# Echocardiographic assessment of cardiac function abnormalities and related risk factors in Thai overweight and obese children

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#### ABSTRACT

| Background               | : | Childhood obesity has become a global concern, with its prevalence steadily increasing over<br>the past decade. This condition negatively impacts the cardiovascular system, increasing<br>the risk of morbidity and mortality in adulthood. This study aimed to identify cardiac<br>function abnormalities and related risk factors among overweight and obese Thai children.   |
|--------------------------|---|--|
| Materials and<br>Methods | : | A cross-sectional observational study of 70 children with body mass index (BMI) >1 standard<br>deviation above the mean for Thai children was conducted at Naresuan University Hospital.<br>Body fat percentage (%Fat) was measured, and standard transthoracic echocardiography<br>was performed. Metabolic profiles were collected from medical records.   |
| Results                  | : | The thickness and diameter of the Left ventricle (LV) wall, including the LV posterior wall, LV internal diameter, and interventricular septum (IVS), were significantly increased in both systolic and diastolic phases in obese children. LV concentric hypertrophy and an abnormal E/E' ratio were found in 27% and 34.3% of participants, respectively. Right ventricular systolic dysfunction indicated by abnormal tricuspid annular plane systolic excursion values was found in 55.7% of all participants. In addition, 27.1% of all obese children had pulmonary hypertension. Significant differences in BMI and %Fat were detected between children with abnormal and normal IVS diastolic (IVSd) ( $P = 0.016$ ). Our univariate and multivariate correlation analyses revealed a significant positive association between abnormal IVSd and %Fat, with an odd ratio (OR) of 1.13 (95% confidence interval [CI]: 1.01–1.27; $P = 0.047$ ) and an adjusted OR of 1.17 (95% CI: 1.01–1.36; $P = 0.04$ ). |
| Conclusions              | : | Cardiac function abnormalities in childhood obesity exhibit a significant positive correlation with BMI and various cardiac dimensions, including ventricular wall thickness. One important related risk factor for increased IVS thickness is %Fat. Therefore, multidisciplinary management of obesity should be initiated as early as possible to prevent future cardiovascular morbidity and mortality.   |
| Keywords                 | : | Cardiac function, children, echocardiogram, obesity, overweight  |

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Nimpum and Jittham: Cardiac function abnormalities and related risk factors in childhood obesity

# **INTRODUCTION**

Thailand is currently facing a growing problem of childhood obesity, with the prevalence increasing steadily over the past decade. A report from the 4<sup>th</sup> National Health Examination Survey in Thailand, conducted in 2008–2009, found that the prevalence of obesity in children aged 6–9 years was 6.7% and 5.8% in children aged 10–14 years.<sup>[1]</sup> A more recent report from the World Health Organization (WHO) in 2022 found that overweight and obesity affected almost 60% of adults in the European region. This report also found that the prevalence of obesity in children aged 5–9 years was 11.6% and 7.1% in children aged 10–14 years.<sup>[2]</sup>

Obesity is a major risk factor for many noncommunicable diseases, including hypertension (HT), diabetic mellitus (DM), and dyslipidemia, which are known as metabolic syndrome. Metabolic syndrome is associated with a two-fold increased risk of coronary and cerebrovascular diseases and a 1.5-fold increased risk of all-cause mortality.<sup>[3]</sup> Obesity has also been linked to obstructive sleep apnea (OSA), obesity hypoventilation syndrome, asthma, and nonalcoholic fatty liver disease.<sup>[4,5]</sup>

The cardiovascular system is the most affected system by obesity, as it can lead to increased morbidity and mortality in adulthood. A previous systematic review of 39 studies found an association between high body mass index (BMI) status in early life and all-cause mortality.<sup>[6]</sup> The review also found an association between high BMI status in early life and coronary heart disease, HT, type 2 diabetes, and obesity. In coronary heart disease, the mortality rate with a history of high BMI during childhood ranged from 1.53 to 5.43 (95% confidence interval [CI] 2.77–10.62).<sup>[6]</sup>

Echocardiography is a standard, noninvasive modality that is widely used to assess cardiovascular function. A systematic review and meta-analysis of echocardiographic studies in adult obesity found that obese adults were 4.2 times more likely to have left ventricular hypertrophy (LVH) than nonobese adults. Eccentric hypertrophy was the most common type of LVH in this review.<sup>[7]</sup>

In children, previous studies have reported that obesity is associated with enlarged left- and right-sided cardiac chambers, thicker left ventricular (LV) walls, and increased LV mass compared to nonobese children. These findings have led to the proposal that cardiovascular dysfunction in childhood obesity is associated with endothelial dysfunction, insulin resistance, increased sympathetic nervous system activity, and increased cardiac ectopic fat.<sup>[8]</sup> A recent prospective study of cardiac geometry found that obese children had larger and thicker left- and right-sided cardiac chambers than nonobese children.<sup>[9]</sup> The vast majority of studies on childhood obesity and cardiac function have been conducted in Europe and the United States. The results of these studies may not be generalizable to other populations, as there may be ethnicity-specific differences in the effects of obesity on the cardiovascular system. The objective of this study was to identify cardiac function abnormalities in Thai overweight and obese children using echocardiography and to investigate the associated risk factors. This study is the first in Thailand to use the newly developed Thai reference BMI chart for children.<sup>[10]</sup>

# **MATERIALS AND METHODS**

This was a cross-sectional observational study conducted among Thai children aged 5-15 years with a BMI greater deviating by more than 1 standard deviation (SD) from the BMI chart for Thai children at the Obesity Clinic, Department of Pediatrics, Naresuan University Hospital, from March 3, 2021, to December 31, 2021. Participants' body weight and percentage of fat (%Fat) were measured using an OMRON HBF-375 bioelectrical impedance analysis device (Omron Healthcare, Inc., Lake Forest, IL, USA), and height was determined using a stadiometer. BMI values were calculated by dividing weight (kg) by height (m<sup>2</sup>). Metabolic parameters, including fasting blood sugar (FBS) and lipid profiles: triglyceride, total cholesterol (TC), and high-density lipoprotein (HDL) levels, were collected from the participant's medical records for analysis. Ethics approval for this study was obtained from the Institutional Review Board (P3-0089/2564) in accordance with the principles outlined in the Declaration of Helsinki.

