation of the renin-angiotensin-aldosterone system and of the sympathetic nervous system in metabolic syndrome leads to an increase in coronary vasoconstriction, which significantly contributes to the imbalance between coronary blood flow and myocardial metabolism.[15] Experimental studies have demonstrated that, even in the early stage of obesity, there is a reduction in coronary endothelium-dependent vasorelaxation.[51]

Acute coronary syndromes are usually triggered by the rupture or erosion of atheromatous plaque; when the plaque ruptures, endothelial tissue factor is exposed to the blood and activates the coagulation cascade, causing thrombus formation.[29]

Arterial hypertension in obesity

The prevalence of hypertension in obese patients in the United States is on the rise and individuals with a BMI greater than 40 have a sevenfold greater likelihood of being hypertensive.[52] Obesity in children and adolescents also leads to hypertension. Chiolero and colleagues (2007) conducted a prevalence study on hypertension and found that this condition was attributed to overweight or obesity in 37% of cases.[53] In Switzerland, Maggio and colleagues (2008) found an association between obese children and systolic hypertension in 47.6% of patients

as well as an increase in left ventricular mass partially caused by high systemic blood pressure. Obese children have a tenfold greater risk of developing hypertension as young adults than non-obese children and a continuous relationship between BMI and arterial pressure has been reported.[7,54] One study reports that 10 Kg of excess body weight is associated with a 3.0-mmHg higher systolic and 2.3-mmHg higher diastolic blood pressure.[55] Stabouli and colleagues[56] reported that obese adolescents have higher blood pressure and greater carotid artery intima-media thickness in comparison to non-obese pairs.

The mechanism of hypertension in metabolic syndrome is highly complex. The obese-related inflammatory state is one of the factors probably responsible for hypertension.[57] The inflammatory state leads to hyperinsulinemia, insulin resistance, dyslipidemia and oxidative stress, along with serious damage to organ systems. Obese patients have increased systemic blood volume. The normal compensatory response to an elevated cardiac output, which should be a drop in peripheral vascular resistance, is hindered in obese patients with hypertension, exhibiting an inappropriately normal total peripheral resistance.[58] Studies have shown that increased sympathetic activity and hypoactivity of the parasympathetic nervous system, even in children, also results in an increased incidence of hypertension by augmenting sodium retention and vascular smooth muscle hypertrophy, affecting glucose delivery to the muscles and postprandial lipid clearance.[59-61] The increasing of the FFAs, along with increased levels of circulating glucose, promotes insulin secretion by the pancreas, resulting in hyperinsulinemia. These events, in turn, can cause increased sodium reabsorption and sympathetic nervous system activity, with subsequent development or worsening of hypertension.[18]

The activation of the renin-angiotensin-aldosterone system also significantly contributes to hypertension in obese patients.[35,59] Adipose tissue is able to synthesize the components of the renin-angiotensin-aldosterone system [35,59]. In this regard, the formation of angiotensin II in the adipose tissue enhances the production of pro-inflammatory and pro-fibrotic cytokines [35,50] and stimulates *per se* vasoconstriction, smooth muscle vascular cell proliferation and endothelial dysfunction[57]. Beside angiotensin II, the elevation of plasma levels of aldosterone might promote myocardial tissue growth.[59]

Left Ventricular involvement in obesity

Cardiac involvement in obesity has been frequently reported in the literature, and the most frequently found abnormalities are: increased left ventricular diameters and mass, eccentric hypertrophy, diastolic dysfunction and, occasionally, systolic dysfunction and heart failure.[62-64] Indeed, obesity has been linked to a spectrum of minor cardiovascular abnormalities, ranging from a hyperdynamic circulation to subclinical structural changes.

Congestive heart failure in obesity

Excess weight has been linked to heart failure and mortality. For each increment of one above 30 on the BMI, the risk of developing heart failure increases 5% in men and 7% in women.[50] Obesity has been associated with systolic and diastolic heart dysfunction. In a cross-sectional study, Ammar and colleagues (2008) found a strong correlation between left ventricular systolic and diastolic dysfunction and central obesity, as measured by the waist-to-hip ratio.[65]

Studies have documented a better chance of survival from cardiac events in patients with decreased left ventricular ejection fraction and a higher BMI in comparison to those with a lower BMI, which is known as the “obesity paradox”. The pathophysiology of the obesity paradox is unknown and some authors state that this paradox could be explained by an additional disease in patients with low BMI, such as lung disease.[66] Kappor and colleagues (2010) have recently reported that the mortality rate in cardiac events is increased in obese patients with a BMI of 45 or more in comparison to lean peers.[67] Moreover, among a cohort of 1790 patients, Frankenstein and colleagues (2009) found that the obesity paradox in patients with stable heart failure did not persist after matching for clinical characteristics and disease severity.[68]

There are studies confirming the relationship between left atrial size and the development of adverse cardiovascular outcomes and those describing a strong correlation between BMI and atrial fibrillation, which deteriorates the cardiac failure.[69,70]

The role of non-invasive image methods in obesity

Metabolic syndrome and its association with vascular and cardiac dysfunction is currently the greatest cause of mortality and this situation is

expected to continue in the future.[71] Noninvasive techniques for evaluating vascular dysfunction, such as flow-mediated dilatation, pulse wave velocity and carotid intima-media thickness and transient elastography to evaluate fatty liver disease[72] are very good surrogate vascular markers. For the early assessment of cardiac dysfunction, tissue Doppler, strain and strain rate have proven useful in patients with obesity and other morbidities.

Endothelial dysfunction with a reduction in the bioavailability of endothelium-derived nitric oxide is an early event in atherosclerotic change. Flow-mediated inflammation is a good way to assess sub-clinical vascular disease and is significantly correlated with invasive tests. Its use with a combination of other exams, such as carotid intima-media thickness and pulse wave velocity, is of very strong clinical importance to the determination of clinical or subclinical atherosclerosis.[73,74,75] However, Biasucci and colleagues (2010) analyzed vascular function in obese and severely obese patients and found that vascular function was paradoxically better among the severely obese individuals. The authors suggested that these kind of patients may be partially protected from atherosclerosis probably by a greater mobilization of endothelial progenitor cells.[76]

In the young population, studies have shown that obesity is associated with increased arterial wall stiffness, as determined by carotid intima-media thickness.[77,78] Diminished flow-mediated dilation has been observed in other pathologies, such as Kawasaki disease and type 1 diabetes mellitus, but there is yet no direct relationship between obesity and altered flow-mediated dilation.[79,80] Further studies are needed, but these are very promising markers for the early assessment of cardiovascular disease, even in young patients.

Transient elastography is a non-invasive method for detection of cirrhosis in patients with chronic liver disease by measuring the liver stiffness. It is a new method to evaluate liver disease instead of biopsy, which is an invasive and with potential life threatening complications. Liver stiffness measurements using transient elastography can be technically difficult in obese patients.[81,82]

Standard and new echocardiography techniques for the determination of coronary flow, early changes in systolic and diastolic left ventricle function are very important tools for assessing obese patients, even in the child population. Transthoracic Doppler echocardiography assessment of coronary flow velocity is an established noninvasive and clinically useful method to provide physiological

information on the coronary circulation in obesity patients.[83] New echocardiography techniques, such as tissue Doppler imaging, strain and strain rate (SR), are useful tools for assessing cardiac dysfunction in adults and children. These techniques permit a quantitative assessment of both global and regional function and timing of myocardial events as well as the assessment of early changes in systolic and diastolic function.[84-86]

Strain and SR assess function in heart segments.[87] Strain is directly related to fiber shortening and strain rate is the speed of fiber shortening, which is a measure of contractility.[88] The longitudinal, radial and circumferential function can be measured by tissue Doppler myocardial imaging and the B-mode imaging using the Speckle tracking technique.[88] These methods are important to assessing subclinical myocardial dysfunction in a wide variety of diseases and the application of strain analysis has been implemented in numerous experimental and clinical studies for the investigation of cardiac function.[88]

Early detection of cardiovascular abnormalities is important because treatment to reverse the process is most likely to be effective earlier in the disease. The potential impact of obesity on biventricular function has not been fully established. Since traditional echocardiographic measurements of ventricular function, such as ejection fraction and mitral inflow for the evaluation of the diastolic function are load-dependent[89,90], the investigation of right and left ventricle subclinical dysfunction in obesity by sensitive newer echocardiographic techniques, such as tissue Doppler imaging (TDI), myocardial strain and strain rate seems promising.

TDI, strain and strain rate have been introduced to better quantify segmental and global dysfunction, with studies showing clinically silent incipient dysfunction in obesity detected by strain and strain rate. Wong and colleagues (2004) used strain and SR to study myocardial function and found that overweight subjects have reduced systolic and diastolic function, even after adjustments for mean arterial pressure, age, gender and left ventricular mass.[91] In 2006, the same authors used the same techniques to demonstrate the existence of right ventricular dysfunction in obese patients.[92] Gong and colleagues (2009) studied 200 patients with metabolic syndrome using strain and SR to evaluate cardiac function in comparison to lean controls and demonstrated left ventricular systolic and diastolic dysfunction in the obese group. In the study, multiple regression

analysis revealed that the waist-to-hip ratio was an independent predictor of systolic dysfunction and that the waist-to-hip ratio and high density lipoproteins (HDL) cholesterol were independent predictors of diastolic dysfunction.[93] Mehta and colleagues (2004) used tissue Doppler and found a decrease in diastolic function in obese children.[94] In a prospective study involving healthy and obese individuals between 10 to 18 years of age, Lorch and colleagues (2006) found a decrease in systolic strain in the obese group in comparison to the lean group.[95] More recently, Ingul and colleagues (2010) have reported an improvement in cardiac function, as evaluated by strain and SR, in obese adolescents after a training program.[96]

The left atrium is important in all phases of the cardiac cycle. During ventricular systole and isovolumic relaxation, it serves as a reservoir that receives blood from the pulmonary venous return and stores energy in the form of pressure. During the early phase of ventricular diastole, the left atrium operates as a conduit for transferring blood into the left ventricle following the opening of the mitral valve due to a pressure gradient and through which blood flows passively from the pulmonary veins into the left ventricle; the contractile function of the left atrium, during the late phase of diastole, increases the left ventricular stroke volume by nearly 20%.[70]

Left atrial size is an expression of chronic left ventricular filling pressures. Early studies had demonstrated the value of left atrial diameter in predicting prognosis of cardiac diseases and in the development of atrial fibrillation. More recently, left atrial volume has been shown to be an important and more accurate measurement of left atrial size and this measurement, indexed to body surface area, has been used to predict prognosis in several heart diseases.[70,97,98] Although left atrial volume seems to correlate with diastolic filling pressures, accurate and direct measurements of the left atrial function have not been established.

Enlargement of the atria is associated with obesity and has been also linked with an increased risk of mortality.[99] Using standard echocardiography techniques, Hirchler and colleagues (2006) concluded that left atrial enlargement is related to abdominal obesity and hypertension in children.[100] Kosar and colleagues (2008) found that obese patients without cardiovascular disease exhibit enlargement of left atrium in standard echocardiography.[101]

Strain and SR methods have emerged as promising methods to evaluate atrial function, but with controversial results. Gulel and colleagues (2009) compared left atrial function using color tissue Doppler imaging in adults with a body mass index ≥ 30Kg/m^2 *versus* those with a BMI < 30 Kg/m2 and found no differences in systolic or diastolic atrial function between groups.[102] On the other hand, Di Salvo and colleagues (2008) studied non-hypertensive children using strain and SR and found reduced left and right atrial function in the obese group.[103] Further studies should be carried out to clarify these controversial results.

In summary, obesity, even without comorbidities, is generally associated with cardiac events. Overt systolic and diastolic dysfunction has been described in obesity. New findings, indicating the occurrence of pre-clinical systolic and diastolic dysfunction, even in young obese patients, suggest that obese patients should be carefully monitored in order to detect incipient dysfunction. Efforts should be made, not only to make obese patients lose weight and control other cardiovascular risk factors, but also to detect incipient atrial and ventricular dysfunction. If these patients should be treated before the development of overt ventricular dysfunction, remains to be established.

Table 1 summarizes the most recent studies using TDI, strain and SR to evaluate cardiac function in obese subjects.

Table 1 - Recent studies using tissue Doppler, strain and SR to evaluate cardiac function in obese subjects

Author and year	**Study population**	**Cutoffs of BMI (Kg/m^2) or waist circumference (cm)**	**Results**	**Commentary**
Metha, Sudhir Ken *et al.,* 2004[88]	Obese children (n=25) Control: 13.8±1.9 years Obese:14.4±2.1 years	BMI>25 (independent of age)	Decrease in diastolic function	Healthy obese children with no comorbidities
Wong, O'Moore-Sullivan *et al.,* 2004[85]	Obese adults (n=109) Control: 46±10 years Overweight:45±11 years Mild obesity: 42±8 years Severe obesity: 43±10 years	Groups 1-BMI:25-29.9 overweight 2-BMI:30-34.9 mild obesity 3-BMI >35 severe obesity	Left ventricular systolic and diastolic dysfunction in patients with moderate to severe obesity	Insulin levels were a significant predictor of systolic and diastolic heart dysfunction
Di Salvo, Pacielo *et al.,* 2006[98]	Obese children (n=150) Control: 12±3 years Obese:12±3 years	Percentile >97th for sex and age (according to CDC)	Systolic dysfunction in both right and left ventricle	Healthy obese children with no comorbidities
Wong, O'Moore-Sullivan *et al.,* 2006[86]	Obese adults (n=112) Control:43±11 years Overweight:44±10 years Mild obesity:41±8 years Severe obesity:44±13 years	BMI:25-29.9 overweight BMI:30-34.9 mild obesity BMI: >35 severe obesity	Increase in BMI associated with increased severity of right ventricle dysfunction	BMI was associated with right ventricular dysfunction, regardless of sleep apnea
Lorch and Sharkey, 2007[89]	Obese children (n=53) Control: 13.9±2.3 Obese: 13.8±2.4	Percentile >95th for sex and age (CDC)*	Systolic and diastolic dysfunction of left ventricle	Retrospective study
Tumuklu, Etikan *et al.,* 2007[99]	Obese adults (n=33) Control:43±11 Moderate obesity:42±6 Severe obesity:42±8	BMI:30-34.9 moderate obesity BMI: >35 severe obesity	Systolic left ventricular dysfunction	Healthy obese subjects with no comorbidities
Di Salvo, Pacielo *et al.,* 2008[97]	Obese children (n=150) Control: 12±3 years Obese :12±3 years	Percentile >97th for sex and age (according to CDC)	Reduced left and right atrial myocardial deformation	Healthy obese children with no comorbidities

Surucu, Tatli *et al.,* 2008[100]	Obese adults (n=25) Control: 53±6 years Obese: 54±8 years	BMI≥27	Right and left ventricular systolic and diastolic dysfunction	Tissue Doppler technique and all subjects of the study with normal angiography
Gong, Tan *et al.,*2009[87]	Obese adults (n=200) Control: 49±10 years Obese: 50±9 years	Waist circumference ≥90cm for men and ≥80cm for women	Left ventricular systolic and diastolic dysfunction	Obese patients with co- morbidities including hypertension, dyslipidemia and hyperglycemia
Gulel, Yuksel *et al.,*2009[96]	Obese adults (n=37) Control: 35±5years Obese: 36±11 years	BMI≥30 Kg/m^2	No difference between groups considering left atrial function	No comorbidities
Orhan AL et al 2010[101]	Obese adults (n=29) Control: 47 ± 7 years Obese:49 ± 8 years	BMI ≥30 Kg/m^2	Left and right ventricular systolic and diastolic dysfunction	No comorbidities

Legend: BMI = body mass index, CDC=Centers for Disease Control and Prevention.

