LEFT VENTRICULAR MASS AND LEFT VENTRICULAR MASS INDEX IN NORMAL MALAY PRIMARY SCHOOL CHILDREN

BY

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ABBREVIATIONS

ASE	American Society of Echocardiography
BMI	Body mass index
BP	Blood pressure
BSA	Body surface area
CO	Cardiac output
DBP	Diastolic blood pressure
HR	Heart rate
ICC	Intraclass correlation coefficient
IVSTd	Interventricular septum thickness during diastolic
IQR	Interquartile Range
LA	Left atrium
LV	Left ventricle
LVH	Left ventricular hypertrophy
LVIDd	Left ventricular internal diameter during diastolic
LVM	Left ventricular mass
LVMI	Left ventricular mass index
LVPW	Left ventricular posterior wall thickness
MLR	Multiple Linear Regression

PWTD	Posterior wall thickness in diastole
RVDs	Right Ventricle internal diameter during systole
RWT	Relative wall thickness
SBP	Systolic blood pressure
SD	Standard deviation
SLR	Simple Linear Regression
SV	Stroke volume
TTE	Transthoracic echocardiography

ABSTRAK

Pengenalan

Jisim ventrikel kiri ("*Left Ventricular Mass* (LVM)") dan indeks jisim ventrikel kiri ("*Left Ventricular Mass Index* (LVMI)") merupakan dua parameter yang penting bagi meramalkan penyakit kardiovaskular pada masa dewasa.

Walaupun pembesaran ventrikelkiri ("*left ventricular hypertrophy*") di kalangan kanak-kanak semakin diberi perhatian tetapi secara relatifnya tidak banyak terdapat data yang diterbitkan mengenai nilai-nilai normal jisim ventrikel kiri di kalangan kanak-kanak yang sedang membesar.

Metodologi

Kajian secara lintang dijalankan pada bulan Oktober dan November, 2009 di Sekolah Kebangsaan Lundang, Kota Bharu. Murid-murid sekolah rendah yang normal daripada prasekolah, darjah 2, 4 dan 6 terlibat dalam kajian ini. Kanak-kanak yang mempunyai sejarah penyakit jantung atau darah tinggi, ketidaknormalan pada pemeriksaan fizikal atau ekokardiogram, dan yang mempunyai BMI yang tidak normal dikecualikan dari kajian. Satu set soalan berkenaan sejarah penyakit atau sebarang penyakit yang dialami oleh murid-murid dan juga kebenaran bertulis diedarkan kepada ibubapa-ibubapa yang terlibat sebelum kajian dijalankan. Pemeriksaan fizikal, penimbangan berat, pengukuran tinggi, bacaan tekanan darah dan pemeriksaan ekokardiogram direkodkan. Bacaan LVM diperolehi daripada kiraan mesin ekokardiogram, manakala bacaan LVMI diperolehi daripada formula LVM/tinggi$^{2.7}$.Carta persentil dibina berdasarkan umur, berat, tinggi,

luas permukaan badan (BSA) dan indeks jisim badan (BMI). Faktor-faktor yang mempengaruhi LVM dan LVMI dikenalpasti menggunakan teknik statistik "Simple Linear Regression". Faktor-faktor klinikal yang dikenalpasti dipilih untuk menentukan faktor yang paling mempengaruhi LVM dan LVMI.

Keputusan

Carta persentil berdasarkan umur merupakan carta yang terbaik hasil daripada kajian ini. Faktor-faktor yang mempengaruhi LVM adalah umur, berat, tinggi, BMI, BSA dan tekanan darah sistolik (SBP). Manakala faktor-faktor yang mempengaruhi LVMI adalah umur, berat, tinggi dan BSA. Untuk bacaan ekokardiogram, *"aortic root (annulus)", "aortic arch'* dan *"MV annulus"* mempengaruhi LVM manakala *"aortic root (annulus)", "aortic arch"* , atrium kiri dan *"MV annulus"* mempengaruhi LVMI. Hasil daripada teknik statistik "Multiple linear regression", kami mendapati berat dan SBP merupakan faktor yang kuat mempengaruhi LVM manakala umur, SBP dan ketinggian mempengaruhi LVMI.

Kesimpulan

Kami telah menemui carta persentil LVM dan LVMI kanak-kanak berumur 5 – 12 tahun, tetapi sekiranya sampel saiz lebih besar, akan membolehkan carta persentil yang lebih baik.