The study protocol was initiated after the participants and/or their parents or legal guardians signed the consent form. Participants with any underlying diseases not listed in the metabolic syndrome prerequisites (e.g., diabetes, high blood pressure [BP], and dyslipidemia) were excluded from the study. In addition, individuals with incomplete metabolic data within 6 months before the study were also excluded.

#### Echocardiographic data

All participants underwent transthoracic echocardiography using a Philips EPIQ CVx (Koninklijke Philips N.V., Amsterdam, Netherlands) machine. All echocardiographic measurements were obtained according to standard guidelines<sup>[11-13]</sup> by a single echocardiographer and validated by a pediatric cardiologist, who was blinded to the result of the patient's BMI and metabolic status. All computed results were derived from the average values obtained over three cardiac cycles.

#### LV systolic function

The LV linear internal diameter and wall thickness were measured in the parasternal long-axis view

using the M-mode technique. Left ventricular ejection fraction (LVEF) was calculated using the modified Simpson's method in the apical four-chamber view. Computation of the LV mass (LVM) by employing the Devereux formula, with subsequent normalization indexed with two methods; body surface area (LVM/BSA)<sup>[14]</sup> and body height in meters to the allometric power of 2.7 (LVM/Ht<sup>2.7</sup>).<sup>[15]</sup> The relative wall thickness (RWT) was calculated.<sup>[12]</sup>

## LV diastolic function

Mitral peak early (E) and late (A) velocities, along with the measurement of mitral deceleration time (MV DTe), were obtained through pulsed-wave Doppler in the apical four-chamber view, with the sample volume placed at the tip of mitral valve leaflets. Lateral early diastolic mitral annulus velocities (E') were evaluated using pulsed-wave tissue Doppler imaging. The E/A and E/E' ratios were calculated.

# Right ventricular function

The right ventricular (RV) systolic function was assessed using tricuspid annular plane systolic excursion (TAPSE). TAPSE was measured by aligning an M-mode cursor parallel to the RV free wall as it meets the tricuspid annulus from the RV apical four-chamber view. The mean pulmonary arterial pressure (mPAP) was calculated using the formula: mPAP = 4 (PRpeak velocity)<sup>2</sup> + right atrial pressure (RAP).<sup>[16]</sup> The RAP pressure was estimated based on the diameter of IVC at end-expiration close to the junction with the hepatic vein (subcostal view) and response to sniffing. All participants had normal volume status on the day of echocardiogram and had <50% IVC collapsibility response to sniffing; we had calculated mPAP with RAP as 8 mmHg.<sup>[12]</sup>

# Definitions

The Thai reference BMI chart for children was defined curve with SD. The severity of obesity was classified as follows: overweight (BMI 1SD - 2SD) and obese (BMI >2SD) following the WHO BMI-based classification for overweight and obesity BMI-for-age (5–19 years).<sup>[17]</sup> The severely obese (BMI >35 kg/m<sup>2</sup>) followed the CDC classification with a cutoff value >35 kg/m<sup>2</sup> due to not being evaluated by the percentile curve.<sup>[18]</sup> %Fat was compared to the normal reference range for age- and sex-matched controls.<sup>[19]</sup>

Metabolic risk factors consist of impaired fasting glucose (FBS  $\geq 100 \text{ mg/dl}$ ) and DM (FBS  $\geq 126 \text{ mg/dl}$ ). According to the Pediatric Obesity Prevention and Treatment Practice Guideline, dyslipidemia involves any of three parameters hypertriglyceridemia levels  $\geq 150 \text{ mg/dl}$ , hypercholesterolemia levels  $\geq 200 \text{ mg/dl}$ , and low HDL levels < 40 mg/dl.<sup>[4]</sup>

HT is defined as systolic BP or diastolic BP  $\geq$  the 95<sup>th</sup> percentile based on age, gender, and height according to the 2017 AAP guidelines.<sup>[20]</sup>

Echocardiographic parameters were indexed to z-scores, developed by the Boston Children's Hospital, with age-, sex-, and BSA-matched controls.[21,22] Abnormal echocardiographic parameters were defined as z-score greater than 2SD. The abnormal LVM/BSA was defined as greater than the 99th percentile with age- and sex-matched controls with cutoff values of more than 95 and 115 g/m<sup>2</sup> for girls and boys, respectively. The abnormal LVM/Ht<sup>2.7</sup> was defined as >51 g/m<sup>2.7</sup>.<sup>[23]</sup> The abnormal RWT was >0.42.<sup>[12]</sup> The RWT allows determining the LV geometry and classification of LV mass increase as either concentric or eccentric hypertrophy as follows:<sup>[24]</sup> concentric remodeling: RWT >0.42 with normal LVM/BSA, concentric hypertrophy: RWT >0.42 with abnormal LVM/BSA, and eccentric hypertrophy: RWT  $\leq 0.42$  with abnormal LVM/BSA.