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3 OBJETIVOS

O objetivo principal deste estudo foi utilizar novas técnicas não invasivas de avaliação da função cardíaca na detecção de disfunção subclínica em crianças e adolescentes obesos.

Como objetivos específicos, estabeleceram-se:

- Comparar dados clínicos tais como frequência cardíaca, índice de massa corporal, pressão sistólica e diastólica de crianças e adolescentes obesos em relação a controles eutróficos pareados por sexo e idade;
- comparar dados laboratoriais, tais como glicemia de jejum, colesterol total e frações *high density lipoprotein* (HDL) e *low density lipoprotein* (LDL), triglicérides entre os dois grupos;
- comparar a função sistólica biventricular por meio das técnicas *strain* e *strain rate* e bidimensional *speckle tracking* e os parâmetros ecocardiográficos padrão (fração de ejeção, tamanho de câmaras cardíacas, massa ventricular esquerda, gradiente átrio direito-ventrículo direito) entre os dois grupos;
- comparar a função diastólica de ventrículo esquerdo utilizando a relação E/A do Doppler do fluxo de entrada da válvula mitral e da relação E/e' obtida a partir da análise do Doppler tissular das paredes septal e lateral do ventrículo esquerdo entre os dois grupos;
- comparar a função diastólica do ventrículo direito utilizando a relação e'/A' obtida da análise do Doppler tissular entre os dois grupos;
- avaliar correlações entre os parâmetros clínicos e ecocardiográficos com *strain* global bidimensional.

4 PACIENTES E MÉTODOS

4.1 Pacientes

4.1.1 Faixa etária

Fizeram parte do estudo crianças e adolescentes de seis a 18 anos de ambos os gêneros.

4.1.2 Critérios de inclusão

Foram incluídos crianças e adolescentes com diagnóstico de obesidade, ou seja, índice de massa corporal (IMC) acima do percentil 95, registrados e em acompanhamento regular na Unidade de Nutrologia Pediátrica do Departamento de Pediatria da Faculdade de Medicina e do Hospital das Clínicas da Universidade Federal de Minas Gerais (UFMG), durante o período de 2009 a 2010.

O grupo controle foi constituído por crianças e adolescentes saudáveis, pareados por gênero e idade, de seis a 18 anos, com IMC abaixo do percentil 85, recrutados nos Ambulatórios de Pediatria da mesma instituição durante o mesmo período.

4.1.3 Critérios de exclusão

Para esta pesquisa, após revisão de prontuários e entrevista com os pais, foram excluídos em ambos os grupos os pacientes com história de obesidade secundária, doenças genéticas, diabetes *mellitus* ou outras doenças endócrinas, cardiopatias adquiridas ou congênitas, hipertensão arterial ou doenças inflamatórias sistêmicas. A exclusão de pacientes com apneia do sono foi baseada exclusivamente nas informações dos pais.

4.2 Protocolo do estudo

Todos os pacientes, durante a consulta na Unidade de Nutrologia Pediátrica do Departamento de Pediatria da Faculdade de Medicina e do Hospital das Clínicas da Universidade Federal de Minas gerais (UFMG), receberam os esclarecimentos do estudo. Após a assinatura no termo de consentimento, foram submetidos, em uma única ocasião, ao ecoDopplercardiograma padrão, avaliação ventricular utilizando as técnicas *strain* e SR e bidimensional *speclke tracking* no serviço de ecocardiografia do Hospital Socor, Ecocenter.

4.3 Métodos

Estudo clínico transversal, observacional com coleta prospectiva dos dados. O aspecto primário de avaliação foi a comparação do *strain* longitudinal do VE utilizando a técnica *speckle tracking* bidimesional entre os dois grupos. Os aspectos secundários foram os dados clínicos, os parâmetros do ecoDopplercardiograma padrão e Doppler tissular para a avaliação das funções cardíacas sistólica e diastólica, além de *strain* e SR global do VE .

4.3.1 Grupos de variáveis

Todos os pacientes foram submetidos a exame clínico, avaliação nutricional utilizando o IMC (kg/m^2), medidas das pressões sistólicas e diastólicas (mmHg) e avaliação laboratorial de acordo com o protocolo utilizado pela Unidade de Nutrologia Pediátrica do Departamento de Pediatria da Faculdade de Medicina e do Hospital das Clínicas da UFMG. Todos os pacientes incluídos na pesquisa realizaram dosagens de triglicérides, colesterol total e suas frações e glicemia de jejum.

- **Cálculo do IMC**

Os participantes foram pesados sem sapatos, usando escala Welmy® com capacidade para 300 kg e precisão de 100 g. A altura foi medida (precisão de 0,5 cm) com estadiômetro. O IMC foi calculado com base na fórmula convencional de peso em quilos dividido pelo quadrado da altura em metros. A obesidade foi definida quando o IMC excedeu o percentil 95 para gênero e idade, com base nos valores de referência[1].

- **Medida da pressão arterial**

A pressão arterial foi determinada utilizando métodos padronizados com manguito de tamanho adequado. Apenas os pacientes com pressão arterial sistólica e pressão arterial diastólica abaixo do percentil 90 para sexo, idade e estatura foram incluídos no estudo[2]. Foram considerados os valores de pressão arterial sistólica e diastólica aqueles do momento do exame ecoDopplercardiográfico.

- **Análise bioquímica**

A avaliação laboratorial referente às dosagens de triglicérides, colesterol total e frações e glicemia de jejum foi realizada de acordo com o protocolo utilizado pela Unidade de Nutrologia Pediátrica do Departamento de Pediatria da Faculdade de Medicina e do Hospital das Clinicas da UFMG. Em todos os pacientes os níveis de glicose foram medidos após jejum de mais de 12 horas pelo método glicose oxidase, utilizando o analisador Hitachi 704. Colesterol total e triglicérides foram medidos com o teste enzimático colorimétrico. Colesterol LDL-C e colesterol HDL-C foram medidos por meio de colorimetria enzimática homogênea.

- **EcoDopplercardiograma padrão e Doppler tecidual**

O ecoDopplercardiograma com mapeamento de fluxo em cores e o Doppler tecidual foram realizados em todos os pacientes utilizando-se *hardware* e *software* disponíveis comercialmente (7 Vivid; GE Vingmed Ultrasound AS, Horten, Noruega) e transdutor de alta resolução de frequência multieletrônicos. As medidas foram realizadas por um único cardiologista. Os valores médios de três ciclos cardíacos consecutivos foram obtidos para todos os parâmetros ecocardiográficos. Diâmetro sistólico do ventrículo esquerdo (VE), diâmetro diastólico final do VE, parede livre do VE e espessura do septo interventricular foram determinados com base nas recomendações da Sociedade Americana de Ecocardiografia[3]. A fração de ejeção do ventrículo esquerdo (FEVE) foi calculada usando o método de Teichhollz[4]. O volume do átrio esquerdo (VAE) foi avaliada pelo método área-comprimento biplano do corte de quatro e duas câmaras e indexado à superfície corpórea[5]. A massa do VE foi calculada usando a fórmula de Devereux e indexada à altura elevada à potência de 2,7, a fim de obter a massa de VE indexada[6]. O pico de velocidade regurgitação tricúspide (RT) foi medido para calcular o gradiente átrio direito-ventrículo direito usando a equação modificada de Bernoulli [(RT velocidade de jato) 2 x 4][7].

Função diastólica foi avaliada a partir do Doppler pulsátil do fluxo mitral e do Doppler tecidual[6]. O Doppler tecidual foi realizado no corte apical quatro câmaras com volume de amostra de 2 mm colocado entre o folheto mitral durante a diástole para gravar perfil de velocidade com varredura de 100 mm/s no fim da expiração. Pico de enchimento precoce (onda E) e enchimento diastólico tardio (onda A), relação E/A, tempo de desaceleração da onda E e o tempo de relaxamento isovolumétrico (TRIV) foram obtidos para todos os pacientes. O TRIV foi medido a partir do final da onda sistólica ao início da velocidade do anel mitral. O Doppler tecidual foi medido na borda medial e lateral do anel mitral e borda lateral do anel tricúspide. As velocidades da onda S, ondas A' e e' foram medidas. Os valores médios das ondas e' septais e laterais foram obtidos. A relação e'/A' das paredes septal e lateral foi avaliada. A relação E/e' foi calculada por meio dos valores médios. A relação e'/A' do VD e das paredes septal e lateral do VE

também foi calculada. Todas as medidas foram aferidas com a observação da média de três batimentos cardíacos consecutivos[6].

- ***Strain* e SR análise**

Strain e SR foram obtidos do volume de amostra de 10 mm na parte basal das seis paredes do VE, nos cortes apical, duas, três e quatro câmaras[8]. O setor de imagem foi reduzido para permitir a mais alta taxa de quadros (>150 quadros/segundo) e o ângulo de imagem para a parede foi mantido o mais baixo possível para permitir melhor alinhamento paralelo à parede de interesse. *Strain* e SR foram medidos no segmento basal das seis paredes do VE. *Strain* e SR global foram obtidos dividindo-se a soma de cada pico sistólico longitudinal e do SR pelo número de paredes. *Strain* e SR foram também obtidos para o VD em sua parede livre na parte basal, utilizando-se o corte apical de quatro câmaras[9].

- **Análise *speckle tracking* bidimensional**

Análise bidimensional *speckle tracking* foi feita em *loops* adquiridos com taxa de quadros acima de 60 por segundo. Análise *speckle tracking* foi realizada nos segmentos basal, medial e apical nos cortes apical, duas, três e quatro câmaras, para avaliar o *strain* longitudinal. *Strain* longitudinal dos 18 segmentos das paredes do VE foi obtido com 2D *speckle tracking software* (GE EchoPAC). Segmentos foram excluídos se a análise era insuficiente, apesar do ajuste manual[10.] A análise da função global pelo *speckle tracking* bidimensional foi feita somando-se o valor do *strain* de todos os segmentos dividido pelo valor total[11].

4.4 Cálculo do tamanho amostral

Como não existem estudos usando o 2D *speckle tracking* para a análise da função do VE em pacientes pediátricos, o tamanho da amostra foi calculado utilizando-se a variável *strain* longitudinal do VE em estudos anteriores envolvendo crianças e adolescentes[12,13]. Desse modo, considerando-se essa variável, uma amostra de 45 pacientes em cada grupo foi calculada afim de se obter um poder amostral de 90% (erro beta de 10%) para se detectar um efeito

clínico de interesse (diminuição da deformação cardíaca a partir de 20% entre os grupos), com nível de significância (alfa) de 0,05 (bicaudal)[14].

4.5 Análise estatística

A normalidade dos dados foi feita utilizando o teste de Kolmogorov-Smirnov a fim de determinar os testes paramétricos *versus* não paramétricos. Para caracterização da amostra, as distribuições de frequência foram utilizadas para as variáveis qualitativas; e as medidas de tendência central (média, mediana, desvio-padrão) foram usadas para variáveis quantitativas. O teste t de Student foi empregado para comparações entre os grupos para as variáveis de distribuição normal e o teste de Mann-Whitney para aquelas de distribuição não-Gaussiana. Coeficiente de Pearson foi usado para determinar as correlações entre variáveis. Análise de regressão linear multivariada foi realizada para analisar as correlações entre o *strain* bidimensional *speckle tracking* e as variáveis clínicas e ecocardiográficas. O coeficiente de determinação foi utilizado para avaliar a acurácia de previsão.[14]A variabilidade intraobservador das variáveis *strain* e SR do VD e do *strain* global bidimensional foi calculada de acordo com o coeficiente intraclasse em amostra de 20 pacientes selecionados aleatoriamente. As análises foram feitas no *Statistical Package for Social Sciences* (SPSS) versão 18.0 (SPSS Inc., Chicago, IL, EUA). O nível de significância de 5% foi considerado em todos os testes estatísticos[14].

4.6 Aspectos éticos

Após aprovação pela Câmara do departamento de Pediatria da Faculdade de Medicina, o Comitê de Ética em Pesquisa (COEP) da UFMG aprovou o estudo com a emissão do Parecer ETIC 130/09 (ANEXO A). Todos os pacientes e seus responsáveis foram esclarecidos sobre a natureza do estudo por meio da leitura e análise do termo de consentimento livre e esclarecido (APÊNDICE A). Os pacientes com obesidade e as crianças e adolescentes saudáveis foram incluídos no estudo somente mediante concordância e assinatura do termo de consentimento por parte do responsável e do próprio paciente conforme a idade. O protocolo de pesquisa não interferiu em qualquer recomendação ou prescrição

médica. Ressalta-se, ainda, que o seguimento clínico-laboratorial e a abordagem terapêutica dos pacientes foram assegurados, mesmo no caso de recusa em participar do estudo.