LVM adalah paling dipengaruhi oleh berat dan SBP manakala LVMI paling dipengaruhi oleh umur, SBP dan tinggi. Kami menghasilkan formula untuk meramalkan bacaan LVM (r^2 = 0.24) dan LVMI (r^2 = 0.40) dengan kesalahan standard 22.97 dan 13.74 berdasarkan analisa yang telah dijalankan. Formula-formula berikut adalah :

$$\text{LVM (g)} = -6.81 + 1.05(\text{beratdalam kg}) + 0.42(\text{SBP})$$

$$\text{LVMI} = 94.23+1.87(\text{umurdalamtahun}) - 80.32(\text{tinggidalam meter}) +0.26(\text{SBP})$$

ABSTRACT

Introduction

Left ventricular mass (LVM) and Left ventricular mass Index (LVMI) aretwo parameters that are considered importantin predicting the outcomes of cardiovascular diseases in adults.Even though there are a lot of interest in the problem of left ventricular hypertrophy in children,there is relatively little published data on normal values of the left ventricular mass (LVM) during the developmental age.

Methodology

A cross sectional study was conducted from October to November,2009 atSekolahKebangsaanLundang, Kota Bharu. Normal primary school children from preschool, Standard 2,4 and 6 were included in this study. Children with history of heart problem or hypertension, abnormal physical examination or echocardiogram findings and abnormal BMI were excluded. A set of questionnaires and consent were obtained from parents prior to the examination. Physical examination, weight, height, blood pressure and echocardiogram measurements were recorded. LVM measurement was calculated by echocardiogram machine and LVMI was calculated by dividing LVM to height in meter power of 2.7 ($LVM/height^{2.7}$). Percentile chartswere created from the data available according to age, weight, height, BSA and BMI. The factors affecting LVM and LVMI were identified using simple linear regression (SLR). Multiple linear regressions (MLR)was performed to determine the final model affecting LVM and LVMI.

Results

The most acceptable percentile chart in our study was percentile chart according to age. Factorsaffecting LVM were age, weight, height, BMI, BSA and SBP. While factors affecting LVMI were age, weight, height and BSA. Echocardiogram measurements found thataortic root, aortic arch and MV annulus affect LVM, whereas aortic root (annulus), aortic arch, Left atrium and MV annulus affect LVMI. From multiple linear regressions, we identified that weight and SBP had strong correlationwith LVM while age, SBP and height had strong correlation with LVMI.

Conclusion

We have provided a pilot percentile chart for LVM and LVMI of normal school children between aged 5 to 12 years old but larger sample size would be able to produce a better percentile chart. LVM was most affected by weight and SBP whereas LVMI were affected by age, SBP and height. We provided a formula to estimate the LVM (r^2= 0.24) and LVMI (r^2= 0.40) with standard error of 22.97 and 13.74. The formula as below:

$$\text{LVM (g)} = -6.81 + 1.05(\text{weight in kg}) + 0.42(\text{SBP in mmHg})$$

$$\text{LVMI} = 94.23 + 1.87(\text{age in years}) - 80.32(\text{height in meters}) + 0.26(\text{SBP in mmHg})$$

INTRODUCTION

1. INTRODUCTION

Left ventricular hypertrophy (LVH) has been shown to be an independent predictor of cardiovascular morbidity. Early detection would preventcomplications such as myocardial ischaemia, congestive heart failure,cardiac arrhythmias and sudden death. Echocardiogram is one of the widely used method to detect LVH by measuring wall thickness and calculating the left ventricular mass (LVM). The M-mode echocardiogram calculates the LVM based on Left Ventricular Internal Diameter, Posterior Wall Thickness and Interventricular Septum Thickness during diastolic. The LVM measurement given was divided by height power of 2.7 to get the left ventricular mass index (LVMI) measurement ($LVMI = LVM/height^{2.7}$).

However, we do not have the proper normal value references for LVM and LVMI in the children. Besides, there are multiple factors such as age, gender, weight, height, body surface area (BSA) and body mass index (BMI) that can influence the LVM and LVMI.

There were total of about 25 echocardiographic parameters measured for the all selected students. In this study, we concentrate on the LVM and LVMI measurements and the factors that have relationship with them such as aortic root (annulus), aortic isthmus, aortic arch, MV annulus and Left atrium (LA).