The abnormal TAPSE was defined as a *z*-score <-2SD. Calculated mPAP from an echocardiogram >20 mmHg was used to define pulmonary HT (PHT) according to the diagnostic criteria for PHT.<sup>[25]</sup>

## Statistical analysis

The Strong Heart Study found that prevalent LVH in obese adolescents and overweight aged 14–20 years was 33.5% and 12.4%, respectively, compared with normal weight participants (3.5%; P < 0.001). For sample size for estimating an infinite population proportion, the following parameters were utilized: P = 0.335, d = 0.12, Z (0.975) = 1.96. The sample size was 60 patients, with a dropout rate of 15%, for a total sample size of 70 patients.<sup>[26]</sup>

Statistical analyses were performed using STATA version 12.0 software (StataCorp, College Station, TX, USA). The Shapiro–Wilk *W*-test was used to analyze the continuous data, which were presented as mean and SD. The one-way ANOVA and independent *t*-test were used to compare the groups. All categorical data were reported as percentages. Abnormal echocardiographic parameters and related risk factors were compared between groups (abnormal and normal) using the Chi-square and Fisher's exact tests. Univariable and multivariable logistic regression analyses were utilized to assess the significant differences in risk related between normal and abnormal groups. The odds ratio (OR) and adjusted OR (AOR) with P < 0.05 were considered significant.

# RESULTS

Seventy obese children were enrolled in this study, of whom 49 (70%) were male. The overall mean age and BMI were 10.47  $\pm$  2.98 years and 30.36  $\pm$  6.52 kg/m<sup>2</sup>, respectively [Figure 1]. Table 1 shows the baseline characteristics and metabolic data for each severity of obesity. Our observations revealed the presence of underlying conditions such as HT, dyslipidemia,

Nimpum and Jittham: Cardiac function abnormalities and related risk factors in childhood obesity

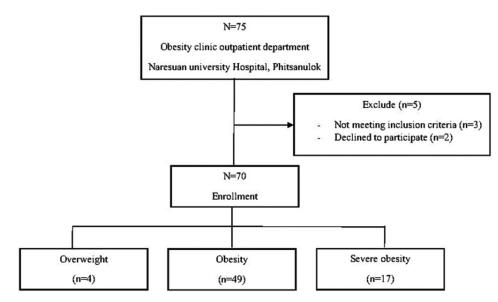


Figure 1: Cascade algorithm for the study design

|  | Table 1: Baseline | characteristics and | metabolic ( | data of | participants |
|--|-------------------|---------------------|-------------|---------|--------------|
|--|-------------------|---------------------|-------------|---------|--------------|

| Characteristics             | Total ( <i>n</i> =70) | Overweight (n=4) | Obese ( <i>n</i> =49) | Severely obese (n=17) |
|-----------------------------|-----------------------|------------------|-----------------------|-----------------------|
| Male, <i>n</i> (%)          | 49 (70.0)             | 3 (75.0)         | 36 (73.5)             | 10 (58.8)             |
| Age (mean±SD)               | 10.47±2.98            | 13.75±1.50       | 9.37±2.64             | 12.88±2.12            |
| BMI (mean±SD)               | 30.36±6.52            | 23.30±1.16       | 27.71±4.08            | 39.65±2.71            |
| HT, n (%)                   | 8 (11.4)              | 0                | 2 (4.0)               | 6 (35.3)              |
| Hypertriglyceridemia, n (%) | 16 (22.9)             | 1 (25.0)         | 7 (14.3)              | 8 (47.1)              |
| Hypercholesterolemia, n (%) | 9 (12.9)              | 0                | 5 (10.2)              | 4 (23.5)              |
| Low HDL, <i>n</i> (%)       | 14 (20.0)             | 1 (25.0)         | 10 (20.4)             | 3 (17.6)              |
| DM, n (%)                   | 2 (2.9)               | 1 (25.0)         | 1 (2.0)               | О́                    |
| Impaired FBS, n (%)         | 12 (17.1)             | 1 (25.0)         | 6 (12.2)              | 5 (29.4)              |
| Percentage fat (mean±SD)    | 30.13±4.30            | 23.28±4.32       | 29.69±3.96            | 32.99±2.84            |

SD: Standard deviation, BMI: Body mass index, DM: Diabetes mellitus, HDL: High-density lipoprotein, FBS: Fasting blood sugar, HT: Hypertension

DM, and impaired FBS in both the obesity and severe obesity groups. Furthermore, the mean %Fat exhibited an upward trend as the severity of obesity increased.

# LV systolic function

The global LVEF was  $58.38\% \pm 3.45\%$ , with no statistically significant difference between the obese cohorts. However, the LV wall thickness and diameter, including the LV posterior wall (LVPW), the LV internal diameter (LVID), and the interventricular septum (IVS), were significantly increased in both systolic (LVPWs, LVIDs, IVSs) and diastolic phases (LVPWd, LVIDd, and IVSd) among the groups under obese categories. On indexing the measurements using *z*-scores with age-, sex-, and BSA-matched controls, all parameters showed no significant difference between obesity groups [Table 2].