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5 RESULTADOS

5.1 Artigo original – Decreased left ventricular strain in obese children and adolescents: a study using speckle tracking and color Doppler myocardial imaging.

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Abstract

Background - Right and left ventricular dysfunction has been described in obese adult patients. A number of studies have also described cardiac dysfunction in obese children and adolescents. **Objective** – The aim of the present study was to investigate left and right systolic and diastolic ventricular dysfunction in obese pediatric patients and compare their echocardiographic findings to those of non-obese controls. **Methods** - Doppler echocardiogram was performed on 50 obese pediatric patients (mean BMI = 29.8 kg/m^2) and 46 lean healthy controls. Systolic and diastolic functions of both ventricles were investigated through conventional Doppler echocardiography as well as new echocardiographic techniques, such as tissue Doppler, color Doppler myocardial imaging (CDMI) and 2D speckle tracking. **Results –** No differences were detected between groups with regard to left ventricular ejection fraction or diastolic parameters , except for a lower mitral A wave (61.6±13.0 vs. 51.9±10.0, p>0.001) and higher E/A ratio (1.8±0.5 vs.2.1±0.4, p=0.007) in the controls. Left ventricular global strain was lower in the obese children using both methods (CDMI: 22.0±2.8 vs. 24.6±2.7, p=0.020; 2D-speclke tracking imaging: 18.4±1.6 vs. 20.4±1.7, p<0.001). Right ventricle strain was significantly higher in the obese group. (29.3±5.4 vs.25.7±4.0, p=0.001). Two-dimensional global strain correlated negatively with age and BMI (r = -0.323, p=0.025 and r = -0.433, p=0.002 respectively). In the multivariate analysis, BMI remained the only significant determinant of 2D global strain. **Conclusion** - The findings of the present study suggested incipient left ventricular systolic dysfunction in obese children (BMI above 95th percentile) when new echocardiogram methods were used to investigate ventricular function and BMI correlated negatively with left ventricular 2D-speckle tracking analyze.

Background

Obesity has become an epidemic in both developed and developing countries. Statistics from the United States of America reveal a 32.2% rate of obesity among adult men and 25.5% among adult women.[1] Reports on the pediatric population (children and adolescents aged two to 19 years) reveal that 11.9% are at or above the 97th percentile of the body mass index (BMI)-for-age growth charts, 16.9% are at or above the 95th percentile and 31.7% are at or above the 85th percentile.[2] It is estimated that five to 10 million individuals in the United States alone have severe obesity (body mass index ≥ 40 kg/m^2).[3] The prevalence of obesity and metabolic syndrome is rapidly increasing in developing countries as well. In Brazil, Silveira *et al.*[4] report a 15.2% prevalence of overweight children in low-income families.

Obesity leads to metabolic syndrome and is associated with dysfunctional adipose tissue, which is most likely a consequence of the enlargement of adipocytes. A chronic state of inflammation triggers this phenomenon, with a reduction in the secretion of adiponectin, an anti-inflammatory cytokine that offers cardiovascular protection.[5] An increase occurs in pro-inflammatory cytokines, such as interleukin-6, interleukin-8, monocyte chemoatttractant protein-1 and tumor necrosis factor-α, which can substantially affect cardiovascular function and morphology.[6,7]

Cardiac involvement in obesity has been well established in adult patients. Structural and functional changes, such left ventricular hypertrophy and diastolic/systolic dysfunction, have been studied in obese humans as well as in animal models.[8,9] However, there are few studies on the pediatric population using pulsed-wave tissue Doppler imaging and color Doppler myocardial imaging to investigate left and right ventricular systolic[10] and diastolic dysfunction[11] and left and right atrial dysfunction.[12,13]

A new echocardiography technique known as two-dimensional (2D) speckle tracking imaging has proven to be an adequate method for assessing ventricular function and detecting sub-clinical dysfunction. Speckle tracking is angle-independent and allows measuring deformation in two dimensions. However, this method has a few limitations, such as low temporal resolution, considerable dependence on a good image and a high frame rate.[14]

The aim of the present study was to compare left ventricular function using color Doppler myocardial imaging strain, strain rate and 2D speckle tracking on obese pediatric patients (BMI > 95th percentile) with no comorbidities and lean controls (BMI < 85th percentile).

Methods

Study and control groups

Obese pediatric patients 6 to 18 years of age with a BMI above the 95th percentile were prospectively recruited from the Nutrition Outpatients Clinic, Hospital das Clinicas, *Universidade Federal de Minas Gerais*, in the city of Belo Horizonte (Brazil). The control group was formed by children aged from six to 18 years with a BMI below the 85th percentile, recruited from Pediatrics Outpatient Clinic of the same institution. Patients with a history of hypertension, diabetes mellitus, endocrinological disorders, hereditary or inflammatory systemic diseases or sleep apnea (according to parents' information) were excluded. The study received approval from the Human Research Ethics Committee of the institution and written informed consent was obtained from all participants and/or parents.

Determination of BMI

The participants were weighed in light clothing without shoes, using a Welmy® scale with a capacity of 300 kg and accuracy of 100 g. Height was measured with a stadiometer (accuracy of 0.5 cm). BMI was calculated using the conventional formula of weight in kilograms divided by the square of height in meters. Obesity was defined when BMI exceeded the 95th percentile for gender and age based on reference values.[15]

Determination of blood pressure

Blood pressure was determined using standard methods with an appropriate-sized cuff on more than three different occasions. Only patients with systolic and diastolic blood pressure values below the 90th percentile for gender and height were included in the study.[16]

Biochemical analysis

In all patients, glucose levels were measured (after overnight fasting > 12 hours) by the glucose-oxidase method using the Hitachi 704 analyzer. Total cholesterol and triglycerides were measured with the enzymatic colorimetric test. Low-density lipoprotein cholesterol (LDL-C) and high-density lipoprotein cholesterol (HDL-C) were measured through homogeneous enzymatic colorimetry.

Standard Doppler echocardiogram and tissue Doppler imaging

A comprehensive Doppler echocardiogram with color flow mapping and tissue Doppler imaging was performed on all patients using commercially available hardware and software (Vivid 7; GE Vingmed Ultrasound AS, Horten, Norway) and an electronic high-resolution multi-frequency transducer. Measurements were performed by a single experienced certified cardiologist. The mean values of three consecutive cardiac cycles were obtained for all echocardiographic parameters. Left ventricle (LV), end-systolic left ventricle diameter, end-diastolic left ventricle diameter, left ventricle free wall and septum thickness were determined based on the recommendations of the American Society of Echocardiography.[17] LV ejection fraction (EF) was calculated using the Teichhollz method.[18] Left atrial volume (LAV) was assessed using the biplane area-length method from apical 4 and 2-chamber views and indexed to body surface area.[19] LV mass was calculated using Devereux's formula and indexed to height to the power of 2.7 in order to obtain the LV mass index.[20] Peak TR velocity was measured to calculate the right ventricle-right atrium gradient using the modified Bernoulli equation [(TR jet velocity)^2 x 4].[21]

Diastolic function was assessed using pulsed Doppler of mitral inflow and pulsed-wave tissue Doppler imaging (PW-TDI).[22] Pulsed-wave Doppler was performed in the apical 4-chamber view, with a 2-mm sample volume placed between the mitral leaflet tips during diastole to record a crisp velocity profile at a sweep speed of 100 mm/s at end expiration. Peak early filling (E wave) and late diastolic filling (A wave) velocities, E/A ratio, deceleration time of early filling velocity and isovolumetric relaxation time (IVRT) were obtained for all patients. IVRT was measured from the end of the systolic wave to the onset of the mitral annular velocity pattern. PW-TDI was measured at the medial and lateral border of the mitral annulus and lateral border of the tricuspid annulus. The velocity of the S, A' and e' waves was measured. Mean values of septal and lateral e' waves were

obtained. The E/e' ratio was derived using mean values. The e'/A' ratio of the LV septal and lateral walls and right ventricle (RV) were also calculated. All measurements were the mean of three heartbeats.

Color Doppler myocardial imaging

Color Doppler-derived strain and strain rate (SR) were obtained by placing a 10-mm sample volume in the basal part of the six LV walls from the apical two, three and four chamber views.[23] The image sector was narrowed to allow the highest frame rate (>150 frames/sec) and the imaging angle to the wall was kept as low as possible to allow better parallel alignment to the wall of interest. Peak systolic strain and SR were measured in the basal segment of the six LV walls. Global strain and SR were obtained by dividing the sum of each longitudinal peak strain and SR by the number of walls. Strain and SR were also obtained for the RV at its basal free wall in the apical 4-chamber view (Figure 1).[24]

Speckle tracking analysis

Two-dimensional speckle tracking analysis was performed in acquired loops of the apical two, three and four chamber views with a frame rate above 40 frames/s. Speckle tracking analysis was performed in the basal, mild and apical segments in the two, three and four-chamber views for longitudinal strain. Longitudinal strain of the 18 segments of the LV walls was obtained with a 2D strain speckle tracking program (GE EchoPAC) that tracks myocardial movement. Segments were excluded if tracking remained insufficient despite manual adjustments.[25] The global 2D speckle tracking strain was calculated by adding the strain of all 18 segments and dividing the value by 18 (Figure 2).[26]

Outcomes and variables analyzed

The primary objective for the purpose of calculating the sample size considered in this study was to compare the LV longitudinal strain using color Doppler-derived strain between the two groups of pediatric patients (obese and non obese) based on previous studies of this variable, since there are no studies using the 2D speckle tracking for the analysis of LV function in obese pediatric patients.[12]. Thus, a sample of 45 patients in each group was calculated to provide a 90% power to detect a clinical effect of interest (decreased cardiac strain from

20% among grops) , with a significance level (alpha) of 0.05 (two-tailed).[27] The others variables studied were clinical data, Doppler echocardiographic parameters and PW-TDI values for the assessment of systolic and diastolic function. LV Doppler global strain and SR were compared between groups.

Statistical analysis

The Kolmogorov-Smirnov test was used to analysis the normality of the data in order to choose parametric vs. non-parametric tests. To characterize the sample, frequency distributions were used for qualitative variables and descriptive measures (mean, median, standard deviation) were used for quantitative variables. The Student's t-test was used for comparisons between groups when variables followed normal distribution and the Mann-Whitney test was used for non-Gaussian distribution. Pearson's correlation coefficients were calculated to determine correlations between variables. Multivariate stepwise linear regression analysis was performed to assess the adjusted correlations between 2D speckle tracking LV global strain, clinical and echocardiographic variables and the coeffient of determination was used to evaluate the accuracy of prediction. A significance level of 5% was considered on all statistical tests.[27] Intra-observer variability in strain and SR values was calculated in a sample of 20 randomly selected obese patients. Analyses were performed using the Statistical Package for Social Sciences version 18.0 (SPSS Inc., Chicago, IL, USA).

Results

Clinical characteristics

Ninety-six patients were recruited – 50 in the obese group (OG) and 46 lean individuals in the control group (CG). Table 1 displays the clinical and demographic data from subjects in both groups. Age, gender, fasting glucose, triglycerides and HDL-C were similar in both groups, whereas heart rate, total cholesterol and LDL-C were significantly higher in the OG. All patients were situated below the 90th percentile for systolic and diastolic blood pressure. However, mean systolic pressure and diastolic pressure were higher in OG.

Standard echocardiography and PW-TDI

LV diameter and mass corrected for height$^{2.7}$ were higher in the OG. The LA dimension and LAV indexed to body surface area were also significantly higher in the obese patients in comparison to the lean controls. No statistically significant difference in EF was detected between groups. The LV E/A ratio and the septal and lateral e'/A' ratio was significantly lower in the obese children . No statistically significant differences between groups were detected with regard to IRTV or E wave deceleration (Tables 2 and 3).

PW-TDI analysis of the mitral annulus revealed lower values in the OG with regard to lateral systolic peak velocity as well as septal and lateral A' . LV E/e' was similar in both groups . The RV e'/A' ratio was significantly lower in the OG (Table 3). Although within the normal range, RV-right atrium gradient (measured by TR jet velocity) was slightly higher in the OG.

Color Doppler myocardial imaging strain and SR

Global strain (obtained from averaging the basal segment strain in all six walls) was significantly lower in the obese patients. When the walls were evaluated separately, strain was found to be lower in the OG in the septal and lateral walls, while strain in the remaining walls did not differ significantly between groups (Table 4). No statistically significant differences between groups were detected with regard to SR of the six walls or global SR. RV strain and SR were significantly higher in the obese group.(Table 4)

Two-dimensional speckle tracking

Global longitudinal strain was significantly lower in the OG. Separate analysis of the LV walls revealed lower longitudinal strain in all walls (mean value of three segments of each wall) in the OG, except the posterior wall, for which values were similar in both groups.(Table 3)

Pearson's correlation and Multivariable analysis

The demographic and clinical variables, BMI, LV mass and LA index were correlated with 2D global strain. Age ($r = -0.323$, $p=0.025$) and BMI ($r = -0.433$ $p=0.002$) correlated negatively with 2D global strain and these variables were therefore incorporated into the multivariable model. In a multivariate linear

regression analysis in which all univariate correlated with LV global strain were considered, only BMI remained correlated with global 2D speckle tracking (p = 0.002) and with a determinant coefficient of 45.9% .(Figure 3)

Reproducibility

Intra-observer variability of 2D-global LV strain, RV strain and SR using intraclass correlation coefficient were 0.89[c], 0.92 [c] and 0.93 [c] respectively.