LITERATURE REVIEW

2. LITERATURE REVIEW

2.1 Anatomy and Physiology of the heart.

The heart is a hollow muscular organ located in thorax between two lungs in the anterior mediastinum. It has four chambers, two atrium and two ventricles. The right and the left sides of the heart divided by the septum and further divided into atrium and ventricle. Between each pair of chambers there are valves preventing any back flow of blood. There are two separate pumps in the right and left. Right side receives blood from the body and sends it to the lungs. The left side receives blood from the lungs and sends it to the systemic circulation.

Heart wall consist of three layers those are endocardium (inner layer), myocardium (middle layer) and epicardium (outer layer). Most cardiac muscle is typically striated muscle. The myocardial cells are linked to one another by intercalateddisks that contain gap junctions. Gap junctions allow depolarization to spread rapidly from cell to cell.

When the heart meets a hemodynamic burden, three mechanisms take place to compensate. First, it uses Frank-Starling mechanism, the ability of heart to change its force of contraction and therefore stroke volume in response to changes in venous return.Second, it augments muscle mass to bear the extra load. This increase in mass is due to hypertrophy of existing myocytes. In pressure overload, the parallel addition of sarcomeres cause increase in myocytes width resulting in increases wall thickness. Thirdly, as in chronic adjustment, there is recruitment of neurohormonal mechanisms to increase contractility (Lorell and Carabello, 2000).

In Frank-Starling mechanism it states that increase in preloadresulting in increases end-diastolic pressure, which increases force of ventricular contraction. The Frank-Starling law explains the factors which control stroke volume and the heart's ability to respond to changes in demand for cardiac output. The capability of the myocardium to generate force depends on the initial length or stretch of the muscle cells prior to contraction. The degree of stretch (preload) of the cardiac muscle cells determines stroke volume. The larger the end diastolic volume the more the muscle fibers are stretched leading to a greater stroke volume.

There are two mechanisms which may clarify this condition. First, the stretching of muscle fibers more than their normal physiological limits results in a greater length-tension relationship. Resting cardiac muscle cells are typically shorter than their optimal length, hence, any increase in the length of cardiac muscle cells from stretching results in a dramatic increase in contractile force.Secondly, the stretching of muscle fibers raises the number of active cross bridges between the actin and myosin filaments. When contraction occurs these increased numbers of cross bridges yield a greater force of contraction.

2.2. Left Ventricular Hypertrophy (LVH)

LVH refers to an increase in the size of myocardial fibers in the main heart pumping chamber. It is usually the response to a chronic volume or pressure overload. The most important pressure overload conditions are systemic hypertension, aortic stenosis and coarctation of aorta. The states associated with left ventricular volume overload are

aortic or mitral valve regurgitation and dilated cardiomyopathy. Pressure overloads cause increase in wall thickness and volume overload cause chamber dilatation.

According to LaPlace's Law, the load on any region of the myocardium is given as below:

$$\frac{Pressure\ x\ radius}{2x\ wall\ thickness}$$

Thus, increase in pressure can be offset by an increase in wall thickness.

In volume overload, there is cavity dilatation with a decrease in ratio wall thickness/chamber dimension this pattern called eccentric hypertrophy. (Lorell and Carabello, 2000)

A diagnosis of LVH may change clinical management for children with conditions such as hypertension (Khoury *et al.*, 2009) and other cardiovascular risk factors. Therefore, it is important to detect it early.

LVH is an independent prognostic factor and clinical outcome for the major cardiovascular events and mortality such as stroke, sudden death, myocardiac infarction,congestive heart failure, cardiac arrhythmias and coronary heart disease(Crowley *et al.*). It has prognostic importance in adults and considered to have similar prognostic value in pediatrics and represents an early stage in progression of

cardiovascular disease. Regardless of other risk factors, those with high LVMI have a risk that is at least double for future cardiovascular morbidity and mortality (Vakili *et al.*, 2001)

2.3. Tools to diagnose LVH

Electrocardiography (ECG) is a convenient tool to detect LVH. It is relatively inexpensive and easily available. It has acceptably high specificity to diagnose LVH but the limitation it has low sensitivity (Waqas et al, 2005)

Echocardiography is widely used to detect LVH. The most commonly practice is by using LVM divided by height in meters to the 2.7^{th} power. LVH is widely defined as a LVMI ($g/m^{2.7}$) more than 95^{th} percentile (Daniels *et al.*, 1995). In adults LVH is identified as a LVMI $>51 g/m^{2.7}$(Daniels, 1999)and in children there is no exact cutoff points. Though the value of $>38.6 g/m^{2.7}$waswproposed from M-mode derived froma single healthy pediatric reference population (192 healthy children 6 to 17 years old) (Daniels *et al.*, 1995).

