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Subclinical hypothyroidism and myocardial function in obese children

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Abstract *Background and aims:* Pediatric obesity is an important health problem representing a major public health concern worldwide in the last decades. An isolated elevation of Thyroid Stimulating Hormone (TSH) with normal levels of thyroid hormones is frequently found in obese children. It has been named Isolated Hyperthyreotropinemia or Subclinical Hypothyroidism (SCH) and may be considered a consequence of obesity. Evidence exists that SCH is related to impairment of both systolic and diastolic myocardial function in the adult population.

The aim of our study is to establish if obesity-related SCH influences myocardial function in children.

Methods and results: We examined 34 obese children and adolescents with SCH and 60 obese children with normal TSH levels who underwent Doppler echocardiographic to evaluate myocardial function.

Global systolic function as assessed by Ejection Fraction (EF) was comparable between groups, however Right Ventricle pressure global systolic function and pressure were significantly reduced in SCH group. Mitral annulus peak systolic (MAPSE) excursion lateral and MAPSE septum resulted significantly reduced in SCH group. Tissue Doppler imaging peak systolic motion (TDI-S) was reduced in SCH group. Diastolic function also showed significant modifications in SCH group.

Conclusion: These results suggest possible involvement of cardiac function in obese children with SCH resulting in both abnormal diastolic function and reduced longitudinal systolic function. This new insight into cardiovascular consequences of obesity-related SCH in children could influence clinical approach to such patients by pediatric endocrinologists.

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Introduction

Pediatric obesity is an important health problem representing a major public health concern in Europe as well as in the USA and even in less developed countries. According to the World Health Organization (WHO) at least 20 million children under the age of 5 years were overweight globally in 2005 [1] with a rising global warning about public health due to possible clinical complications related to this condition.

Health complications related to obesity have long been considered as problems of adulthood, however it is now definitely clear that some of these outcomes could already be detected in childhood. A robust body of literature suggests that obese individuals are, in fact, at high risk of developing dyslipidemia, hypertension and impaired glucose tolerance, with the consequent increase of the risk for cardiovascular as well as metabolic diseases [2].

Cardiovascular consequences of obesity have been extensively investigated; obesity has been associated with heart failure [3], left ventricle (LV) dilation, increased LV wall stress and compensatory LV hypertrophy [4]. Most studies reported an abnormal diastolic function [5,6] without consistent association with systolic dysfunction and a spectrum of minor cardiovascular changes [3]. Therefore, childhood obesity should not only be considered a risk factor for cardiovascular diseases in adulthood, but also a cause of subclinical impairment of cardiac function in children [7].

Recently, an increasing attention has been devoted to endocrine concerns, such as thyroid function, in obese children [8,9]. Studies have shown that a moderate elevation of serum Thyroid Stimulating Hormone (TSH) concentrations, associated with serum free T4 (fT4) values in the normal range, is frequently found in obese children. This laboratory finding is generally defined as Subclinical Hypothyroidism (SCH). There have been, however, some claims to adopt the expression Isolated Hyperthyreotropinemia to define this condition in obese children. This is due to the observation that it seems to be rather a benign consequence of obesity than a thyroid disease since weight loss leads to a normalization of elevated TSH levels. Moreover this finding seems not to be associated with other significant anomalies [10,11]. Furthermore the underlying pathways of this alteration are not fully understood [12] and, therefore, there is not a clear consensus neither about the proper terminology nor about the need for treatment of SCH in obese children [13].

Using intramyocardial ultrasonic techniques, which allow the detection of early ultrastructural and regional functional systolic and diastolic abnormalities of the heart, it has been demonstrated that SCH is related to impairment of both systolic and diastolic myocardial function in adults [14]. Particularly, TSH concentration has been found to be inversely related to LV contractility, consistently with the known inotropic effects of thyroid hormone [15].

Since pediatric obesity and SCH have been shown to be associated, having both detrimental cardiovascular consequences, and since in literature we found no studies concerning this issue, the aim of our study is to evaluate cardiac function in obese children with obesity-related SCH. To establish whether SCH influences myocardial function in children, possibly further increasing the risk for cardiovascular diseases in this high risk population, would represent an interesting clinical insight.

Methods

We examined 34 obese children and adolescents with SCH (18 girls), and 60 obese children with normal TSH levels, matched for BMI, waist circumference, age, gender and pubertal development. They were referred to the Department of Pediatrics, Second University of Naples, for obesity between 2005 and 2008 and underwent cardiologic evaluation in the Department of Pediatric Cardiology of Monaldi Hospital. Subjects with known presence of diabetes or using medications altering blood pressure, glucose or lipid metabolism, with goiter or known thyroid disease or thyroid autoimmunity were excluded. The ethical committee of the Second University of Study of Naples approved the study. Informed consent was obtained by parents and, where appropriate, by children. Obesity was defined according to the body mass index (BMI) 95th percentile for age and sex using the definition of the International Task Force for Obesity in Childhood and the charts for Italian population [16]. Obesity degree was evaluated using the *z*-score BMI, calculated with the LMS method [17]. Anthropometric measures were assessed at the time of the first visit. Waist circumference was measured by the same operator to the nearest centimetre with a flexible steel tape measure while the subjects were standing, after gently exhaling, as the minimal circumference measurable on the horizontal plane between the lowest portion of the rib cage and iliac crest. Standard deviation (SD) scores for waist circumference have been calculated using normative values for Italian population [18]. Systolic blood pressure (SBP) and diastolic blood pressure (DBP) were measured three times while the subjects were seated, and the two last measurements were averaged for the analysis and we calculated SD according to normative values [19]. The pubertal stage was assessed using Tanner criteria.

After an overnight fasting, blood samples were obtained for triglycerides, high density lipoprotein (HDL) cholesterol, insulin, serum glucose, thyroid hormones (TSH, fT3, fT4) and anti-thyroglobulin (Tg-Ab) and anti-peroxidase antibodies (TPO-Ab).

Serum fasting glucose levels were measured with glucose oxidase method. Triglycerides and HDL cholesterol were measured by an Olympus AU 560 apparatus using an enzymatic colorimetric method. Immunoreactive insulin was assayed by IMX (Abbott Diagnostics, Santa Clara, CA). The mean intra- and interassay coefficients of variations were 4.7% and 7.2%, respectively. The degree of insulin resistance was determined using a homeostasis model assessment (HOMA), [insulin (mU/l) $\times$ glucose level (mmol/l)/22.5].

Thyroid hormones (TSH, fT3, and fT4) and TPO-Ab and Tg-Ab were determined by high-specific solid-phase technique-chemiluminescenceimmunoassays (Perkinelmer, Turku, Finland).

TPO-Ab and Tg-Ab levels higher than 60 UI/ml were considered positive, and autoimmune thyroiditis was diagnosed. SCH was diagnosed when TSH was higher than