Discussion

The present study has shown that LV strain is reduced in obese children and adolescents when compared to controls, which may suggest incipient systolic involvement in obesity. Several mechanisms have been proposed to explain ventricular dysfunction, such as an increased mass in response to a larger intravascular volume, increased preload and increased afterload.[28]

LV mass

Obesity is independently associated with LV mass. The present study has shown that this association holds true in children with a BMI above the 95th percentile. The increase in LV mass occurs to compensate the higher hemodynamic load in obese patients.[8,29] Moreover, LV hypertrophy is an early marker in the sequence of cardiac events [30] , but in the univariate analysis, did not correlated with 2D- speckle tracking. The present study did not aim to characterize the cardiac hypertrophy, however eccentric hypertrophy is the most common form, even with associated hypertension.[11,31]

LV systolic function in obesity

In adults, a number of studies have shown systolic and diastolic dysfunction with the use of conventional Doppler echocardiography.[32] However, some studies have failed to detect abnormalities with conventional indices of systolic function, such as EF.[33] Therefore, this may not be a good index to express systolic function in obesity, which is known to be associated with increased in preload and afterload.[8] With the introduction of new techniques, such as TDI, strain and SR, incipient systolic dysfunction has been described in obesity.[34] Tumuklu *et al.*[29] found subclinical changes in left ventricular systolic function detected by strain and

SR imaging. In a studying involving morbidly obese patients, Barbosa *et al.*[3] report a decrease in lateral S velocity of the LV and RV strain detected by PW-TDI.

In pediatric patients, Lorch *et al.*[10] and Di Salvo *et al.*[12] studied the cardiac effect of obesity in non-hypertensive children and also found similar results to those reported for adults, suggesting that obesity exerts an early effect on ventricular function. In the present study, conventional indices of systolic function, such as EF, did not differ between the obese and non-obese patients, whereas LV strain was found to be lower in the obese children and adolescents. Using the CDMI technique, basal strain was significantly lower in the obese patients only in the septal and lateral walls (Table 4). Unlike PW-TDI, CDMI has the advantage of discriminating between active and passive cardiac motion, but is angle-dependent and requires good quality images, thereby hindering the acquisition of reliable, reproducible results. On the other hand, 2D speckle tracking is considered a more robust technique and easier to use than both PW-TDI and CDMI.[35] In the present study, 2D speckle tracking was able to detect lower strain in the obese patients in all walls, except the posterior. Global 2D speckle tracking was clearly lower in the obese group ($p < 0.001$) (Table 5).

LV diastolic function in obese individuals

Diastolic dysfunction has been reported in adult obese patients, especially when obesity is associated with metabolic syndrome, and may lead to atrial dysfunction.[36,37] Sharpe *et al.*[38] found obesity to be correlated with diastolic dysfunction in children and adolescents, once again suggesting that LV diastolic dysfunction may be an early finding in obesity. Dhuper *et al.*[11] found diastolic dysfunction using PW-TDI. In the present study, the E/A ratio was significantly lower in the obese group , which may be an indication that an incipient abnormal relaxation pattern is present even in the early stage. Since obesity leads to LV hypertrophy, it seems reasonable to speculate that obese children may have a tendency toward impaired myocardial relaxation. In fact, in the present study, LV mass was higher in obese group than in controls. A decreased e' is recognized as one of the markers of diastolic dysfunction.[39] In the present study, however, neither e' nor the E/e' ratio differed between groups. The E/e' ratio is load independent and can be used to predict filling pressures.[22] Since an abnormal E/e' ratio is associated with elevated filling pressure, it is not surprising that this ratio remains

within the normal range in obese children, in whom increased mass and incipient LV dysfunction have not been present long enough to increase filling pressure.

Obesity in adults and metabolic syndrome have been linked with RV dysfunction in previous studies. Using PW-TDI imaging, Wong *et al.,*[24] Tadic *et al.*[40] and Surucu *et al.*[41] found right ventricular dysfunction to be present in obesity. Using CDMI, Barbosa *et al.*[3] established incipient right ventricular dysfunction in morbid obesity. Di Salvo *et al.*[12] also describe right ventricular dysfunction in non-hypertensive obese children, which was not found in the present study. The systolic RV parameter (S) was similar in both groups when assessed using PW-TDI. However, the strain and SR values were significantly higher in the OG. Since this is different from the findings in obese adults,[3,36] it may be that systolic RV function is not an early abnormality in obesity and only develops in long-standing obesity. PW-TDI RV systolic velocity and strain correlate well with invasively determined right ventricular stroke volume.[42,43] Thus, another possible explanation for the increased RV strain and SR is that the incipient systolic dysfunction in obese children is initially masked by the hyperdynamic state present in obesity and that RV dysfunction is only detected by these techniques later on in obesity. Moreover, although RV pressure was higher in the OG, pulmonary hypertension, which is potentially involved in RV dysfunction, was not present in these individuals. The RV ‘e’/A ratio was significantly lower in the OG, which suggests an incipient impaired myocardial relaxation pattern in these children and adolescents.

Limitations of the study

The usual limitations about strain and SR angle dependence and the highly speckle tracking requirement on image quality should be considered.

Conclusion

The present study demonstrated that obesity in children, even in the absence of other comorbidities, is associated with decreased left ventricular myocardial deformation, as demonstrated by the use of new imaging techniques, such as CDMI and 2D speckle tracking. BMI correlated negatively with global 2D speckle tracking. The hyperdynamic state in obesity may explain the higher RV strain and SR values found in obese children and adolescents. The detection of incipient LV dysfunction in obese children may be further important evidence to

stimulate physicians and health policies to strongly fight obesity in this population.

Disclosure

The authors have no relationship with industry or other conflicts of interest to declare.

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Table 1: Demographic and clinical data

Parameters	***Obese (n=50)***	***Control (n=46)***	***p-value***
Age (years)	11.7±3.4	11.5±3.1	0.409
Height (cm)	151.8±14.5	144.5±18.6	0.034
Weight (Kg)	71.0±22.7	38.3±14.0	<0.001
BMI (Kg/m^2)	29.9±5.4	17.7±2.6	<0.001
SBP (mmHg)	97.2±13.0	90.5±10.0	0.007
DBP (mmHg)	63.0±10.0	58.1±6.3	0.006
HR (bpm)	80.4±11.8	74.3±8.3	0.011
F. glucose (mg/dl)	83.1±7.9	82.6±5.9	0.765
Totalcholesterol(mg/dl)	172.9±43.0	143.0±31.6	0.003
HDL-C mg/dl	43.1±10.8	46.3±9.2	0.213
LDL-C mg/dl	102.5±28.6	83.07±28.9	0.008
Triglycerides mg/dl	89.5±31.3	76.0±23.8	0.095

Legend: bpm = beats per minute; DBP = diastolic blood pressure; F = female; HR = heart rate; BMI = body mass index; M = male; SBP = systolic blood pressure; DBP = diastolic blood pressure; F. glucose (fasting glucose)

Table 2: Echocardiographic parameters in obese and healthy controls

M mode	***Obese (n=50)***	***Control (N = 46)***	***P-value***
LVd (mm)	44.5±4.6	40.7±5.6	<0.001
LVs (mm)	27.5±3.4	25.9±3.3	0.020
EF (%)	68.2±6.2	68.3±5.3	0.931
Ao (mm)	25.3±3.4	22.6±3.1	<0.001
LAd (mm)	31.4±4.0	27.1±4.4	<0.001
LAV (ml)	34.2 ± 11.7	27.0 ± 10.8	0.001
LAVi (ml/m2)	14.8±1.3	11.4±1.3	<0.001
VS (mm)	8.8 ± 1.5	8.8 ± 1.5	<0.001
PW (mm)	8.7 ± 1.4	7.1 ± 1.1	<0.001
LV mass/height$^{2.7}$	51.0 ± 10.8	40.3 ± 12.7	<0.001

Legend: LVd = left ventricular end diastolic diameter; LVs = left ventricular end systolic diameter; EF = ejection fraction (Teichholz method); Ao = ascending aortic diameter; LAd = left atrial diameter; LAVi = indexed left atrial volume; VS = ventricular septal end-diastolic thickness; PW = posterior wall end-diastolic thickness; LV mass/height$^{2.7}$ = indexed left ventricular mass

Table 3: Doppler, PW-TDI, CDMI strain and strain rate in healthy obese individuals

Parameters	*Obese (n=50)*	*Control (n=46)*	*p-value*
E (cm/s)	111.3±17.1	108.6±16.6	0.439
E/A	1.8 ± 0.5	2.1 ± 0.4	0.007
TRIV (m/s)	64.4± 6.5	62.5± 6.5	0.175
DT (m/s)	201.8±28.7	196.6±36.4	0.435
e' septal (cm/s)	13.3±1.7	13.4±1.7	0.997
A'septal (cm/s)	6.8±1.7	5.9±1.0	<0.001
S septal (cm/s)	8.1±1.0	7.8±1.0	0.128
e' lateral (cm/s)	18.2±3.4	19.1±2.8	0.530
A' lateral (cm/s)	7.7±2.0	6.6±1.4	0.012
e'/A' septal ratio	2.0±0.4	2.3±0.5	0.008
e'/A' lateral ratio	2.5±0.7	3.0±0.8	0.002
S lateral (cm/s)	9.8±2.2	10.8+1.9	0.018
E/e' ratio	7.1±1.4	6.7±1.1	0.498
LV G ST(%)	22.7±2.8	24.5±2.7	0.020
LV G SR(1/s)	1.7±0.2	1.9±0.3	0.114
RV e'(cm/s)	15.5±2.5	15.8±3.7	0.301
RV A'(cm/s)	10.4±2.6	8.9±1.9	0.004
RV e'/A'	0.9±0.4	1.2±0.3	0.007
RV S(cm/s)	13.8± 1.7	13.7± 1.6	0.655
RV ST (%)	29.3±5.4	25.7 ± 4.0	0.001
RV SR (1/s)	2.2±0.8	1.8± 0.5	0.027
RV/RA grad (mmHg)	20.7±3.7	19.1±3.4	0.041

Legend: A = A wave of the mitral inflow; A' septal = Tissue Doppler A' at septal mitral annulus; A' lateral = tissue Doppler A' at lateral mitral annulus; DT = deceleration time of E wave; e' septal = tissue Doppler e' at septal mitral annulus; e' lateral = tissue Doppler e' at lateral mitral annulus; E = E wave of mitral inflow; E/A = ratio of E wave of mitral inflow by A wave of mitral inflow; e'/A' septal= ratio of e' by A' of septal mitral annulus, e'/A' lateral= ratio of e' by A' of lateral mitral annulus, E/e' = ratio of E wave mitral inflow by mean e'; LV G ST= left ventricular global strain; LV G SR = left ventricular global strain rate; RV = right ventricular; RV A' = tissue Doppler A' at RV free wall; RV e' = tissue Doppler e' at RV free wall; RV e'/Á' = RV e' to A' ratio; RV S = systolic tissue Doppler velocity at tricuspid lateral annulus; RV ST = right ventricular Doppler based strain; RV SR = Doppler based RV strain rate; S lateral = systolic tissue Doppler velocity at mitral lateral annulus; RV/RA grad = right ventricle/right atrium gradient.

Table 4 : Longitudinal CDMI of strain(%)

Wall	***Obese (n=50)***	***Control (N = 46)***	***p-value***
Septal (%)	21.2±3.2	24.0±4.1	0.007
Lateral (%)	21.4±4.7	26.6±5.1	<0.001
Inferior (%)	21.1±4.9	22.3±6.1	0.309
Anterior (%)	25.5±6.9	28.2±5.1.	0.185
Posterior (%)	29.9±5.6	25.1±5.3	0.052
Anteroseptal (%)	21.8 ± 4.8	22.3 ± 4.2	0.690
Global (%)	22.0±2.8.	24.6±2.7	0.020

Legend: Septal = CDMI of basal segment of septal wall; Lateral = CDMI of basal segment of lateral wall; Inferior = CDMI of basal segment of inferior wall; anterior = CDMI of basal segment of anterior wall; posterior = CDMI of basal segment of posterior wall; Anteroseptal = CDMI of basal segment of anteroseptal wall; global = global basal CDMI

Table 5: Longitudinal 2D speckle tracking

Wall	***Obese (n=50)***	***Controls (N = 46)***	***P-value***
Septal (%)	19.3±2.7	20.7±2.4	0.009
(B,M,A)	N=48	N=46	
Lateral (%)	16.8±2.4	18.9±2.7	<0.001
(B,M,A)	N=43	N=43	
Inferior (%)	20.0±2.4	21.9±2.9	0.001
(B,M,A)	N=48	N=46	
Anterior (%)	18.3±2.7	21.8±3.0	<0.001
(B,M,A)	N=48	N=41	
Posterior (%)	17.8±2.6	18.8±2.6	0.064
(B,M,A)	N=46	N=45	
Anteroseptal (%)	17.9 ± 2.7	20.6 ± 2.8	<0.001
(B,M,A)	N=42	N=44	
Global (%)	18.4±1.6	20.4±1.7	<0.001
	N=48	N=46	

Legend: Septal = 2D speckle tracking of septal wall; Lateral = 2D speckle tracking of lateral wall; Inferior = 2D speckle tracking of inferior wall; anterior = 2D speckle tracking of anterior wall; posterior = 2D speckle tracking of posterior wall; Anteroseptal = 2D speckle tracking of anteroseptal wall; global = Global 2D speckle tracking; (B,M,A) = sum of basal segment (B), medial segment (M) and apical segment (A) / 3