#### LV mass

The overall calculated mean LVM was  $168.39 \pm 69.30$  g. The mean LVM in each group was  $151.87 \pm 57.36$  g,  $148.85 \pm 59.17$  g, and  $228.60 \pm 67.08$  g in the overweight, obese, and severely obese groups, respectively, with a significant difference among the obese cohorts (P < 0.001). Consequently, when LVM was indexed to BSA (LVM/BSA) and height (LVM/Ht<sup>2.7</sup>), the overall mean LVM/BSA and LVM/Ht<sup>2.7</sup> were  $97.59 \pm 25.60$  g/m<sup>2</sup> and  $35.60 \pm 13.79$  g/Ht<sup>2.7</sup>, respectively. The mean LVM/ BSA in each group was  $91.31 \pm 17.61$ ,  $96.00 \pm 24.70$ , and  $103.67 \pm 29.68$  g/m<sup>2</sup> in the overweight, obesity, and severely obese groups, respectively, with no significant difference in obesity groups (P = 0.506). The mean LVM/ Ht<sup>2.7</sup> in each group was  $26.59 \pm 4.99$ ,  $37.91 \pm 13.23$ , and  $31.06 \pm 15.22$  g/Ht<sup>2.7</sup> in the overweight, obesity, and severely obese groups, respectively, with no significant difference in obesity groups (P = 0.083). The overall mean RWT was  $0.52 \pm 0.09$  which is higher than the cutoff value (>0.42). The mean RWT in each group was 0.46  $\pm$  0.04, 0.53  $\pm$  0.09, and 0.53  $\pm$  0.08 in the overweight, obesity, and severely obese groups, respectively, with no significant difference in obesity groups (*P* = 0.319) [Table 2].

#### LV diastolic function

The LV diastolic function of all participants was normal. The mean MV E/A ratio was  $1.79 \pm 0.30$ , with a mean *z*-score ratio of  $-0.66 \pm 0.50$ . The mean E/E' was

| Echocardiographic                           |                       |                  | Mean±SD               |                       |         |
|---|-----------------------|------------------|-----------------------|-----------------------|---------|
| parameters                                  | Total ( <i>n</i> =70) | Overweight (n=4) | Obese ( <i>n</i> =49) | Severely obese (n=17) | Р       |
| LV systolic function                        |                       |                  |                       |                       |         |
| LVPW systolic (cm)                          | 1.18±0.16             | 1.17±0.18        | 1.12±0.15             | 1.33±0.10             | <0.001* |
| LVPW systolic (Z)                           | -1.53±0.88            | -1.32±0.96       | -1.63±0.80            | -1.30±1.06            | 0.377   |
| LVID systolic (cm)                          | 2.83±0.60             | 2.98±0.58        | 2.66±0.48             | 3.28±0.72             | <0.001* |
| LVID systolic (Z)                           | -1.00±1.53            | -0.42±1.26       | -1.14±1.51            | -0.73±1.66            | 0.486   |
| IVS systolic (cm)                           | 1.15±0.18             | 1.11±0.13        | 1.09±0.16             | 1.32±0.13             | <0.001* |
| IVS systolic (Z)                            | -0.81±0.77            | -0.85±0.35       | -0.80±0.82            | -0.82±0.73            | 0.992   |
| LVPW diastolic (cm)                         | 1.09±0.20             | 0.98±0.16        | 1.04±0.19             | 1.24±0.16             | <0.001* |
| LVPW diastolic (Z)                          | 1.71±1.44             | 1.02±0.58        | 1.81±1.41             | 1.58±1.64             | 0.531   |
| LVID diastolic (cm)                         | 4.19±0.64             | 4.31±0.63        | 3.99±0.57             | 4.75±0.52             | <0.001* |
| LVID diastolic (Z)                          | -1.95±1.34            | -1.48±1.00       | -2.02±1.44            | -1.86±1.10            | 0.710   |
| IVS diastolic (cm)                          | 1.16±0.19             | 1.06±0.10        | 1.12±0.18             | 1.29±0.15             | 0.002*  |
| IVS diastolic (Z)                           | 1.55±1.15             | 1.12±0.53        | 1.73±1.11             | 1.12±1.27             | 0.127   |
| LVM (g)                                     | 168.39±69.30          | 151.87±57.36     | 148.85±59.17          | 228.60±67.08          | <0.001* |
| LVM/BSA (g/m <sup>2</sup> )                 | 97.59±25.60           | 91.31±17.61      | 96.00±24.70           | 103.67±29.68          | 0.506   |
| LVM/HT <sup>2.7</sup> (g/m <sup>2.7</sup> ) | 35.60±13.79           | 26.59±4.99       | 37.91±13.23           | 31.06±15.22           | 0.083   |
| RWT   | 0.52±0.09             | 0.46±0.04        | 0.53±0.09             | 0.53±0.08             | 0.319   |
| LVEF (%)                                    | 58.38±3.45            | 57.90±1.47       | 58.75±3.91            | 57.41±1.92            | 0.375   |
| Diastolic function                          |                       |                  |                       |                       |         |
| E/A ratio                                   | 1.79±0.30             | 1.73±0.30        | 1.79±0.31             | 1.78±0.30             | 0.911   |
| E/A ratio (Z)                               | -0.66±0.50            | -0.87±0.46       | -0.61±0.49            | -0.75±0.52            | 0.435   |
| E/E'  | 9.10±1.58             | 10.45±1.80       | 8.93±1.63             | 9.25±1.27             | 0.163   |
| E/E' ( <i>Z</i> )                           | 2.08±1.12             | 3.13±1.25        | 1.93±1.15             | 2.28±0.89             | 0.083   |
| DTe   | 131.81±27.38          | 143.40±52.78     | 130.41±22.83          | 133.12±33.24          | 0.649   |
| DTe ( <i>Z</i> )                            | -0.37±0.83            | -0.34±1.49       | -0.31±0.75            | -0.56±0.92            | 0.566   |
| RV function                                 |                       |                  |                       |                       |         |
| TAPSE (mm)                                  | 18.0±1.5              | 18.4±1.1         | 18.2±1.6              | 17.3±0.8              | 0.095   |
| TAPSE (Z)                                   | -2.05±1.35            | -2.07±0.62       | -2.08±1.33            | -1.95±1.58            | 0.940   |
| IVC diameter (cm)                           | 1.43±0.30             | 1.61±0.30        | 1.38±0.29             | 1.51±0.31             | 0.147   |
| mPAP (mmHg)                                 | 18.34±3.29            | 17.65±3.71       | 18.50±3.35            | 18.06±3.19            | 0.817   |