The other method to assess LVH is by cardiac geometry. LV estimation depends on wall thickness and diastolic chamber dimension. Parietal thickness and its relation to LV chamber size have been distinguish to measure LVH for more than 30 years (Sjogren, 1971)

$$RWT = \frac{2\ x\ posterior\ wall\ thickness}{LV\ diastolic\ diameter} \quad OR$$

$$\frac{Septal\ wall\ thickness + Posterior\ wall\ thickness}{LV\ diastolic\ diameter}$$

*RWT: Relative wall thickness

Cutoff levels for LVM and RWD were created to evaluate LV geometry. LV can be classified into four categories: normal, concentric remodeling, eccentric hypertrophy and concentric hypertrophy. Normal geometry had LVM and RWT below 95th percentile. Concentric remodeling was described as normal LVMI but elevated RWT. Eccentric hypertrophy was defined as elevated LVMI with normal RWT and concentric hypertrophy explained as both LVMI and RWT more than 95th percentile.

2.4 Echocardiograph examination in Paediatrics

Echocardiograph examination is a test that uses high-frequency sound waves (ultrasound) to produce an image of the heart's internal anatomy. A transducer (small probe) is placed on the child's chest and sends out ultrasonic sound waves at a high frequency. A small amount of clear gel is applied between the transducer and chest to ensure there is proper skin contact. When the probe is placed in certain positions and at certain angles, the ultrasonic sound waves move through the skin and other body tissues to the heart tissues, where the waves "echo" the heart structures. The probe picks up the reflected waves and sends them to a computer. The computer software translates the echoes into an image of the heart structures including the walls and valves. The

procedure is painless and usually lasts less than 30 minutes. No preparation is needed for the examination.

In paediatrics, echocardiogram is used to diagnose congenital heart defects and acquired heart disease such as infectious, neuromuscular or metabolic disorders. Transthoracic echocardiography (TTE) is an ideal tool for cardiac assessment because it is non-invasive, portable, and efficacious in providing detailed anatomic, hemodynamic, and physiologic information of the paediatric heart(Lai *et al.*, 2006). M-mode (one dimensional) echocardiography makes it possible to assess and quantitate non-invasively certain aspect of cardiac anatomy and function.

2.5Left Ventricular Mass (LVM)

LVM is generally calculated as the difference between the epicardium delimited volume and the left ventricular chamber volume multiplied by an estimate of myocardial density(Foppa et al., 2005).LVM can be measured in various techniques. The gold standard is an autopsy; however it is invasive and can be done as post mortem only. Echocardiography is the most widely technique used for assessment of LVM. It can be estimated using M-mode (one dimensional), two-dimensional imaging and even three dimensional imaging.

M-mode imaging allows better endocardial border definition if adequate ultrasound beam positioning and ventricle shape approaches normality. M-mode is preferred because of its technical feasibility and availability.

Two-dimensional imaging estimates ventricular diameter measurement and detects regional motion abnormalities but it is limited due to lower lateral resolution and frame rates. Furthermore it is time consuming.

For the real time three-dimensional echocardiography, this method is able to document accurate real time LVM estimation measurements via wall thickness and volume without limitations of geometrical assumptions. However this is not in general use yet even though the calculation and estimation have been mainly worked out but there are not much data on percentiles (3D) especially in children.

By M-mode technique, LVM is calculated using the mathematical principle, based on the LVIDd (Left Ventricular Internal Diameter in Diastole), PWTD (Posterior Wall Thickness in Diastole) and IVSTd (Interventricular Septum Thickness in Diastole) measurement. There are three formulas to estimate LVM. First formula is the original calculations from Troy and coworkers based on volume formula(Troy *et al.*, 1972).Second formula suggested by Devereux and colleagues using the Penn convention as the border definition criteria. Their prediction equation in this pivotal study was derived from necropsy findings of 34 patients (Devereux and Reichek, 1977).

Third formula, Devereux and colleagues recommended a new adjusted equation, validated on necropsy findings of 52 individuals (Devereux *et al.*, 1986), using the American Society of Echocardiography (ASE) convention and accounting for the discrepancy in about 20%.