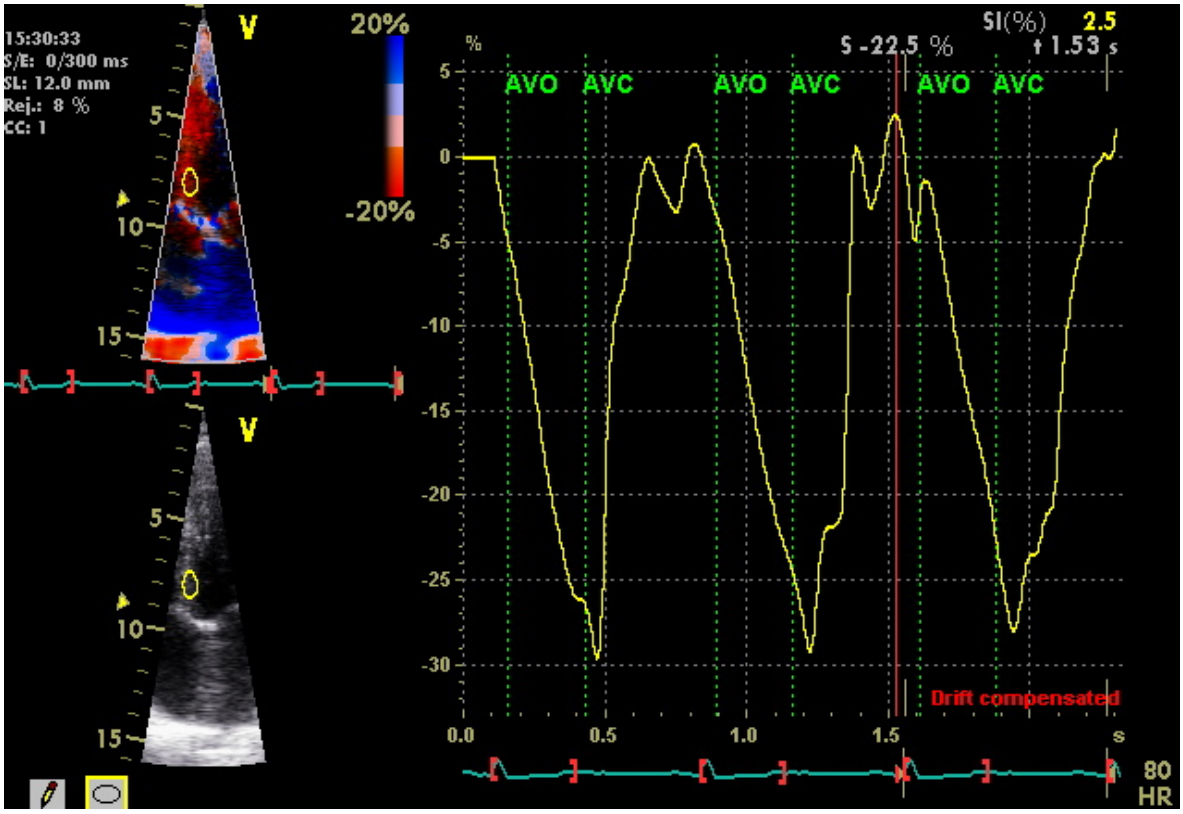

Figure 1: Color Doppler myocardial imaging of peak systolic strain obtained at basal segment of interventricular septum; narrowed sector enables maximal yield in frame rate (ideally>150/s), optimizing clarity and data acquisition

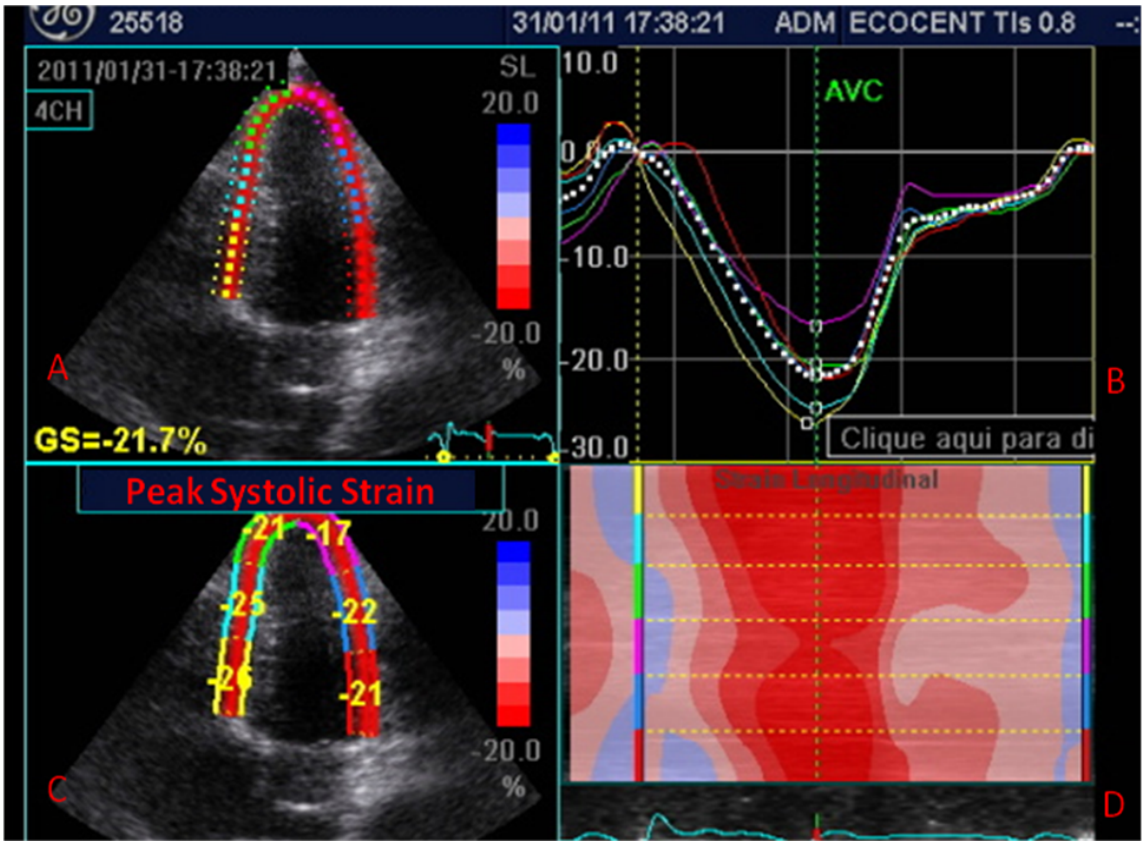

Figure 2: Two-dimensional strain (speckle tracking) of healthy patient. Apical 4-chamber view. A-Tracked apical loop of the six myocardial segments, GS= global strain B-Average segmental strain graphically displaced. C- Color display of peak systolic strain. D- M mode representation of peak systolic strain.

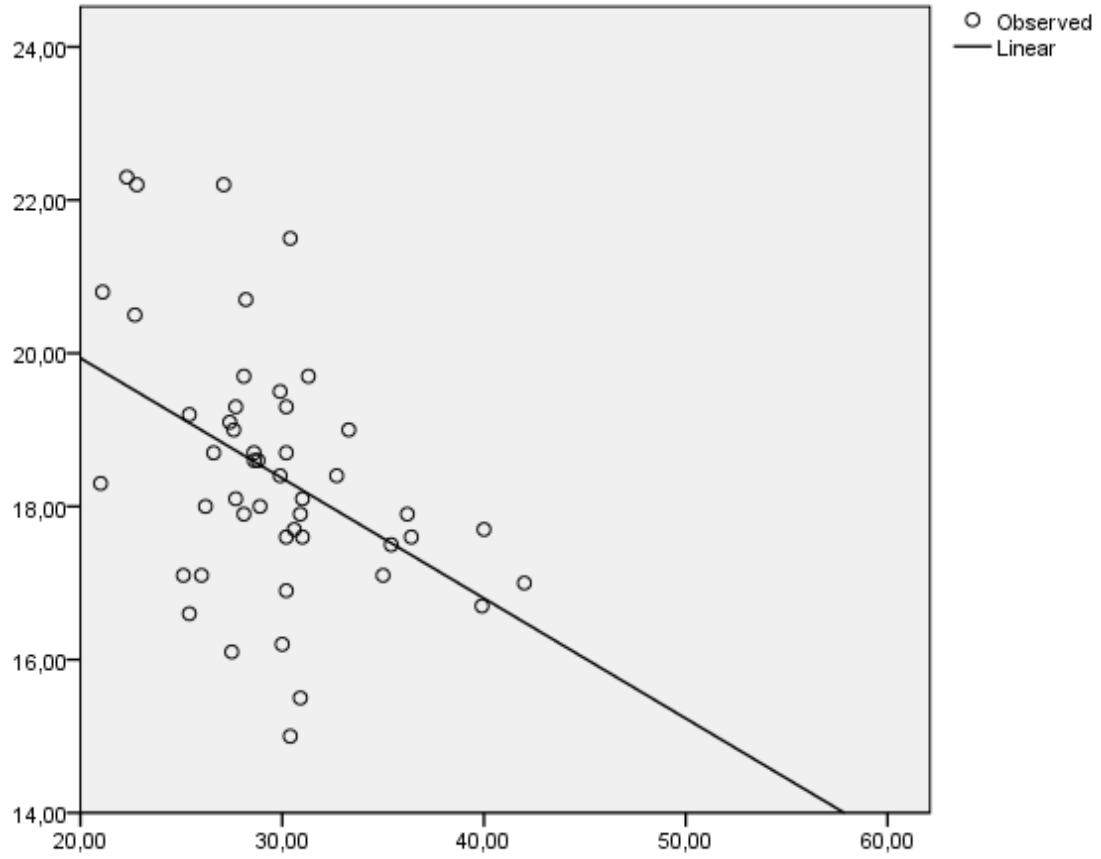

Figure 3: Correlation of global 2D speckle tracking (%) with the BMI (Kg/m^2) in obese group. Pearson correlation analysis, r= -0.433, P= 0.002 and a determinant coefficient of 45.9%.

6 CONSIDERAÇÕES FINAIS

A obesidade exógena, ou seja, devida ao excesso de gordura decorrente de um balanço positivo de energia entre ingestão e gasto calórico, é um fator de risco bem estabelecido para doenças metabólicas e cardiovasculares. Causas genéticas e o meio ambiente contribuem para esse risco. Recentes avanços aumentaram o entendimento do mecanismo celular no qual o tecido adiposo deixou de ser considerado apenas como um reservatório passivo de energia, passando, então, a assumir o papel de órgão endócrino com importante papel nos efeitos adversos locais e sistêmicos[1,2].

O IMC é uma ferramenta útil para avaliar gordura corpórea. Os valores de IMC correlacionam-se de forma segura com os riscos que a obesidade determina para a saúde, especialmente para os riscos cardiovasculares.[1] **Crianças com percentil de IMC abaixo de 85 estão associadas a baixo nível de complicações,** porém, quando o IMC está acima do percentil 95, o nível de gordura corporal está alto e os riscos são elevados[1]. A sensibilidade do percentil 95 de IMC para as curvas de crescimento do *Center of Disease Control and Prevention* (CDC)[3] para identificar crianças e adolescentes obesos em diversos estudos variou de 54 a 100%, com alta especificidade (96 a 99%) e valor preditivo positivo de 56 a 99%, concluindo que existem poucos pacientes com diagnóstico incorreto de obesidade utilizando o IMC como parâmetro[4].

A circunferência abdominal é utilizada principalmente em pacientes adultos como indicador de risco na síndrome metabólica.[1] Em crianças e adolescentes, comparando com o IMC, a circunferência abdominal fornece melhor estimativa da gordura visceral e prediz melhor os riscos para a saúde, especialmente em adolescentes. [1] Porém, sua capacidade de identificar obesidade não é maior que a do IMC e atualmente não existem guias específicos para sua aplicação clinica[4].

Obesidade e síndrome metabólica em adultos estão bem-estabelecidas, não existindo consenso em relação à definição de síndrome metabólica em crianças. Cook *et al.*[5] propuseram uma definição para adolescentes quando três ou mais dos seguintes fatores estão presentes: triglicérides ≥ 110 mg/dL, **colesterol HDL ≤ 40 mg/dL, IMC > percentil 95, glicose de jejum ≥110 mg/dL,**

pressão arterial ≥ percentil 90 para idade e altura[6,7]. A obesidade está associada ao estado de inflamação crônica e aumenta a morbidade e mortalidade na hipertensão, dislipidemia, diabetes *mellitus*, insuficiência cardíaca, doenças respiratórias, acidente vascular cerebral e doença coronariana[7].

Pacientes com IMC alto estão associados à história familiar positiva de doenças cardiovasculares. Aproximadamente um terço de crianças e adolescentes obesos, hipertensos ou não hipertensos apresenta história familiar positiva para doenças cardiovasculares como infarto agudo do miocárdio e acidente vascular cerebral[4].

A disfunção cardíaca subclínica em crianças e adolescentes obesos sem o diagnóstico de síndrome metabólica já está bem documentada[8,9] e é um processo que aumenta a morbidade e mortalidade, podendo ocorrer de forma lenta, crônica e precoce[9].

O diabetes *mellitus* tipo 2 tem aumentado de forma importante em adolescentes. Geralmente não acompanha os sintomas tais como poliúria e polidipsia, consequentemente, sua identificação requer avaliação laboratorial para crianças com risco. A hiperinsulinemia, um marcador de resistência à insulina, influencia a pressão sanguínea (através do sistema renina-angiotensina) e a concentração de lipoproteínas (via aumento da lipólise)[10]. Consequentemente, crianças e adolescentes com IMC acima do percentil 95 apresentam elevado risco de serem hipertensos e tornarem-se adultos hipertensos[11,12]. Em relação a concentrações de lipoproteínas, pacientes pediátricos obesos apresentam perfil lipídico desfavorável comparado com crianças e adolescentes com peso normal, incluindo altos valores de LDL-C e triglicérides e baixas concentrações de HDL-C. Além disso, estudos mostram que crianças obesas apresentam 50% de chance de apresentarem colesterol total aumentado[13]. O desenvolvimento lento da aterosclerose, um marcador de doenças cardiovasculares, acontece em uma fase precoce e está diretamente relacionado à concentração de lipoproteínas no plasma[14].

Além das alterações metabólicas e cardiovasculares, crianças obesas exibem elevado risco de alterações neurológicas como pseudotumor cerebral, desordens psicológicas, ressaltando-se depressão e ansiedade, alterações ortopédicas, apneia do sono e alterações cutâneas, como acantose *nigrans*[1].

O efeito da obesidade já pode estar relacionado com o período pré-natal. O aumento na incidência de diabetes gestacional, excesso de ganho de peso durante a gravidez, mães fumantes e gravidez na adolescência expõe mais fetos a um meio intrauterino obesogênico, levando futuramente a risco mais alto de obesidade, diabetes e outras doenças metabólicas[15,16].