#### Table 2: Echocardiographic data

\*P<0.001, LV: Left ventricle, LVPW: LV posterior wall, LVID: LV internal diameter, IVS: Interventricular septum, LVEF: LV ejection fraction, LVM/BSA: LV mass/body surface area, HT: Hypertension, E/A: Early/late, DTe: Deceleration time, TAPSE: Tricuspid annular plane systolic excursion, IVC: inferior vena cava, RWT: Relative wall thickness, mPAP: Mean pulmonary arterial pressure, SD: Standard deviation, RV: Right ventricular

 $9.10 \pm 1.58$ , and the mean MV DTe was  $131.81 \pm 27.38$  s. When indexed to *z*-scores with age-, sex-, and BSA-matched controls, we found an abnormal range of mean E/E' ratio *z*-score showed  $2.08 \pm 1.12$ , and none of these parameters demonstrated statistically significant differences between obesity groups, as presented in Table 2.

#### **Right ventricular function**

The mean TAPSE was  $1.80 \pm 0.15$  mm in all participants, with no significant difference between obesity groups (P = 0.095). The mean TAPSE *z*-score was  $-2.05 \pm 1.35$ , within the lower normal range, and also showed no significant difference between obesity groups. The mPAP was  $18.34 \pm 3.29$  mmHg in all participants [Table 2].

We analyzed the relationship of all significant echocardiographic parameters and BMI using scatter plots, as shown in Figure 2.

Echocardiographic parameters were classified into two categories: normal and abnormal, as detailed in our study definition. In the LV systolic function, abnormal LVPWd and IVSd were found in 54.3% and 55.7%, respectively. The abnormal LVM/BSA and LVM/Ht<sup>2.7</sup> were 55.7% and 70%, respectively.

In the LV diastolic function, abnormal E/E' was observed in 34.3% of participants. In the RV systolic function, abnormal TAPSE was found in 55.7% of participants. The results also showed 27.1% of obese children with PHT. Other parameters exhibited a marginal deviation from the normative values [Table 3].

When the classification of LVM relies on RWT, we found concentric remodeling at 57.14% and concentric hypertrophy in 27.14% of all participants [Table 4].

All echocardiographic parameters and related risk factors were subjected to a comparative analysis between the normal and abnormal clusters. We identified a statistically significant difference in BMI and %Fat between the abnormal and normal IVSds (P = 0.016). The %Fat within the cohort with abnormal IVSd was  $31.06 \pm 3.83\%$ , whereas the group with normal IVSd exhibited a %Fat of  $28.95 \pm 4.63\%$ , revealing a significant difference between these two groups (P = 0.041) [Table 5]. In the univariate and multivariate correlation analyses, we found that only %Fat was significantly positively correlated with abnormal IVSd. The OR was 1.13 (95% CI: 1.01-1.27; P = 0.047), and the AOR was 1.17 (95% CI: 1.01-1.36; P = 0.040).

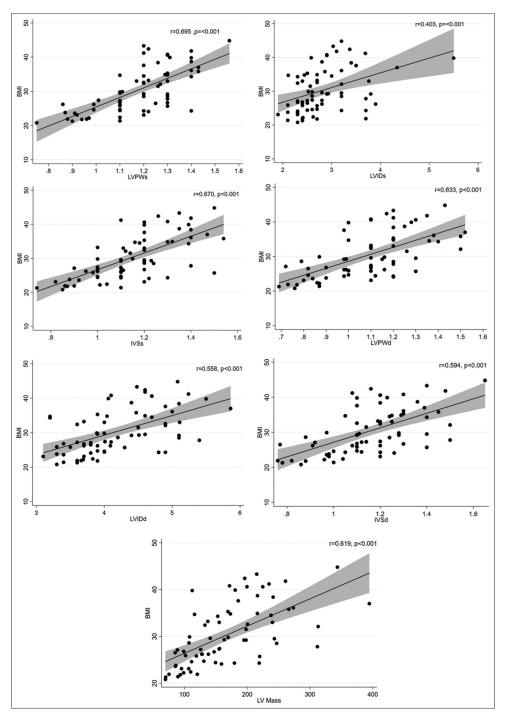


Figure 2: Scatter plot of the relationship between significant echocardiographic parameters and BMI (each figure with X axis defines as BMI and Y axis defines as echocardiographic parameters listed from top to bottom: LVPWs, LVIDs, IVSs, LVPWd, LVIDd, IVSd, LV mass)

# DISCUSSION

Childhood obesity has shown a significant correlation between BMI and various echocardiographic parameters such as cardiac dimensions, ventricular wall thickness, and LVM. Overall, LV systolic and diastolic functions were normal. However, we observed an increased E/E' ratio in LV diastolic function, which reflects an intermediate increase in LV filling pressure.<sup>[27]</sup> These findings align with previous reviews comparing obese and normal-weight children.<sup>[8,9]</sup> Obesity cardiomyopathy is a major concern for children with long-standing obesity, as it can develop in adulthood. This condition is thought to be caused by compensatory remodeling in response to increased ventricular pressure or volume and circulatory hemodynamics. Consequently, obese individuals develop atrial and ventricular hypertrophy, alongside elevated stroke volume and cardiac output.<sup>[28]</sup> This assertion is supported by a retrospective study in children with hypertrophic cardiomyopathy (HCM), revealing that obese children with HCM exhibit greater LVPW thickness when compared to their nonobese counterparts (P = 0.001).<sup>[29]</sup> The RWT is used to determine the LV geometry and classification of LVM increase. Our data showed LV concentric hypertrophy in one-third (27%) of obese children in accordance with previous works.<sup>[26]</sup> Our study underscores the presence of obesity-related cardiomyopathy, showing a significant correlation with the severity of obesity in children.

The RV function in obese children was evaluated using TAPSE. Our study found that RV function was lower than normal, especially in the severe obesity group (mean  $17.3 \pm 0.8$  mm). When TAPSE was indexed with standard *z*-scores, 55% of the participants had abnormal TAPSE *z*-scores. The TAPSE cutoff value is <17 mm with a high specificity of abnormal RV systolic function in adults. The right heart dysfunction associated with obesity may be caused by a hypermetabolic state, LV dysfunction, chronic hypoxia in sleep disorder, and PHT.<sup>[30]</sup> Interestingly, the evidence of PHT from an echocardiogram in our study had been found in

# Table 3: Prevalence of abnormalechocardiographic parameters in obese children,indexed with standard Z-score and percentile

| Echocardiographic<br>parameters | Abnormal,<br><i>n</i> (%) | Normal,<br><i>n</i> (%) |
|---------------------------------|---------------------------|-------------------------|
| LV systolic function            |                           |                         |
| LVPW systolic                   | 1 (1.4)                   | 69 (98.6)               |
| LVID systolic                   | 4 (5.7)                   | 66 (94.3)               |
| IVS systolic                    | 0                         | 70 (100.0)              |
| LVPW diastolic                  | 38 (54.3)                 | 32 (45.7)               |
| LVID diastolic                  | 1 (1.4)                   | 69 (98.6)               |
| IVS diastolic                   | 39 (55.7)                 | 31 (44.3)               |
| LVEF                            | 4 (5.7)                   | 66 (94.3)               |
| LVM/BSA                         | 39 (55.7)                 | 31 (44.3)               |
| LVM/Ht <sup>2.7</sup>           | 49 (70.0)                 | 21 (30.0)               |
| Diastolic function              |                           |                         |
| E/A ratio                       | 0                         | 70 (100.0)              |
| E/E'                            | 24 (34.3)                 | 46 (65.7)               |
| DTe                             | 1 (1.4)                   | 69 (98.6)               |
| TAPSE                           | 39 (55.7)                 | 31 (44.3)               |
| IVC diameter                    | 0                         | 70 (100.0)              |
| PHT                             | 19 (27.1)                 | 51 (72.9)               |

LV: Left ventricle, LVPW: LV posterior wall, LVID: LV internal

diameter, IVS: Interventricular septum, LVEF: LV ejection fraction, LVM/BSA: LV mass/body surface area, HT: Hypertension, E/A: Early/late, DTe: Deceleration time, TAPSE: Tricuspid annular plane systolic excursion, PHT: Pulmonary hypertension, IVC: Inferior vena cava one-third (27%) of all obese participants. The prevalence of PHT in childhood obesity has not been published, but a study of children with OSA found a prevalence of only 1.8%, which was not associated with high BMI.<sup>[31]</sup> A recent systematic review and meta-analysis of adult studies found no significant association between BMI and risk of PHT.<sup>[32]</sup> Metabolic derangements in obesity can contribute to myocardial dysfunction, such as endothelial dysfunction, insulin resistance, increased sympathetic nervous system activity, and increased cardiac ectopic fat.<sup>[8]</sup> Our study found that only a %Fat was a significant risk factor for abnormal IVSd. A large cross-sectional study of Chinese adults found that %Fat was closely associated with both systolic and diastolic cardiac function, but metabolic syndrome (HT, DM, and dyslipidemia) was not a significant risk factor.<sup>[33]</sup> Another study also underscored that %Fat, rather than BMI, independently correlated with cardiovascular risk factors as determined through logistic regression analysis.<sup>[34]</sup>

From our study, the echocardiographic parameters, especially wall thickness and dimension, were not different between the three obesity groups when *z*-scores were compared. That may mean more obese patients with higher BMI have higher wall thickness that is appropriate for the BMI or may be justification for using absolute wall thickness instead of *z*-score as a marker for future bad outcomes.

The clinically relevant concern for obese children is their quality of life. Our recent study of cardiovascular performance in obese children, evaluated using the 6-min walk test (6MWT), found that obese children with overall normal LV systolic function had lower 6MWT performance than normal-weight children. Higher %Fat and TC levels were also associated with reduced 6MWT performance.<sup>[35]</sup>

#### Limitations of the study

Echocardiography assessment in obese children and adults is difficult due to acoustic shadowing from excessive subcutaneous fat. The current gold standard for evaluating cardiac geometry and function is magnetic resonance imaging (MRI) which is a more sensitive and reproducible method. However, cardiac MRI is more expensive than echocardiography and only available in cardiac center hospitals in our region. Echocardiography should be the first technique used to evaluate cardiac

Table 4: Classification of left ventricle mass relies on relative wall thickness and left ventricle mass/body surface area

| Class of LVH           | Total ( <i>n</i> =70), <i>n</i> (%) | Overweight (n=4), n (%) | Obese ( <i>n</i> =49), <i>n</i> (%) | Severely obese ( <i>n</i> =17), <i>n</i> (%) |
|------------------------|-------------------------------------|-------------------------|-------------------------------------|--|
| Normal                 | 10 (14.29)                          | 1 (25)                  | 7 (14.29)                           | 2 (11.76)                                    |
| Concentric remodeling  | 40 (57.14)                          | 3 (75)                  | 30 (61.22)                          | 7 (41.18)                                    |
| Concentric hypertrophy | 19 (27.14)                          | 0                       | 11 (22.45)                          | 8 (47.06)                                    |
| Eccentric hypertrophy  | 1 (1.43)                            | 0                       | 1 (2.04)                            | 0  |

LVH: Left ventricular hypertrophy

| Table 5: Comparison of related risk factors  |
|--|
| between abnormal and normal interventricular |
| septum diastolic categories                  |

| Factors                            | IVSd                        |                           |        |  |
|------------------------------------|-----------------------------|---------------------------|--------|--|
|                                    | Abnormal<br>( <i>n</i> =39) | Normal<br>( <i>n</i> =31) | Р      |  |
| BMI (mean±SD)<br>BMI, <i>n</i> (%) | 30.65±5.68                  | 30.00±7.53                | 0.681  |  |
| Overweight                         | 0                           | 4 (12.9)                  | 0.016* |  |
| Obese                              | 32 (82.1)                   | 17 (54.8)                 |        |  |
| Severely obese                     | 7 (17.9)                    | 10 (32.3)                 |        |  |
| Percentage fat (mean±SD)           | 31.06±3.83                  | 28.95±4.63                | 0.041* |  |
| HT, n (%)                          | 5 (12.8)                    | 3 (9.7)                   | 0.681  |  |
| Dyslipidemia, n (%)                |                             |                           |        |  |
| Hypertriglyceridemia               | 7 (18.0)                    | 9 (29.0)                  | 0.273  |  |
| Hypercholesterolemia               | 4 (10.3)                    | 5 (16.1)                  | 0.466  |  |
| Low HDL                            | 8 (20.5)                    | 6 (19.4)                  | 0.904  |  |
| DM, n (%)                          | 0                           | 2 (6.5)                   | 0.055  |  |
| Impaired FBS, n (%)                | 4 (10.3)                    | 8 (25.8)                  |        |  |

\*P<0.001, SD: Standard deviation, BMI: Body mass index, DM: Diabetes mellitus, HDL: High-density lipoprotein, FBS: Fasting blood sugar, HT: Hypertension, IVSd: Interventricular septum diastolic

function in obese children, and those at high risk for cardiovascular dysfunction should be referred for cardiac MRI. There was no previous study standard *z*-score of echocardiographic parameters in Thai children, which might be unclear of abnormal parameters *z*-score from differences in ethnicity. The study could have been strengthened by data on waist-hip circumference ratio and skin fold thickness, the one important maker of obesity other than BMI for analysis.

# **CONCLUSIONS**

Cardiac function abnormality in childhood obesity is significantly correlated with BMI and cardiac dimensions, ventricular wall thickness, and LVM. There is an increase in E/E' ratio, reflecting an intermediate increase in LV filling pressure. There is also evidence of decreased RV systolic function and PHT. The %Fat is an important risk factor for abnormal IVS thickness. Multidisciplinary management of obesity should be initiated as early as possible to prevent future cardiovascular morbidity and mortality.

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# Conflicts of interest

There are no conflicts of interest.

# REFERENCES

- 1. Yamborisut U, Mo Suwan L. Prevalence of childhood and adolescent obesity in Thailand: A review. J Med Assoc Thai 2014;97:44-51.
- 2. Fryar C, Carroll M, Ogden C. Prevalence of Overweight,

Obesity, and Severe Obesity among Children and Adolescents Aged 2-19 Years: United States, 1963-1965 Through 2015-2016. National Center for Health Startistics; 2018. p. 1-6.

- 3. Engin A. The definition and prevalence of obesity and metabolic syndrome. Adv Exp Med Biol 2017;960:1-17.
- 4. Ratanachuek S, Thaweekul P, Eamopas O, Suthutvoravut U. Clinical practice guideline of prevention and management childhood obesity 2014. Thai Ped, [Internet]. Available from: https://www.thaipediatrics.org/?p=700. [Last accessed on 2021 Jan 5].
- Csige I, Ujvárosy D, Szabó Z, Lőrincz I, Paragh G, Harangi M, et al. The Impact of Obesity on the Cardiovascular System. J Diabetes Res;2018:3407306.
- 6. Park MH, Falconer C, Viner RM, Kinra S. The impact of childhood obesity on morbidity and mortality in adulthood: A systematic review. Obes Rev 2012;13:985-1000.
- 7. Cuspidi C, Rescaldani M, Sala C, Grassi G. Left-ventricular hypertrophy and obesity: A systematic review and meta-analysis of echocardiographic studies. J Hypertens 2014;32:16-25.
- 8. Cote AT, Harris KC, Panagiotopoulos C, Sandor GG, Devlin AM. Childhood obesity and cardiovascular dysfunction. J Am Coll Cardiol 2013;62:1309-19.
- 9. Mangner N, Scheuermann K, Winzer E, Wagner I, Hoellriegel R, Sandri M, *et al.* Childhood obesity: Impact on cardiac geometry and function. JACC Cardiovasc Imaging 2014;7:1198-205.
- 10. National Growth Reference for Children Age 5-19 years. Bureau of Nutrition, Department of Health: Ministry of Public Health; 2020.
- 11. Lai WW, Geva T, Shirali GS, Frommelt PC, Humes RA, Brook MM, *et al.* Guidelines and standards for performance of a pediatric echocardiogram: A report from the task force of the pediatric council of the American Society of Echocardiography. J Am Soc Echocardiogr 2006;19:1413-30.
- 12. Nagueh SF, Smiseth OA, Appleton CP, Byrd BF 3<sup>rd</sup>, Dokainish H, Edvardsen T, *et al.* Recommendations for the evaluation of left ventricular diastolic function by echocardiography: An update from the American Society of Echocardiography and the European association of cardiovascular imaging. Eur Heart J Cardiovasc Imaging 2016;17:1321-60.
- 13. Tissot C, Singh Y, Sekarski N. Echocardiographic evaluation of ventricular function-for the neonatologist and pediatric intensivist. Front Pediatr 2018;6:79.
- 14. Devereux RB, Alonso DR, Lutas EM, Gottlieb GJ, Campo E, Sachs I, *et al.* Echocardiographic assessment of left ventricular hypertrophy: Comparison to necropsy findings. Am J Cardiol 1986;57:450-8.
- 15. de Simone G, Daniels SR, Devereux RB, Meyer RA, Roman MJ, de Divitiis O, *et al.* Left ventricular mass and body size in normotensive children and adults: Assessment of allometric relations and impact of overweight. J Am Coll Cardiol 1992;20:1251-60.
- 16. Abbas AE, Fortuin FD, Schiller NB, Appleton CP,

Moreno CA, Lester SJ. Echocardiographic determination of mean pulmonary artery pressure. Am J Cardiol 2003;92:1373-6.

- 17. WHO BMI-Based Classification for Overweight and Obesity BMI-for-Age (5-19 Years). Available from: https://www.who.int/tools/growth-reference-data-for-5to19 years/indicators/bmi-for-age. [Last accessed on 2021 Jan 05].
- 18. BMI and BMI Categories for Children and Teen. Available from: https://www.cdc.gov/obesity/basics/childhood-defining.html. [Last accessed on 2021 Jan 05].
- 19. McCarthy HD, Cole TJ, Fry T, Jebb SA, Prentice AM. Body fat reference curves for children. Int J Obes (Lond) 2006;30:598-602.
- 20. Flynn JT, Kaelber DC, Baker-Smith CM, Blowey D, Carroll AE, Daniels SR, *et al.* Clinical practice guideline for screening and management of high blood pressure in Children and Adolescents. Pediatrics 2017;140:e20171904.
- 21. Colan SD. Normal echocardiographic values for cardiovascular structures. In: Lai WW, Cohen MS, Geva T, Mertens L, editors. Echocardiography in Pediatric and Congenital Heart Disease. Appendix1. West Sussex, UK: Wiley-Blackwell; 2009. p. 765-85.
- 22. BCH Z Score Calculator. Available from: https://zscore. chboston.org. [Last accessed on 2021 Jan 05].
- 23. Ganau A, Devereux RB, Roman MJ, de Simone G, Pickering TG, Saba PS, *et al.* Patterns of left ventricular hypertrophy and geometric remodeling in essential hypertension. J Am Coll Cardiol 1992;19:1550-8.
- 24. Díaz A, Zócalo Y, Bia D. Reference intervals and percentile curves of echocardiographic left ventricular mass, relative wall thickness and ejection fraction in healthy children and adolescents. Pediatr Cardiol 2019;40:283-301.
- 25. Humbert M, Kovacs G, Hoeper MM, Badagliacca R, Berger RM, Brida M, et al. 2022 ESC/ERS Guidelines for the diagnosis and treatment of pulmonary hypertension. Eur Heart J 2022;43:3618-731.
- 26. Chinali M, de Simone G, Roman MJ, Lee ET, Best LG, Howard BV, *et al.* Impact of obesity on cardiac geometry

and function in a population of adolescents: The strong heart study. J Am Coll Cardiol 2006;47:2267-73.

- 27. Mitter SS, Shah SJ, Thomas JD. A test in context: E/A and E/e' to assess diastolic dysfunction and LV filling pressure. J Am Coll Cardiol 2017;69:1451-64.
- 28. Ren J, Wu NN, Wang S, Sowers JR, Zhang Y. Obesity cardiomyopathy: Evidence, mechanisms, and therapeutic implications. Physiol Rev 2021;101:1745-807.
- 29. Balaji S, DiLorenzo MP, Fish FA, Etheridge SP, Aziz PF, Russell MW, *et al.* Impact of obesity on left ventricular thickness in children with hypertrophic cardiomyopathy. Pediatr Cardiol 2019;40:1253-7.
- 30. Rudski LG, Lai WW, Afilalo J, Hua L, Handschumacher MD, Chandrasekaran K, *et al.* Guidelines for the echocardiographic assessment of the right heart in adults: A report from the American Society of Echocardiography endorsed by the European Association of Echocardiography, a registered branch of the European Society of Cardiology, and the Canadian society of Echocardiography. J Am Soc Echocardiogr 2010;23:685-713.
- 31. Burns AT, Hansen SL, Turner ZS, Aden JK, Black AB, Hsu DP. Prevalence of pulmonary hypertension in pediatric patients with obstructive sleep apnea and a cardiology evaluation: A retrospective analysis. J Clin Sleep Med 2019;15:1081-7.
- 32. Pu S, Yin L, Wen B, He J. The association of body mass index with the risk of pulmonary hypertension in adults: A systematic review and meta-analysis of observational studies. Front Med (Lausanne) 2021;8:680223.
- 33. Zeng Q, Sun XN, Fan L, Ye P. Correlation of body composition with cardiac function and arterial compliance. Clin Exp Pharmacol Physiol 2008;35:78-82.
- 34. Zeng Q, Dong SY, Sun XN, Xie J, Cui Y. Percent body fat is a better predictor of cardiovascular risk factors than body mass index. Braz J Med Biol Res 2012;45:591-600.
- 35. Jittham W, Hirunpoom J, Nimpun D. Obesity-related factors that affect 6-minute walk test performance in Thai obese children. J Child Obes 2022;7:124.