Formula 1(Troy *et al.*, 1972):

$$\text{LV mass (Troy)} = 1.05\ ([\text{LVIDd} + \text{PWTD} + \text{IVSTd}]^3 - [\text{LVIDd}]^3)\ \text{g.}$$

Formula 2(Devereux and Reichek, 1977) :

$$\text{LVM (Penn)} = 1.04\ ([\text{LVIDd} + \text{PWTD} + \text{IVSTd}]^3 - [\text{LVIDd}]^3) - 13.6\ \text{g.}$$

Formula 3(Devereux *et al.*, 1986):

$$\text{LVM (ASE): } 0.8\ (1.04\ ([\text{LVIDd} + \text{PWTD} + \text{IVSTd}]^3 - [\text{LVIDd}]^3)) + 0.6\ \text{g.}$$

All the measurements of septum and posterior wall in left ventricular diameter in diastole. Comparison between M-mode measurements of border in multiple criteria as below(Foppa *et al.*, 2005):

1) Troy: measures from leading to trailing edge in septum and from leading edge to posterior wall.
2) Penn: same as Troy criteria but excludes echoes from parietal walls in septum
3) ASE: measures leading to leading edge in in both septum and posterior wall.

However there are constraint factors in the LVM formula. All necropsy validation studies have limited sample size and this formula may not perform adequately in distorted ventricles.

There are multiple factors affecting LVM. A study in Muscatine involving 904 normal children, aged 6 to 16 years found that a strong positive linear association of LVM with age, weight, height, systolic and diastolic blood pressure.These factors need to be considered when interpreting LVM in childhood (Malcolm *et al.*, 1993).

2.6. Left Ventricular Mass Index (LVMI)

There are some physiologic variations effecting the LVM, such as body size including height, weight, body surface area (BSA), body mass index (BMI) and free-fat mass. The best way is still debated and unclear.

BSA correction reduces variability due to body size and gender (Devereux *et al.*, 1984), but underestimates LVM in upper range of the body surface area distribution (de Simone *et al.*, 1992). A study by Szewczykowska et al in 2009amonghealthy children aged 2 weeks to 18 years found there were significant correlation of LVM with BSA and with age. There were no significant gender dependent differences in LVM values(Szewczykowska, 2009)

Height to the power of 2.7 ($Height^{2.7}$) derived from regression models in normal samples from De Simone and coworkers (de Simone *et al.*, 1992) is the most accurate estimation of LV hypertrophy and risk for pathologic changes in the heart structure, especially in obese subjects. Other studies,Zoccali and colleagues and Liao and colleagues also found LVH indexed by $height^{2.7}$ to be a better predictor of cardiovascular events than LVH indexed using body surface area.Zoccali studied a

group of patients undergoing dialysis(Zoccali et al., 2001). Liao and colleagues (Liao *et al.*, 1997) studied 988 patients and identified progressive increments in death rates with both body surface area and better correlation with height$^{2.7}$ indexing criteria.

Gender differences in LVM are first noticed around puberty. It can be minimized by adequate indexing of body size. Before puberty, LVM is only modestly higher in boys than in girls. Most of the sex differences in adult LVM follows differences in body size and is due to a greater "physiological" LV hypertrophy in men than in women. (de Simone *et al.*, 1995).

In conclusion, LVMI calculated as LVM in grams divided by height in meters to the 2.7th power has been widely used in adults and also in children.

2.7. Percentile charts

There are percentiles chart available for LVMI (LVM g/m$^{2.7}$) constructed for normal healthy non obese children aged 0-18 years oldin Cincinnati Children's Hospital Medical Center. In this study, children less than9 years old were noted to have indices that varied with age, therefore LVMI must be compared with percentile charts and for the younger children, a better indexing method is needed.LVM/height$^{2.7}$ curves of 5th, 10th, 25th, 75th, 90th and 95th quantiles were constructed according to age. Results of their study showed for children aged more than 9 years, median LVM/height$^{2.7}$ ranged from 27 to 32 g/m$^{2.7}$ and had little differences with age.In those aged 9 years, quantiles of LVM/height$^{2.7}$ vary little, and values > 40 g/m$^{2.7}$ in girls and > 45 g/m$^{2.7}$ in boys can be considered

abnormal (> 95th percentile). However, for patients aged less than 9 years, the index varies with age. Thus, measured LVM/height$^{2.7}$ must be compared with percentile curves. This variation in LVM/height$^{2.7}$ in younger children indicates that a better indexing method is needed for this age group (Khoury et al, 2009)

2.8Factors effecting LVM

There are various factors that determine LVM and hypertrophy. Recognized factors are age, ethnicity, familial predisposition, obesity and blood pressure. Other clinical factors such as diabetes and metabolic disease, primary valvular and myocardiac disease, environment exposure, lipid level, pulmonary function, heart rate and hematocrit also affect LVH (Foppa *et al.*, 2005)

For age, LVM increases with aging, particularly parietal thickness both in normotensive and hypertensive patient (de Simone *et al.*, 2005). Heart size increases during infancy and adolescence due to increase in body size. One study in 2008 in Cincinnati Children's Hospital Medical center noted (Crowley *et al.*) single method of indexing LVM to height is not appropriate in younger children because there are differential growth rates of myocardium and the rest of the body. This resulting LVMI is higher in children aged less 9years old compared with those aged more than 9 years old (Khoury *et al.*, 2009).

For ethnicity, LVH is higher prevalent in certain ethnics. For example, in African-American and Hispanic are found to have higher prevalence for LVH(Foppa *et al.*, 2005, Kizer *et al.*, 2004).

There was evidence of contribution of familial predisposition to the risk of LVH. It appears to contribute to increase LV wall thickness causing concentric remodeling and concentric LVH (Schunkert *et al.*, 1999).

Environment exposure such as alcohol consumption, salt intake, smoking and sedentary life style has been associated with an increase in LVM (Foppa, 2005). Low birth weight at 1 year old also one of the risk factor of LVH, concordant with Baker's Theory of the fetal and early life origin of chronic disease (Vijayakumar, 1995)

2.9 LVM and blood pressure

Burke et al has shown that the increase BP is related to increase LVM(Burke *et al.*, 1987). Studies of normal and hypertensive children have found that systolic blood pressure (SBP) and LVMI are positively associated across a wide range of blood pressure values, with no clear blood pressure threshold to predict pathological increase in LVMI (Sorof *et al.*, 2002).

LVH which is defined as LVMI > $51 g/m^{2.7}$ in adults showed 4-fold risk of cardiovascular morbidity in hypertensive adults. It is recognized as target organ damage

in several clinical practice guidelines, representing an intermediate unfavorable prognostic marker(Chobanian *et al.*, 2003). In children, it represents an early stage in the progression of cardiovascular disease. It remains to be determined whether treatment of hypertensive children results in reversion of LVMI and resolution of the LVH (Sorof *et al.*, 2002).

2.10 LVM and body mass index (BMI)

Obesity is increasingly predictable as an independent predictor of cardiovascular morbidity and mortality (Seidell *et al.*, 1999). The increase in LVM in obesity is probably more than a simple physiologic adaptation. The proposed mechanism for left ventricular dilatation in obesity is that the increased vascularity of adipose tissue creates a higher circulating blood volume causing left ventricular dilatation, as well as increased sympathetic predominance (Messerli *et al.*, 1981).

Patients with obesity are usually associated with hypertension and other metabolic diseases which also can lead to LVH. Adjusting by height$^{2.7}$ minimize the interference of obesity. In obesity without any complication, it is not a risk factor for LVH when indexed by either BSA or height$^{2.7}$(Foppa *et al.*, 2005)

OBJECTIVES

3. OBJECTIVES

3.1 General objectives:

To explore relationship between LVM and LVMI with clinical and echocardiograph parametersin normal Malay primary school children.

3.2 Specific objectives:

1) To create a pilot percentile chart for left ventricular mass and left ventricular mass index in normal Malay primary school children based on age, gender, weight, height,body surface area (BSA) and body mass index (BMI).

2) To investigate relationship between clinical parameters(age, weight, height, body mass index, body surface area, systolic blood pressure and diastolic blood pressure) with left ventricular mass and left ventricular mass index in normal Malay primary school children.

3) To explore relationship between echocardiographic parameters (Aortic root diameter, aortic isthmus, aortic arch, MV annulus and left atrium) with left ventricular mass and left ventricular mass index in normal Malay primary school children.

3.3 RESEARCH HYPOTHESIS

1. There is no difference in percentile charts for LVM and LVMI based on age group, gender, weight, height, BSA or BMI.

2. There is significant linear relationship between age, weight, height, BMI, BSA,systolic blood pressure and diastolic blood pressure with LVM and LVMI in normal Malay primary school children

3. There is significant relationship between echocardiogram parameters (Aortic root diameter, aortic isthmus, aortic arch, MV annulus and left atrium) with LVM and LVMI in normal Malay primary school children.

METHODOLOGY

4. METHODOLOGY

4.1 Study Design

A cross sectional study involving 102normal children was conducted fromOctober toNovember, 2009 in Sekolah Kebangsaan Lundang, Kota Bharu, Kelantan. In this school there were 3 classes in standard 1 to standard 6 and 2 classes in preschool. Stratified random sampling was used to select the samples. A classwas selected randomly from preschool, standard 2, Standard 4 and Standard 6 from the above school. A classroom consisted of about 30 students. All students from each selected class who consented and met the inclusion criteria were included as samples.

4.2 Inclusion and exclusion criteria

Inclusion criteria:

- Age 5 to 12 years old.
- All asymptomatic students from selected classes
- All students whose parents consented for the study

Exclusion criteria:

- Children with history of heart disease or related cardiovascular disease.
- Children with abnormal findings noted during physical examination or after echocardiography (e.g.: CRHD)
- Children with BMI <3rd centile and >95th centile.

4.3 Sample size

We used PS program(Power and sample size calculation program) version 3.0.43 to estimate the sample size.

Table 4.1 Sample size calculations.

	SD	Detectable difference (Δ^2)	Power	Sample size
Weight (kg)	11.8	5	0.8	88
Height (cm)	30.27	5	0.8	576
BSA(m^2)	0.34	0.1	0.8	182
Age (years)	4.2	1	0.8	278

The above tables showed sample size calculation for various clinical parameters with their SD and expected detectable differences based on previous study. We need to study between 88 to 576 per group to be able to reject our null hypothesis that the population means between the groups are equal with probability (power) 0.8.

4.4 Sampling methods

Stratified random sampling methods were used. All students from selected classes of Preschool, Standard 2, 4 and 6 were involved. A set of questionnaire were distributed to them to obtain the background data and past medical history (Questionnaire enclosed in Appendix 6). A written consent was asked from parent.

All students had undergone measurement of weight, height and blood pressure. Physical examination for clinical assessment performed by the investigator, followed by echocardiograph examination by Paediatric Cardiologist or Paediatrician trained in performing echocardiographic examination.

4.5 Measurement issues (validity)

Blood Pressure

Blood pressure for each student was measure using electronic BP measurement (OMRONAutomatic blood pressure monitor with intellisense Model T8). Measurement done in sitting position with arm supported at the level of heart over the right arm using the appropriate cuff. Measurement was repeated twice if BP abnormal. However in limited time, the duration of repeated BP was less than an hour.

Normal value for the SBP and DBP was based on the blood pressure levels specific for gender, age and height percentile (Percentile chart enclosed in Appendix 1 and 2).

Weight

Weight was measured using a weight scale which was already calibrated (SECA 700 mechanical column scale, US). All candidates were weight using the same weighting scale with shoes off. The weight measured in kilograms (kg) to one decimal point.

Height

Height was measured using a stadiometer (SECA 217 portable stadiometer, US). All candidates were instructed to shoes off and stand up straight. The height was recorded by the investigator. The measurements were recorded in centimeters (cm) to two decimal points.

Body mass index (BMI)

BMI was calculated using the formula:

$$BMI = Weight\ (kg) / height\ (m^2)$$

Students with abnormal BMI ($<3^{rd}$ or $>95^{th}$centile, according to BMI percentile by CDC) were excluded.

Echocardiography

Echocardiography (M-mode) was done to all candidates by Paediatric Cardiologist or Paediatrician trained in performing echocardiographic examination, assisted by two trained staff nurse in Hospital Universiti Sains Malaysia. A SonoSite Micromaxx device (SonoSite Inc., Bothell, Washington, USA) with a 2.5 – 3.5MHz linear transducer was used. The measurements were performed according to recommendations of the American Society of Echocardiography (ASE) in M-Mode. LVM was calculated with the Deveroux formula by the machine(Devereux et al., 1986). LVMI was calculated by LVM (g)/height ($meter^{2.7}$) (De Simone, 1999).

The parameters measured were:

- Right ventricle :
    - Right ventricular wall during diastolic (RVWd)