Os cuidados ao paciente obeso devem basear-se em medidas que realcem os padrões de conduta que levem ao controle de peso, ou seja, resultem na modificação do comportamento no contexto individual e familiar. A prevenção é o caminho ideal em vez de se tentar reverter o quadro já estabelecido. Orientações na mudança de hábitos são de fundamental importância nesse processo. O estímulo ao aleitamento materno, o limite na ingestão de alimentos hipercalóricos, o aumento no consumo de frutas e vegetais, o estímulo a exercícios físicos e a redução de atividades sedentárias são os principais alvos no processo.[17] Atualmente, sendo o *fast food*, computadores e os jogos eletrônicos a rotina das crianças e adolescentes, não e fácil persuadir esses pacientes a mudanças de hábitos e estilo de vida. Vale ressaltar que a atividade física tem efeito terapêutico no perfil lipídico, principalmente no metabolismo de triglicérides e no HDL-C[1].

É necessário desenvolver programas usando crianças e adolescentes como público-alvo e utilizar abordagem multidisciplinar[17]. Pediatras devem estimular programas em comunidades e em escolas com a intenção de prevenir a obesidade. Influência familiar tem importante papel nesse contexto. Pais obesos têm o risco dobrado de terem filhos obesos na fase adulta, mesmo quando não obesos quando crianças[18].

Todas as crianças e adolescentes com diagnóstico de obesidade, dependendo da gravidade do quadro, devem ser submetidos a exames de rastreamento para doenças metabólicas, endócrinas e exames de imagem para detectar disfunção cardíaca, vascular e polissonografia para o diagnóstico da apneia do sono[4].

O ecoDopplercardiograma é uma ferramenta clínica, não invasiva e bem estabelecida para analisar função ventricular direita e esquerda regional e global. Utilizando novos métodos de análise de função cardíaca, como *strain* Doppler e *speckle tracking* bidimensional, o presente estudo demonstrou que a obesidade está associada à diminuição dos índices de contratilidade do ventrículo esquerdo e que essas alterações incipientes na função ventricular são um achado precoce

na obesidade, podendo ocorrer já na infância e na ausência de comorbidades associadas.

A universalização desses novos métodos diagnósticos abre novas perspectivas na abordagem aos pacientes obesos, permitindo detectar de forma precoce disfunção cardíaca subclínica e tratá-los antes que evoluam para a forma mais estabelecida da doença.

Em relação ao tratamento, deve ter implicações no cuidado primário e em ambientes terciários. O cuidado à criança e adolescentes obesos é de difícil abordagem, requer tempo, pode ser frustrante e custoso. O objetivo principal é estabelecer hábitos saudáveis, estruturar planos para manejo do peso com dietas de baixo valor calórico e, raramente, abordagem medicamentosa ou cirúrgica[18]. A obesidade é uma doença crônica, então, esses pacientes necessitam de *follow-up* mesmo após perda de peso e uma variedade de estratégias deve ser desenvolvida para manutenção do peso saudável. A detecção de disfunção ventricular esquerda precoce em crianças e adolescentes obesos reforça que o pediatra deve intervir de forma preventiva e precoce, no sentido de reduzir a ocorrência das formas mais graves na vida adulta.

Concluindo, para os milhares de pessoas que já são obesas, existe acentuada necessidade de tratamentos mais eficazes para a perda de peso. A implementação de protocolos para tratar esses pacientes deve ser estabelecida por médicos, nutricionistas, especialistas em atividades físicas e proporcionar extenso suporte familiar. O entendimento da relação entre obesidade e o desenvolvimento de condições médicas associadas pode também auxiliar na melhora da saúde, independentemente da perda de peso. O melhor entendimento de vários fatores causais que levam à obesidade e suas cormorbidades permitirá o desenvolvimento de terapias mais específicas e mais efetivas[15,19].

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ANEXOS E APÊNDICES

ANEXO A – Parecer ético

CÂMARA DO DEPARTAMENTO DE PEDIATRIA – FM - UFMG

Parecer 67/08

Título do Projeto: Avaliação cardíaca da função sistólica e diastólica pelo Doppler tecidual em crianças e adolescentes portadores de obesidade.

Interessados:
Cleonice de Carvalho Coelho Mota
Henrique de Assis Fonseca Tonelli
José Augusto Almeida Barbosa

Histórico:

O estudo enfoca a questão da obesidade infantil cuja prevalência tem aumentado em várias regiões do mundo, inclusive no Brasil. Dados do IBGE mostram que a prevalência aumentou de 4% para 18% nos últimos trinta anos para crianças e adolescentes. Dentre as conseqüências da obesidade podem citar maior risco para desenvolvimento da síndrome metabólica, diabetes mellitus tipo II, hipertensão arterial, dislipidemia, alterações hepáticas e alterações cardíacas. A obesidade é vista como uma doença crônica e associada com estas alterações.

Estudos mostram alterações cardíacas em crianças e adolescentes com obesidade, comparados com eutróficas, que podem ser identficadas pelo Doppler tissular para avaliação da função sistólica e diastólica. Deste modo, pelos efeitos da obesidade a longo prazo, uma avaliação precoce da disfunção ventricular, sistólica e/ou diastólica e o Doppler tissular pode ser um método útil e fornecer informações clínicas importantes. A medida da massa do ventrículo esquerdo é importante para o diagnóstico de hipertrofia em crianças com doenças cardiovasculares e um bom parâmetro para avaliar hipertrofia induzida pela obesidade e hipertensão arterial sistêmica.

O estudo propõe avaliar a função ventricular sistólica e diastólica em crianças e adolescentes portadores de obesidade atendidos nos ambulatórios de Nutrologia Pediátrica e de Cardiologia Pediátrica do HC da UFMG. Portanto, o estudo poderá trazer maior contribuição para o conhecimento sobre o tema bem.

Mérito:

Trata-se de um estudo transversal que inclui uma amostra de conveniência de pacientes com obesidade, atendidos no Ambulatório de Nutrologia Pediátrica do Hospital das Clinicas da UFMG, no período de janeiro de 2009 a dezembro de 2010. Da amostra serão incluídas somente crianças e adolescentes na faixa etária de 5-19 anos. As crianças com idade igual ou inferior a 4 anos não serão incluídas em virtude da necessidade de sedação para realizar o exame.

Os pacientes serão pareados por sexo e idade com um grupo de crianças e adolescentes eutróficos (controle). Estes pacientes serão recrutados no Ambulatório de Cardiologia Pediátrica (Sopro Inocente).

Serão constituídos três grupos: pacientes obesos; obesos que perderam peso durante o estudo; e grupo controle. Os pacientes com obesidade serão subdivididos em 4 grupos, em função da presença de hipertensão arterial sistêmica e alteração do perfil lipídico. Serão verificadas as seguintes situações: obesidade e ausência de alterações (hipertensão e perfil lipidico); obesidade e alterações do perfil lipidico; obesidade com hipertensão arterial sistemica; obesidade e associações com hipertensão arterial e obesidade.

Os pesquisadores envolvidos na pesquisa possuem experiência e competência para realizar os procedimentos técnicos e outros procedimentos previstos na metodologia.

Fontes financiadoras:

Os pesquisadores pretendem enviar o projeto para agencias financiadoras de pesquisa para recursos a serem destinados para realização dos exames, segundo as normas da DEPE-HC.

O aparelho para realização do Eco-Dopplercardiograma com fluxo em cores já está disponível na Faculdade de Medicina da UFMG.

Aspectos éticos:

Os pesquisadores se comprometem a divulgar os resultados sob forma de artigos, apresentações em congressos e uma tese de doutorado. Os dados gerados serão de uso exclusivo em pesquisa. Não há riscos para os participantes. Os benefícios da pesquisa são decorrentes de melhor conhecimento sobre o tema investigado e sua aplicação na prática clínica médica no acompanhamento dos pacientes obesos.

No TCLE está descrito que os pacientes podem se desligar da pesquisa sem prejuízo, ficando garantida a continuidade do tratamento convencional e assistência médica. Os pacientes no grupo controle, se apresentarem alguma alteração no exame, serão excluídos do estudo e encaminhados para completar a propedêutica e tratamento.

Parecer:

Pela aprovação do projeto.

Joel Alves Lamounier
01/10/2008

UNIVERSIDADE FEDERAL DE MINAS GERAIS
COMITÊ DE ÉTICA EM PESQUISA - COEP

Parecer nº. ETIC 130/09

Interessado(a): Profa. Cleonice de Carvalho Coelho Mota
Departamento de Pediatria
Faculdade de Medicina - UFMG

DECISÃO

O Comitê de Ética em Pesquisa da UFMG – COEP aprovou, no dia 31 de março de 2010, a inclusão da coleta de sangue e a dosagem de adiponectinas nos sujeitos do projeto de pesquisa intitulado **"Avaliação cardíaca da função sistólica e diastólica pelo Doppler tecidual em crianças e adolescentes portadores de obesidade"** bem como o Termo de Consentimento Livre e Esclarecido.

O relatório final ou parcial deverá ser encaminhado ao COEP um ano após o início do projeto.

Profa. Maria Teresa Marques Amaral
Coordenadora do COEP-UFMG

Av. Pres. Antonio Carlos, 6627 – Unidade Administrativa II - 2° andar – Sala 2005 – Cep:31270-901 – BH-MG
Telefax: (031) 3409-4592 - e-mail: coep@prpq.ufmg.br

Universidade Federal de Minas Gerais
Hospital das Clínicas
Diretoria de Ensino, Pesquisa e Extensão

DECLARAÇÃO

Declaramos para fins de comprovação no Comitê de Ética e Pesquisa em Seres Humanos – COEP/UFMG que o projeto de pesquisa intitulado, **"AVALIAÇÃO CARDÍACA DA FUNÇÃO SISTÓLICA E DIASTÓLICA PELO DOPPLER TECIDUAL EM CRIANÇAS E ADOLESCENTES PORTADORES DE OBESIDADE"** de responsabilidade da Profª Cleonice de Carvalho Coelho Mota, foi recebido na Diretoria de Ensino, Pesquisa e Extensão/HC-UFMG para registro e avaliação.

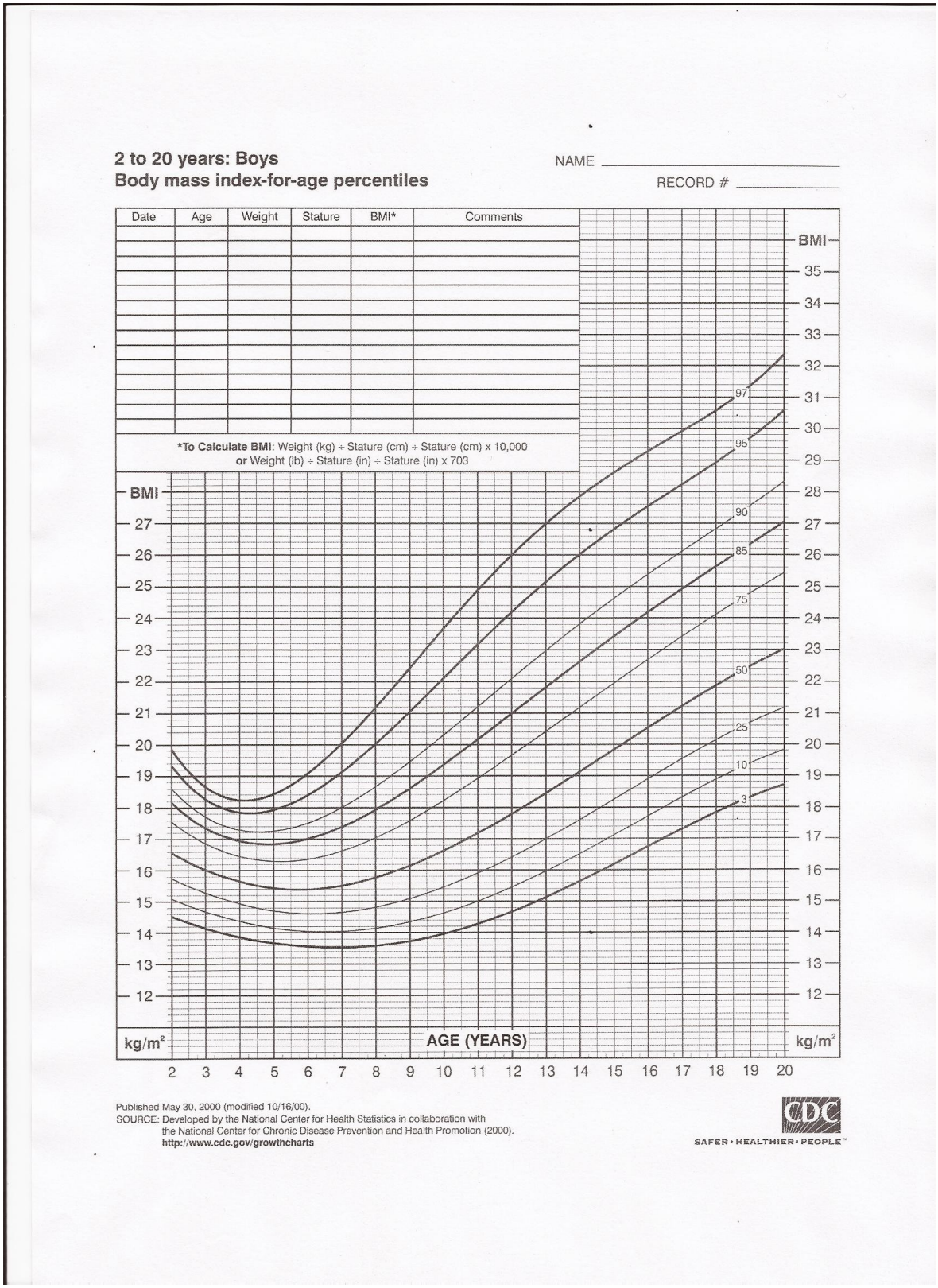
Belo Horizonte, 0342 de abril de 2009.

Elzi do Carmo Cota
Secretária da DEPE/HC-UFMG

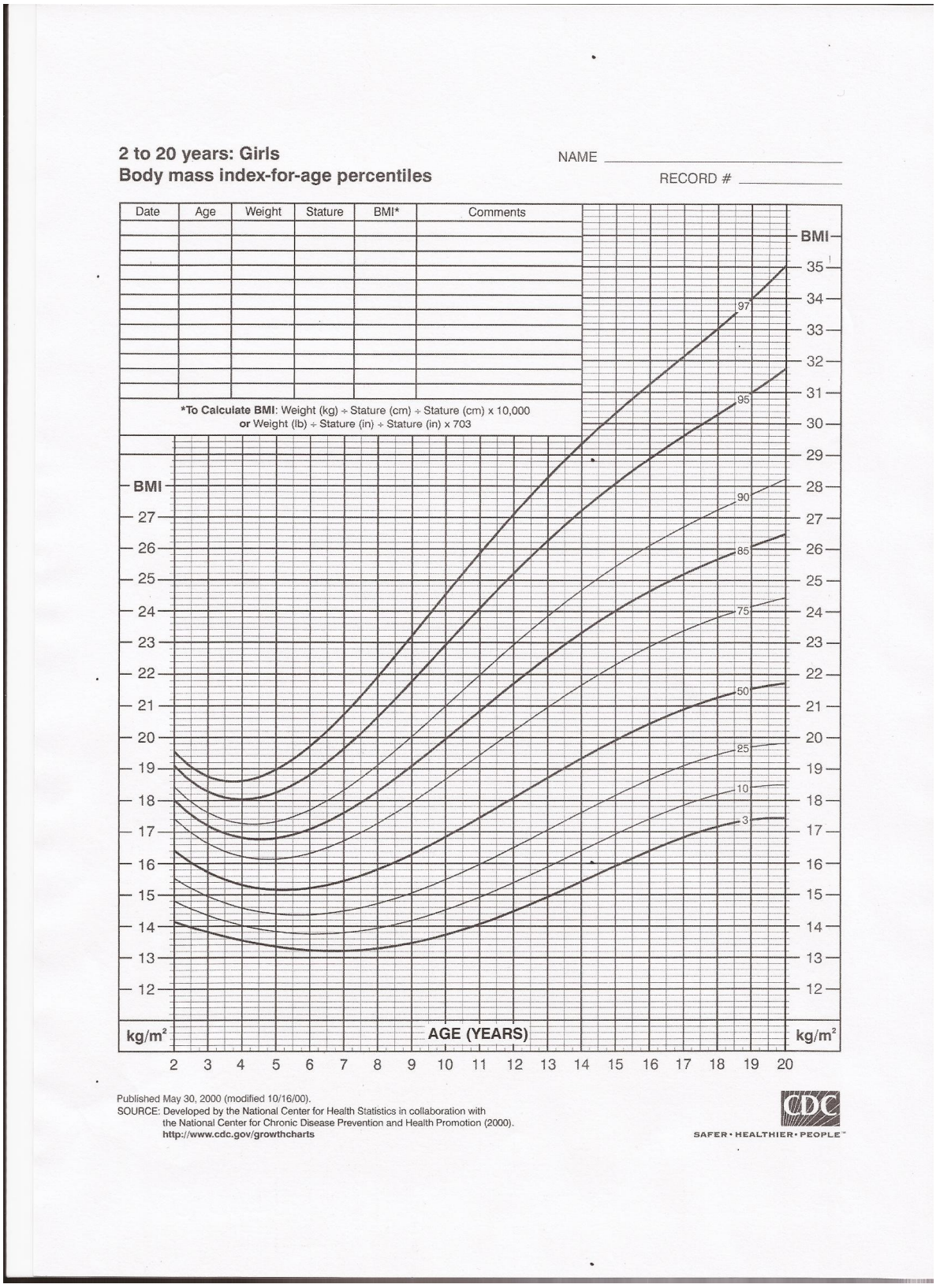
Av. Prof. Alfredo Balena, 110 – 1º andar – ala leste
Bairro Santa Efigênia - CEP 30130.100 – Belo Horizonte – MG
Telefones: 31-3409-9375 / 3409-9379 - FAX 31-3409-9380 – depe@hc.ufmg.br

ANEXO B - Curvas IMC

Meninos



Meninas


2 to 20 years: Girls
Body mass index-for-age percentiles
NAME
RECORD #
Date
Age
Weight
Stature
BMI*
Comments
*To Calculate BMI: Weight (kg) ÷ Stature (cm) ÷ Stature (cm) x 10,000
or Weight (lb) ÷ Stature (in) ÷ Stature (in) x 703
BMI
kg/m²
AGE (YEARS)
97
95
90
85
75
50
25
10
3
Published May 30, 2000 (modified 10/16/00).
SOURCE: Developed by the National Center for Health Statistics in collaboration with the National Center for Chronic Disease Prevention and Health Promotion (2000).
http://www.cdc.gov/growthcharts
SAFER · HEALTHIER · PEOPLE™

ANEXO C - Carta de aceitação do artigo de revisão (*Vascular Health Risk and Management*)

Para: jalmeidabarbosa@uol.com.br
Assunto: Dove Medical Press: Submission accepted for publication
Enviada: 13/05/2011 18:58

Dear Dr Barbosa,

I am pleased to inform you that your submission, "Cardiovascular dysfunction in obesity and role of new diagnostic imaging techniques - the role of the non-invasive image methods", has been accepted for publication in "Vascular Health and Risk Management". The publication processing is accessible here:
http://www.dovepress.com/invoice.php?pa=edit&invoice_id=2979&l=QzZDZXrsUgbRnPxDjB1JcGMw117485
(Please note that you can modify your address on the invoice if necessary.)

Your manuscript will be sent for copy editing (if you have requested it) and typesetting. After typesetting has been completed author proofs will be sent to you for you to correct as needed. We will then send your corrections to be incorporated into the author proofs by the typesetter. You have the option of reviewing the corrected proofs again or we will publish your manuscript immediately after the corrected proofs have been received.

You will be notified that your paper has been published and subscribers to the new article notification service for the journal your paper is published in will also be informed.

If you have any questions about the production process please contact us at any time. We also welcome your feedback.

Yours sincerely

Jeanette Pearce
Dove Medical Press
www.dovepress.com - open access to scientific and medical research
17801

APÊNDICE A - Protocolo de pesquisa

Protocolo obesidade infantil

Número : **DVD:** **Data :** _____/_____/_____

		Idade :	Percentil IMC:
Rua :		Cidade :	CEP :
Telefone:	Peso: |__|__|__|	Altura: : |__|__|__|	Sup Corpórea: : |__|__|__|
Data Nascimento : ____/____/____	PA: _____/_____	Responsável:	

PA |__/__| mmHg

Percentil Pressão sistólica:

Percentil Pressão diastólica:

Perfil lipídeo data:- ----------

Triglicérides mg/dl:

Colesterol total mg/dl:

LDL:

HDL:

Glicemia de jejum mg/dl:

Outras doenças _____

Medicamentos _____

FC	____	IM :	__	El' (cm/s)	___.__
VD (mm)	___	IAo :	__	Al'(cm/s)	___.__
VEd (mm)	___	IT :	__	Sl (cm/s)	___.__
VEs (mm)	___	Vel IT	___	**Frame Rate Strain Bid**	___.__
SIV (mm)	___	Grad RT	___	Strain bid S basal	-___.__
PP (mm)	___	**Frame rate TD**	___	Strain bid S med	-___.__
FE (%)	___	**Strain VE**		Strain bid S apic	-___.__
FS (%)	___	Strain basal S	-___.__	Strain bid L basal	-___.__
Ao (mm)	___	Strain basal L	-___.__	Strain bid L med	-___.__
AE (mm)	__	Strain basal I	-___.__	Strain bid L apic	-___.__
VAE	____	Strain basal A	-___.__	Strain bid I basal	-___.__
VD		Strain basal P	-___.__	Strain bid I med	-___.__
Strain VD(%)	____	Strain basal AS	-___.__	Strain bid I apic	-___.__
SR VD	__.___	**Strain Rate VE**		Strain bid A basal	-___.__
E' VD (cm/s)	___.__	SR basal S	-__.___	Strain bid A med	-___.__
A' VD(cm/s)	___.__	SR basal L	-__.___	Strain bid A apic	-___.__
S VD (cm/s)	___.__	SR basal I	-__.___	Strain bid P basal	-___.__
Valva Mitral		SR basal A	-__.___	Strain bid P med	-___.__
E VE (cm/s)	____	SR basal P	-__.___	Strain bid P apic	-___.__
A VE (cm/s)	____	SR basal AS	-__.___	Strain bid AS basal	-___.__
DT (ms)	____	Es' (cm/s)	___.__	Strain bid AS méd	-___.__
Triv (ms)	____	As' (cm/s)	___.__	Strain bid AS apic	-___.__
Reg Valvar: 1-Aus 2- L 3-Mod 4-Imp		Ss (cm/s)	___.__		

APÊNDICE B - Termo de consentimento

Crianças até 6 anos

Por meio deste termo de consentimento, informamos que estamos desenvolvendo uma pesquisa no Hospital das Clínicas da UFMG para estudar o efeito da obesidade no coração da criança, pois alguns estudos mostram que crianças obesas podem ter problemas no coração.

Este estudo quer, então, por meio do ecoDopplercardiograma (exame que avalia a função cardíaca e o tamanho do coração), analisar se realmente as crianças obesas têm alterações no coração.

Esse exame, que é um ultrassom do coração e tem duração de aproximadamente 45 minutos, é indolor, não invasivo e não requer qualquer tipo de sedação.

Esse exame poderá ser feito novamente após a perda de peso, se for de sua vontade.

O exame do coração somente será realizado após sua autorização e assinatura neste termo de consentimento.

Garantimos, ainda, que serão resguardadas sua identidade e privacidade e que os resultados deste estudo somente serão utilizados para os fins de pesquisa com objetivo de aumentar os conhecimentos da Medicina.

Os custos de transporte até a clínica onde o exame será realizado serão pagos pelos pesquisadores.

Finalmente, você tem o direito de recusar a participar do trabalho em qualquer etapa, sabendo-se que continuará a receber o tratamento convencional, tendo, assim, garantidos sua assistência médica e o controle médico que está realizando no Hospital das Clínicas.

Nome dos pesquisadores: José Augusto Almeida Barbosa

Cleonice de Carvalho Coelho Mota

Endereço: Presidente Antônio Carlos, 6.627, Unidade Administrativa II. 2º andar, sala 2005. CEP: 31270-901-BH-MG telefax (031)3409-4592, coep@prpq.ufmg.br
Endereço do pesquisador: Estrada de Nova Lima, 345/703 - Belvedere. Belo Horizonte CEP- 30320-760.

Eu, _____, responsável pelo paciente_____, entendi tudo que foi explicado sobre essa pesquisa e concordo em participar. Este estudo será feito pelo Dr. José Augusto Almeida Barbosa do Hospital das Clínicas da UFMG. Confirmo que fui selecionado de forma voluntária para participar desta pesquisa. Eu assinei e recebi uma cópia deste termo de consentimento.

Eu,_____, responsável pelo paciente _____, entendi tudo que foi explicado sobre esta pesquisa e concordo em permitir a participação do menor _____ para a avaliação ecocardiográfica.

Este estudo será feito pelo Dr. José Augusto Almeida Barbosa, do Hospital das Clínicas da UFMG. Confirmo que o paciente _____foi selecionado de forma voluntária para participar desta pesquisa. Eu assinei e recebi uma cópia deste termo de consentimento.

Data e local:_____

Assinatura do responsável:

Assinatura do pesquisador:

Crianças de 7 a 12 anos (paciente)

Por meio deste termo de consentimento, informamos que estamos desenvolvendo uma pesquisa no Hospital das Clínicas da UFMG para estudar o efeito da obesidade no coração da criança, pois alguns estudos mostram que crianças obesas podem ter problemas no coração.

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Finalmente, você tem o direito de recusar a participar do trabalho em qualquer etapa, sabendo-se que continuará a receber o tratamento convencional, tendo, assim, garantidos sua assistência médica e o controle médico que está realizando no Hospital das Clínicas.

Os custos de transporte até a clínica onde o exame será realizado serão pagos pelos pesquisadores.

Nome pesquisadores: José Augusto Almeida Barbosa

Cleonice de Carvalho Coelho Mota

Endereço: Presidente Antônio Carlos, 6.627, Unidade Administrativa II. 2º andar, sala 2005. CEP: 31270-901-BH-MG telefax (031)3409-4592, coep@prpq.ufmg.br.
Endereço do pesquisador: Estrada de Nova Lima, 345/703 Belvedere. Belo Horizonte CEP: 30320760.

Eu, paciente_____, entendi tudo que foi explicado sobre esta pesquisa e concordo em participar. Este estudo será feito pelo Dr. José Augusto Almeida Barbosa, do Hospital das Clínicas da UFMG. Confirmo que fui selecionado de forma voluntária para participar desta pesquisa. Eu assinei e recebi uma cópia deste termo de consentimento.

Eu,_____, responsável pelo paciente _____, entendi tudo que foi explicado sobre esta pesquisa e concordo em permitir a participação do menor _____ para a avaliação ecocardiográfica.

Este estudo será feito pelo Dr. José Augusto Almeida Barbosa, do Hospital das Clínicas da UFMG. Confirmo que o paciente _____foi selecionado de forma voluntária para participar desta pesquisa. Eu assinei e recebi uma cópia deste termo de consentimento.

Data e local:_____

Assinatura do responsável:

Assinatura do paciente:

Assinatura do pesquisador:

Crianças de 13 a 17 anos (pais)

Por meio deste termo de consentimento, informamos que estamos desenvolvendo uma pesquisa no Hospital das Clínicas da UFMG para estudar o efeito da obesidade no coração da criança, pois alguns estudos mostram que crianças obesas podem ter problemas no coração.

Este estudo quer, então, por meio do ecoDopplercardiograma (exame que avalia a função cardíaca e o tamanho do coração), analisar se realmente as crianças obesas têm alterações no coração.

Este exame, que é um ultrassom do coração e tem duração de aproximadamente 45 minutos, é indolor, não invasivo e não requer qualquer tipo de sedação.

O exame do coração somente será realizado após sua autorização e assinatura neste termo de consentimento.

Este exame poderá ser feito novamente após a perda de peso, se for de sua vontade.

Garantimos, ainda, que serão resguardadas sua identidade e privacidade e que os resultados deste estudo somente serão utilizados para os fins de pesquisa com objetivo de aumentar os conhecimentos da Medicina.

Finalmente, você tem o direito de recusar a participar do trabalho em qualquer etapa, sabendo-se que continuará a receber o tratamento convencional, tendo, assim, garantidos sua assistência médica e o controle médico que está realizando no Hospital das Clínicas.

Os custos de transporte até a clínica onde o exame será realizado serão pagos pelos pesquisadores.

Nome pesquisadores: José Augusto Almeida Barbosa

Cleonice de Carvalho Coelho Mota

Endereço: Presidente Antônio Carlos, 6.627, Unidade Administrativa II. 2º andar, sala 2005. CEP: 31270-901-BH-MG telefax (031)3409-4592, coep@prpq.ufmg.br
Endereço pesquisador: Estrada de Nova Lima, 345/703 Belvedere. Belo Horizonte CEP: 30320760.

Eu, responsável pelo paciente_____, entendi tudo que foi explicado sobre esta pesquisa e concordo em participar. Este estudo será feito pelo Dr. José Augusto Almeida Barbosa, do Hospital das Clínicas da UFMG. Confirmo que fui selecionado de forma voluntária para participar desta pesquisa. Eu assinei e recebi uma cópia deste termo de consentimento.

Eu,_____, responsável pelo paciente _____, entendi tudo que foi explicado sobre esta pesquisa e concordo em permitir a participação do menor _____ para a avaliação ecocardiográfica.

Este estudo será feito pelo Dr. José Augusto Almeida Barbosa, do Hospital das Clínicas da UFMG. Confirmo que o paciente _____foi selecionado de forma voluntária para participar desta pesquisa. Eu assinei e recebi uma cópia deste termo de consentimento.

Data e local:_____

Assinatura do responsável:

Assinatura do pesquisador:

Crianças de 13 a 17 anos (paciente)

Por meio deste termo de consentimento, informamos que estamos desenvolvendo uma pesquisa no Hospital das Clínicas da UFMG para estudar o efeito da obesidade no coração da criança, pois alguns estudos mostram que crianças obesas podem ter problemas no coração.

Este estudo quer, então, por meio do ecoDopplercardiograma (exame que avalia a função cardíaca e o tamanho do coração), analisar se realmente as crianças obesas(gordinhas) têm alterações no coração.

Este exame, que é um ultradsom do coração e tem duração de aproximadamente 45 minutos, é indolor, não provoca dor e não requer qualquer tipo de remédio.

O exame do coração somente será realizado após sua autorização e assinatura neste termo de consentimento (esta folha).

Este exame poderá ser feito novamente após a perda de peso, se for de sua vontade.

Garantimos ainda que serão resguardadas sua identidade e privacidade e que os resultados deste estudo somente serão utilizados para os fins de pesquisa com objetivo de aumentar os conhecimentos da Medicina.

Finalmente, você tem o direito de recusar a participar do trabalho em qualquer etapa, sabendo-se que continuará a receber o tratamento convencional, tendo, assim, garantidos sua assistência médica e o controle médico que está realizando no Hospital das Clínicas.

Os custos de transporte até a clínica onde o exame será realizado serão pagos pelos pesquisadores.

Nome pesquisadores: José Augusto Almeida Barbosa

Cleonice de Carvalho Coelho Mota

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Endereço do pesquisador: Estrada de Nova Lima, 345/703 Belvedere. Belo Horizonte CEP: 30320760.

Eu, paciente_____, entendi tudo que foi explicado sobre esta pesquisa e concordo em participar. Este estudo será feito pelo Dr. José Augusto Almeida Barbosa, do Hospital das Clínicas da UFMG. Confirmo que fui selecionado de forma voluntária para participar desta pesquisa. Eu assinei e recebi uma cópia deste termo de consentimento.

Eu, responsável pelo paciente _____, entendi tudo que foi explicado sobre esta pesquisa e concordo em permitir a participação do menor _____ para a avaliação ecocardiográfica.

Este estudo será feito pelo Dr. José Augusto Almeida Barbosa, do Hospital das Clínicas da UFMG. Confirmo que o paciente_____foi selecionado de forma voluntária para participar desta pesquisa. Eu assinei e recebi uma cópia deste termo de consentimento.

Data e local:_____

Assinatura do paciente:

Assinatura do pesquisador:

Até 6 anos (para o grupo-controle)

Por meio deste termo de consentimento, informamos que estamos desenvolvendo uma pesquisa no Hospital das Clínicas da UFMG para estudarmos o coração das crianças obesas.

Este estudo quer, então, saber se crianças obesas apresentam alterações no coração.

Sabemos que você não tem problema de obesidade nem cardíaco, mas gostaríamos de pedir para estudar seu coração por meio do exame de ecoDopplercardiograma. Este exame é gratuito e não apresenta contraindicações, não trazendo prejuízo algum à sua saúde a sua realização.

Este exame tem duração de aproximadamente 45 minutos e não requer qualquer tipo de sedação, é indolor e não invasivo.

Estamos garantindo que este exame só será feito se você consentir e assinar este termo de consentimento.

Garantimos, ainda, que você terá resguardadas sua identidade e privacidade e os resultados deste estudo somente serão utilizados para fins de pesquisa com o objetivo de aumentar os conhecimentos da Medicina.

Sua participação neste estudo é voluntária, não havendo pagamento ou recebimento de benefícios.

Os custos de transporte até a clínica onde o exame será realizado serão pagos pelos pesquisadores.

Finalmente, será resguardado o direito de recusa a participar do trabalho em qualquer etapa. Você não terá ônus com a realização deste exame.

Pesquisadores: José Augusto Almeida Barbosa

Cleonice de Carvalho Coelho Mota

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Endereço pesquisador: Estrada de Nova Lima, 345/703, Belvedere. Belo Horizonte. CEP: 30320760

Eu, _____, entendi tudo que foi explicado sobre esta pesquisa e concordo em participar. Este estudo será feito pelos Drs. José Augusto Almeida Barbosa e Cleonice de Carvalho Coelho Mota, do Hospital das Clínicas da UFMG.

Confirmo que fui selecionado de forma voluntária para participar desta pesquisa. Eu assinei e recebi uma cópia desta autorização.

Eu, responsável por _____, entendi tudo que foi explicado sobre esta pesquisa e concordo em permitir a participação do menor _____ para a avaliação ecocardiográfica.

Este estudo será feito pelo Dr. José Augusto Almeida Barbosa, do Hospital das Clínicas da UFMG. Confirmo que _____foi selecionado de forma voluntária para participar desta pesquisa. Eu assinei e recebi uma cópia deste termo de consentimento.

Data e local:_____

Assinatura do responsável:

Assinatura do pesquisador:

Crianças de 7 a 12 anos (para o grupo-controle)

Por meio deste termo de consentimento, informamos que estamos desenvolvendo uma pesquisa no Hospital das Clínicas da UFMG para estudarmos o coração das crianças obesas.

Este estudo quer, então, saber se crianças obesas apresentam alterações no coração.

Sabemos que você não tem problema de obesidade nem cardíaco, mas gostaríamos de pedir para estudar seu coração por meio do exame de ecoDopplercardiograma. Este exame é gratuito e não apresenta contraindicações, não trazendo prejuízo algum à sua saúde a sua realização.

Este exame tem duração de aproximadamente 45 minutos e não requer qualquer tipo de sedação, é indolor e não invasivo.

Estamos garantindo que este exame só será feito se você consentir e assinar este termo de consentimento.

Garantimos, ainda, que você terá resguardadas sua identidade e privacidade e os resultados deste estudo somente serão utilizados para fins de pesquisa com o objetivo de aumentar os conhecimentos da Medicina.

Sua participação neste estudo é voluntária, não havendo pagamento ou recebimento de benefícios.

Os custos de transporte até a clínica onde o exame será realizado serão pagos pelos pesquisadores.

Finalmente, será resguardado o direito de recusa a participar do trabalho em qualquer etapa. Você não terá ônus com a realização deste exame.

Pesquisadores: José Augusto Almeida Barbosa

Cleonice de Carvalho Coelho Mota

Endereço: Presidente Antônio Carlos, 6.627, Unidade Administrativa II. 2º andar, sala 2005. CEP: 31270-901-BH-MG telefax (031)3409-4592, coep@prpq.ufmg.br

Eu, _____, entendi tudo que foi explicado sobre esta pesquisa e concordo em participar. Este estudo será feito pelos Drs. José Augusto Almeida Barbosa e Cleonice de Carvalho Coelho Mota, do Hospital das Clínicas da UFMG.

Confirmo que fui selecionado de forma voluntária para participar desta pesquisa. Eu assinei e recebi uma cópia desta autorização.

Eu, responsável por _____, entendi tudo que foi explicado sobre esta pesquisa e concordo em permitir a participação do menor _____ para a avaliação ecocardiográfica.

Este estudo será feito pelo Dr. José Augusto Almeida Barbosa, do Hospital das Clínicas da UFMG. Confirmo que _____foi selecionado de forma voluntária para participar desta pesquisa. Eu assinei e recebi uma cópia deste termo de consentimento.

Data e local:_____

Assinatura do responsável:

Assinatura do paciente:

Assinatura do pesquisador:

Crianças de 13 a 17 anos (pais) (para o grupo-controle)

Por meio deste termo de consentimento, informamos que estamos desenvolvendo uma pesquisa no Hospital das Clínicas da UFMG para estudarmos o coração das crianças obesas.

Este estudo quer, então, saber se crianças obesas apresentam alterações no coração.

Sabemos que você não tem problema de obesidade nem cardíaco, mas gostaríamos de pedir para estudar seu coração por meio do exame de ecoDopplercardiograma. Este exame é gratuito e não apresenta contraindicações, não trazendo prejuízo algum à sua saúde a sua realização.

Este exame tem duração de aproximadamente 45 minutos e não requer qualquer tipo de sedação, é indolor e não invasivo.

Estamos garantindo que este exame só será feito se você consentir e assinar este termo de consentimento.

Garantimos, ainda, que você terá resguardadas sua identidade e privacidade e os resultados deste estudo somente serão utilizados para fins de pesquisa com o objetivo de aumentar os conhecimentos da Medicina.

Sua participação neste estudo é voluntária, não havendo pagamento ou recebimento de benefícios.

Os custos de transporte até a clínica onde o exame será realizado serão pagos pelos pesquisadores.

Finalmente, será resguardado o direito de recusa a participar do trabalho em qualquer etapa. Você não terá ônus com a realização deste exame.

Pesquisadores: José Augusto Almeida Barbosa
Cleonice de Carvalho Coelho Mota

Endereço: Presidente Antônio Carlos, 6.627, Unidade Administrativa II. 2º andar, sala 2005. CEP: 31270-901-BH-MG telefax (031)3409-4592, coep@prpq.ufmg.br
Endereço pesquisador: Estrada de Nova Lima, 345/703, Belvedere. Belo Horizonte CEP: 30320760.

Eu, _____, entendi tudo que foi explicado sobre esta pesquisa e concordo em participar. Este estudo será feito pelos Drs. José Augusto Almeida Barbosa e Cleonice de Carvalho Coelho Mota, do Hospital das Clínicas da UFMG.

Confirmo que fui selecionado de forma voluntária para participar desta pesquisa. Eu assinei e recebi uma cópia desta autorização.

Eu, responsável por _____, entendi tudo que foi explicado sobre esta pesquisa e concordo em permitir a participação do menor _____ para a avaliação ecocardiográfica.

Este estudo será feito pelo Dr. José Augusto Almeida Barbosa, do Hospital das Clínicas da UFMG. Confirmo que _____foi selecionado de forma voluntária para participar desta pesquisa. Eu assinei e recebi uma cópia deste termo de consentimento.

Data e local:_____

Assinatura do responsável:

Assinatura do pesquisador:

Crianças de 13 a 17 anos (paciente) (grupo-controle)

Por meio deste termo de consentimento, informamos que estamos desenvolvendo uma pesquisa no Hospital das Clínicas da UFMG para estudarmos o coração das crianças obesas (gordinhas).

Este estudo quer, então, saber se crianças obesas (gordinhas) apresentam alterações no coração.

Sabemos que você não tem problema de obesidade nem cardíaco, mas gostaríamos de pedir para estudar seu coração por meio do exame de ecoDopplercardiograma. Este exame é gratuito e não apresenta contraindicações, não trazendo prejuízo algum à sua saúde a sua realização.

Este exame tem duração de aproximadamente 45 minutos e não requer qualquer tipo de sedação, é indolor e não invasivo.

Estamos garantindo que este exame só será feito se você consentir e assinar este termo de consentimento.

Garantimos, ainda, que você terá resguardadas sua identidade e privacidade e os resultados deste estudo somente serão utilizados para fins de pesquisa com o objetivo de aumentar os conhecimentos da Medicina.

Sua participação neste estudo é voluntária, não havendo pagamento ou recebimento de benefícios.

Os custos de transporte até a clínica onde o exame será realizado serão pagos pelos pesquisadores.

Finalmente, será resguardado o direito de recusa a participar do trabalho em qualquer etapa. Você não terá ônus com a realização deste exame.

Pesquisadores: José Augusto Almeida Barbosa

Cleonice de Carvalho Coelho Mota

Endereço: Presidente Antônio Carlos, 6.627, Unidade Administrativa II. 2º andar, sala 2005. CEP: 31270-901-BH-MG telefax (031)3409-4592, coep@prpq.ufmg.br

Eu, _____, entendi tudo que foi explicado sobre esta pesquisa e concordo em participar da avaliação ecográfica. Este estudo será feito pelos Drs. José Augusto Almeida Barbosa e Cleonice de Carvalho Coelho Mota, do Hospital das Clínicas da UFMG.

Confirmo que fui selecionado de forma voluntária para participar desta pesquisa. Eu assinei e recebi uma cópia desta autorização.

Este estudo será feito pelo Dr. José Augusto Almeida Barbosa, do Hospital das Clínicas da UFMG. Confirmo que _____foi selecionado de forma voluntária para participar desta pesquisa. Eu assinei e recebi uma cópia deste termo de consentimento.

Data e local:_____

Assinatura do paciente:

Assinatura do pesquisador: