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EFFECT OF EXERCISE INTENSITY AND DIET INTERVENTION ON CARDIAC FUNCTION AMONG OBESE CHILDREN AND ADOLESCENTS

Master's thesis in Exercise Physiology and Sports Science

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Abstract

Introduction: Childhood obesity is an important risk factor for the early cardiovascular disease. Studies show conflicting results on whether it is the diet or physical inactivity that play the most important role in treating childhood obesity and possible health consequences.

Objectives: The aim of the study was to measure the cardiac function before and after three months intervention including only diet, continuous moderate exercise (CME) and high intensity aerobic interval training (AIT) in obese children/adolescents; to compare the cardiac function among exercise (CME+AIT) combined diet intervention with diet intervention only.

Method: A randomized controlled trial study was performed. In total 29 obese (ISO-BMI $\geq$ 30 kg/m^2) children (16 girls,13 boys) with mean age 11.3 ± 2.4 years and ISO-BMI 32.9 ± 3.3 kg/m^2 were randomized to either of three months intervention groups: Diet (32.8 ± 3.1 kg/m^2), CME (34.8 ± 4.3 kg/m^2) and AIT (31.2 .± 2.2 kg/m^2) respectively. The CME performed training at 70% of maximal heart rate (HR_{max}) for 47 minutes and the AIT performed 4×4 minutes training at 85-95% of HR_{max} with 3 minutes active interval (60% HR_{max}) in between. Both intervention groups performed the training session twice in the lab and once at home in each week for consecutive 12 weeks. Diet intervention together with AIT and CME were counseled together with their caregiver for healthy food choices for every second weeks for consecutive three months of intervention period. Anthropometric measurement with body composition, maximal oxygen uptake and resting echocardiography were done before and after intervention program. Mean ± standard deviation was calculated. Paired t-test and one way ANOVA test was used to compare the mean differences within and between the groups from baseline to three months test. The statistical significance of $p< 0.05$ was set.

Result: In total 21 subjects completed the three months intervention. BMI tended to reduce in all three groups. Left ventricular end-diastolic volume indexed to body surface area (LVEDVI) increased almost significantly in the CME group by 24.5% (p=0.09) and AIT group by 30.5% (p=0.2) respectively. Ejection fraction increased significantly in the AIT by 16.3% (p=0.05). The CME improved lean body mass (LBM) (p=0.04) significantly as well as AIT improved LBM almost significantly (p=0.07). The resting heart rate significantly reduced by 10 BPM (p=0.05) and the upright blood pressure had a tendency towards reduction by 6 mmHg (p=0.21). Maximal oxygen uptake did not improve after intervention. When exercise (CME+AIT) combined diet intervention was compared with diet intervention only, exercise combined diet intervention improved LVEDV by 24.6% (p=0.02) and LVEDVI by 26.9% (p=0.03) and almost significantly shortened IVRT (p=0.08); diet intervention reduced IVRT (p=0.006) after intervention. LBM significantly improved among exercise combined diet intervention by 1.7% (p= 0.003). The other variables remained unchanged in both groups after intervention.

Conclusion: Aerobic interval training combined with diet advice improved cardiac function more than moderate exercise and only diet intervention. The exercise intervention (CME+AIT) improved more variables than the diet intervention alone.

Limitation and strength: Significant difference was not achieved in several parameters due to small sample size**.** However the safe, well-controlled and highly defined exercise intensity intervention regimen is a strength of this study.

Keywords: obesity, children, adolescents, continuous moderate exercise, aerobic interval training, diet

List of abbreviations

BMI: Body Mass Index

WC: Waist Circumference

FM: Fat Mass

FFM: Fat Free Mass

BP: Blood Pressure

AIT: Aerobic Interval training

CME: Continuous Moderate Training

LV: Left ventricle

LVM: Left ventricular mass

LA: Left atrium

LVEDV: Left ventricular end diastolic volume

LVEDVI: Left ventricular end diastolic volume index

LVESV: Left ventricular end systolic volume

SV: Stroke volume

SVI: Stroke volume index

CO: Cardiac output

COI: Cardiac output index

HR: Heart rate

LVOT: Left ventricular outflow tract

$\mathbf{V_{maxLVOT}}$: Maximal velocity in the left ventricular outflow tract

E: Peak early mitral inflow velocity

A: Late mitral inflow velocity

DT: Deceleration time of early mitral inflow velocity

IVRT: Isovolumic Relaxation time

DT: Deceleration time

S′: Peak systolic tissue Doppler velocity

e′: Peak early diastolic Doppler velocity

A′: Peak late diastolic tissue Doppler velocity

E/A: Mitral ratio of peak early to late diastolic filling velocity

E/e′: Mitral filling pressure

$HR_{max:}$ Heart Rate at the peak of exercise

VO_{2max}: Maximal oxygen uptake

SD: Standard Deviation

ADHD: Attention Deficit Hyperactivity Disorder

BOD POD: Body Composition Tracking System Analysis

AV plane: Atrio-ventricular plane

CVD: Cardiovascular Disease

CHD: Chronic Heart disease

CDC: Centers for Disease Control

LVH: Left Ventricular Hypertrophy

SHS: Strong Heart Study

FFA: Free Fatty Acids

CRP: C-Reactive Protein

IL-6: Interleukin-6

PGC- 1∂: Peroxisome-proliferator- activated receptor gamma co-activator 1∂

LDL: Low Density Lipoprotein

HDL: High Density Lipoprotein

Contents

Introduction

1.1. Prevalence of childhood obesity

The prevalence of childhood overweight/obesity has doubled to tripled between early 1970s and late 1990s in the USA and the most industrialized countries as well as; in the urban areas of several lower income countries (Y. Wang & Lobstein, 2006). The prevalence further increased from 4.2% in 1990 to 6.7% in 2010 and is estimated to reach to 9.1% by 2020 (De Onis, Blössner, & Borghi, 2010). In Norway, Young-HUNT 3 study concluded that a total of 20% of the girls and 22% of the boys in secondary schools; and 25% of girls and 27% of boys in high school are classified as overweight or obese. One in five girls and one in four boys can be classified as either overweight or obese and prevalence is higher among boys (Krokstad & Knudtsen, 2011). The epidemic has levelled off or stabilized in most of the countries like Australia, Europe, Japan and America. However the prevalence is still increasing in some of the countries like China, Vietnam and Germany (Rokholm, Baker, & Sørensen, 2010). Therefore, the research into the causes, prevention and treatment of childhood obesity should remain a priority.

1.2. Definition of overweight and obesity

Obesity is defined as the abnormal fat accumulation in the body, which impairs the health (WHO, 2011). Body mass index (BMI) has been the preferred measure for evaluating obesity among children and adolescents from 2 to 18 years of age, which is expressed as weight (kilograms)/ height (meters^2). The cut-off points for the childhood overweight and obesity is similar to that of the adult (>18 years); overweight BMI > 25 kg/m^2 and obesity BMI ≥ 30 kg/m^2 (Cole, Bellizzi, Flegal, & Dietz, 2000). The cutoffs for an ISO-BMI based on age and sex have been extrapolated from data obtained from six different countries (Cole et al., 2000).

Center for disease control (CDC, 2009) also defines the childhood overweight as a BMI at or above 85th percentile and lower than 95th percentile and obesity as a BMI at or above 95th percentile for children of same age and sex (CDC, 2009).

1.3. Determinants for childhood obesity

Childhood obesity is normally due to the imbalance between the calorie uptake and the energy utilization. When the physical activity is reduced, the excess un-utilized energy deposits in the body causing obesity (CDC, 2009). The behavioral factors include eating behavior, increased energy intake, lack of safe and easy access places for physical activity, unsupportive family for physical activity, sedentary lifestyle such as watching television, consuming more energy-

dense foods or snacks with large portion sizes, and having reduced physical activity increases the risk for obesity (CDC, 2009).

1.4. Consequences of childhood obesity

1.4.1. Childhood obesity and cardiovascular risk in adulthood

The growing prevalence and severity of obesity among children/adolescents leads to serious health consequences. It can adversely affect almost every body system resulting in deleterious physical health consequences, which includes type 2 diabetes, hypertension, stroke, certain cancers, disability, obstructive sleep apnea, metabolic syndrome, liver disease, cardiovascular disease (CVD) and psychosocial health impairment (S. R. Daniels, 2009). The metabolic risk factors which contributes to the development of CVD among obese children include low level of high density lipoprotein (HDL), elevated triglycerides level, increase in inflammatory biomarkers such as interleukin-6 (IL-6) and C-reactive (CRP) protein, high blood pressure (BP) and impaired glucose tolerance (Sacheck, 2008). The risk of developing type 2 diabetes, hypertension, dyslipidemia, and carotid-artery atherosclerosis increased when the obese child grows to become the obese adult and the risk of these outcomes among the overweight and obese children who became normal weight by adulthood was similar to those among persons who were never overweight or obese before (Juonala et al., 2011). Overweight/obesity during adolescence leads to premature mortality and morbidity in adulthood (Reilly & Kelly, 2011) regardless of the adult obesity (Bjørge, Engeland, Tverdal, & Smith, 2008). The rate of premature death from the endogenous cause is doubled among the highest quartile of BMI compared to the lowest quartile and the significant associations persist even after adjusting baseline glucose level, cholesterol level and blood pressure (Franks et al., 2010).

A study done by Baker et al showed that BMI at the age of 7 to 13 years for boys and 10 to 13 years for girls was positively associated with risk for fatal and non-fatal coronary heart disease (CHD) event later in adulthood. This association was linear for each age and was found stronger for the boys than for the girls. The risk increased with increase in BMI (Baker, Olsen, & Sørensen, 2007). Different studies concluded that obese subjects during midlife have a greater likelihood of mortality after the age of 65 years from CHD independent of the presence of hypertension, hypercholesterolemia and smoking (Bjørge et al., 2008; Mazzone & Fantuzzi, 2006; Reilly & Kelly, 2011).

1.4.2. Adult obesity: consequence of childhood obesity

Childhood obesity is an important predictor for adult obesity. The Bogalusa Heart Study performed on 2617 participants showed that 77% of the obese children remained obese (BMI $\geq$30 kg/m^2) as adult and 58% of obese children and adolescents (5-17 years old) had at least

one of the major cardiovascular risk factors normally observed at old age (Freedman, Dietz, Srinivasan, & Berenson, 2009).

The process of obesity starts from early fetal life. The complex interaction of inherited gene effects and in-utero environment may combine in the developing fetus to program pathways leading to future obesity. The obese mother can have a disturbed metabolism in pregnancy, and the growing fetus, therefore have a higher percentage of body fat and insulin resistance leading to an early origin of future obesity (Freeman, 2010). On the contrary under nutrition can also lead to future obesity. Barker's hypothesis stated that under nutrition in utero leads to permanent changes in tissue structure, function and metabolism that predispose to CHD later in life. This is also called thrifty phenotype, reduced fetal growth, and these individuals can, in an affluent environment, develop metabolic disorders, such as obesity and type 2 diabetes (Barker, 2007).

1.5. Degree of obesity

Even though there are multiple long term deleterious health effect of obesity, BMI equal and above 30 kg/m^2 impaired the cardiac health with premature atherosclerosis, increased risk of myocardial infarction and heart failure; and increased mortality largely by cardiovascular deaths, particularly in extreme weight categories (Berrington de Gonzalez et al., 2010). Incase of overweight children/adolescents, the cardiovascular risk factors was found elevated with further abnormalities in those with obesity (BMI $>95^{th}$ percentile) which means that even modest degrees of excess adiposity contribute to cardiovascular risk (Zhu et al., 2008).

When obesity becomes severe, it is associated with alteration in the cardiac structure and function (Pascual et al., 2003). The severity of the defect is associated with both the degree and duration of obesity (Alpert, Lambert, Panayiotou, et al., 1995; Nakajima et al., 1985).

1.6. Cardiac morphological and functional changes due to obesity

1.6.1. Mechanism contributing for cardiac changes due to obesity

Figure 1.1 shows the mechanism contributing for the cardiac morphological changes among the obese.

Hemodynamics changes due to obesity

Increased body weight is associated with an increase in both lean and fat mass as well as and in surface area. The total body oxygen consumption and energy requirement to move the excess weight increased for obese subjects compared to lean individuals (Paul Poirier et al., 2006). The circulatory blood volume in obese is increased (Alexander et al., 1962) and the

systemic vascular resistance is decreased (Messerli Fh & et al., 1981). This and the associated increase in total blood volume, is accompanied by a compensatory increase in stroke volume and cardiac output (de Divitiis et al., 1981). The cardiac output increases to maintain the blood supply to the excess fat mass (Messerli Fh & et al., 1981).

This continuous increase in the cardiac output eventually leads to left ventricular dilatation and increased left ventricular wall stress, which result in eccentric hypertrophy as an additional effect of left ventricular wall stress. When the left ventricular wall is not able to bear the increased stress, overt ventricular failure with systolic and diastolic dysfunction occur (Crowley, Khoury, Urbina, Ippisch, & Kimball, 2011).

The renin-angiotensin-aldosterone system is highly active among obese leading to the increase level of sodium in the blood (Goodfriend, Kelley, Goodpaster, & Winters, 1999). Angiotensin II is also believed to cause the myocardial hypertrophy and fibrosis causing myocardial dysfunction (Brilla, Matsubara, & Weber, 1993). The sympathetic nervous system is also active in obese (Corry & Tuck, 1999) as an effect of insulin resistance (Festa, D'Agostino, Hales, Mykkänen, & Haffner, 2000) and activation of renin-angiotensin-aldosterone system (Goodfriend et al., 1999). Both high cardiac output and sodium retention trigger the production of high level of natriuretic peptide level (Goodfriend et al., 1999). However in obese adolescent, the level of natriuretic peptide is low due to an abundance of the natriuretic peptide receptors in the adipose tissue, resulting in elevation of the blood pressure (T. J. Wang et al., 2004). Reduced or impaired myocardial hormone release may be another etiology of the reduction of natriuretic level (Licata, Volpe, Scaglione, & Rubattu, 1994). An increase in systemic vascular resistance observed in obese individual results in a sustained rise in blood pressure causing eccentric left ventricular hypertrophy. In severe cases, the atria and ventricles begin to fail causing heart failure. This is known as the obesity related cardiomyopathy (Alpert, 2001) (Figure 1.1).

Adiponectine and inflammation

Adiponectine is a cytokine produced by adipocytes. It mediates paracrine and endocrine communication between macrophages and adipocytes which creates a positive feedback loop to aggravate inflammatory changes in adipose tissue (Suganami, Nishida, & Ogawa, 2005) and protect myocardium by inhibiting the insulin-mediated myocardial hypertrophy (Shibata et al., 2004). The level of adiponectine is decreased in obese despite the fact that it is secreted from adipose tissue (Arnaiz et al., 2010). This triggers an increase in inflammatory protein, decreased high density lipoprotein (HDL) (Arnaiz et al., 2010) and increased triglycerides level (Pilz et al., 2005). It also stimulates the premature atherosclerosis in children and adolescent (Pilz et al., 2005). Increased insulin resistance also reduce the adiponectine level among the obese (Arnaiz et al., 2010). The persistent inflammation reduces the cardiac contractility, induces the cardiac hypertrophy, and promotes apoptosis; a process that contributes to undesirable myocardial remodeling (Aukrust, Gullestad, Ueland, Damås, & Yndestad, 2005).

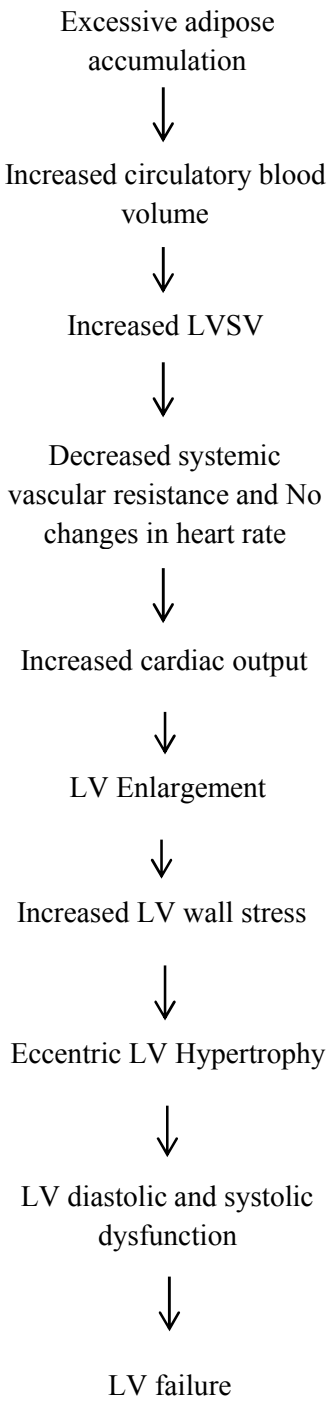

Figure 1.1. Diagram shows the mechanism contributing for changes in the cardiac structure among obese children. (Modified from (Alpert, 2001). Abbreviations: LV, left ventricle; LVSV, left ventricular stroke volume

1.6.2. Cardiac morphological changes due to obesity

Early echocardiographic signs of childhood obesity include increased left ventricular wall dimension and mass (Van Putte-Katier et al., 2008). Several studies have shown that obese individuals develop a significant cardiac remodeling compared to lean controls, with increased left atrial diameter, left ventricular end diastolic diameter, left ventricular mass (LVM), and left ventricular regional wall hypertrophy (Di Bonito et al., 2008; Di Salvo et al., 2006; Van Putte-Katier et al., 2008).

Chinali et al concluded that left ventricular hypertrophy was more common in obese compared to overweight and normal weight adolescents (Chinali et al., 2006). Increased level of LVM is appropriate for a higher hemodynamic load in overweight adolescent. In obese adolescents this increase LVM exceeds beyond the needed limit for compensating cardiac workload. This is associated with mildly reduced left ventricular chamber and mid-wall function, and increased left atrial contribution for the left ventricular filling. Stroke volume increases significantly with mild lowering of the ejection fraction (EF) and mid-wall shortening in obese adolescents compared to normal weight and overweight groups (Chinali et al., 2006). Increase in left ventricular mass may progress to left ventricular dilatation with increasing BMI (Chinali et al., 2006). The LVM and left ventricular dilation is strongly associated with the degree and severity of obesity (Li et al., 2004) and is more prominent among higher degree obesity (Schuster et al., 2009). The left ventricular hypertrophy is amplified when obesity is associated with diabetes in childhood (Shah et al., 2011). Reduction in weight helps to reduce the early cardiac changes in obese (Ippisch et al., 2008).

1.6.3. Cardiac functional changes due to obesity

Diastolic function is defined as the ability of the ventricle to fill without an impaired diastolic pressure. Diastolic dysfunction is an abnormal relaxation of the myocardium. Diastolic dysfunction leads to impaired LV filling during rest or exercise to a normal end diastolic volume without an abnormal increase in LV end-diastolic or mean left atrial pressure (Grossman, 2000).

The increase in LVM progressively reduces LV diastolic filling in case of morbid obesity causing diastolic dysfunction (Alpert, Lambert, Terry, et al., 1995). Diastolic dysfunction is an abnormal relaxation of the myocardium. Ingul et al. found that obese adolescent have impaired diastolic function than lean counterparts (Ingul C, 2010). The left ventricular diastolic dysfunction causes the left atrium to exert greater force to pump blood into the left ventricle. This persistent pressure overload in the left atrium results in left atrial dilatation. Thus the left atrial dilatation is predicted as another indicator for left ventricular diastolic dysfunction and has been shown in obese children (Stephen R. Daniels, Witt, Glascock, Khoury, & Kimball, 2002). Mitral Doppler inflow velocities and tissue Doppler early diastolic velocity show that E/e′ ratio, E′, E/A ratio and the deceleration time are significantly different

between lean and obese adolescence, indicating decreased left ventricular diastolic function in obese adolescence (Sharpe et al., 2006).

The diastolic dysfunction is an important predictor for mortality. The Strong Heart Study performed on 3008 middle-aged and elderly adults concluded that the reduction in the mitral ratio of peak early to late diastolic filling velocity (E/A) is associated with increased risk of the cardiac mortality, independently or not independent with covariates. Mitral E/A>1.5 increased all cause mortality and cardiac mortality by 2-folds independent with covariates; E/A<0.6 increased all cause mortality and cardiac mortality by 2- fold not independent with the covariates (Bella et al., 2002). Furthermore, increase in mortality among the central obesity is mediated partly by LV dysfunction, especially diastolic dysfunction (Ammar et al., 2008).

Systolic function among the obese is enhanced initially (Berry & Sattar, 2011) which later decline with the progression of time (Alpert, Lambert, Panayiotou, et al., 1995). However the study done by Ingul C resulted that the stroke volume, ejection fraction and peak systolic tissue Doppler velocity are impaired in obese adolescents compared to lean counterparts (Ingul C, 2010).

1.7. Cardiorespiratory fitness in overweight and obese children

Cardiorespiratory fitness is the best way to measure the physiological strength and to determine the aptitude of cardiovascular and pulmonary system (F. B. Ortega, Ruiz, Castillo, & Sjostrom, 2007). It is determined by maximal oxygen uptake (VO_{2max}); defined as the highest rate at which the oxygen is taken up and utilized by the body during maximum exercise (Bassett & Howley, 2000). Cardiorespiratory fitness is closely associated with the total abdominal body fat (F. Ortega, Ruiz, Castillo, & Sjöström, 2008). The absolute VO_{2max} has found to be lower among obese children (10-16 years) than lean counterpart but no group difference observed when normalized with allometric scaling (Milano, Rodacki, Radominski, & Leite, 2009). Aerobic fitness is low to-moderately associated with cardiovascular disease risk (F. B. Ortega et al., 2007) among children and adolescents and study showed that the relationship persist even after controlling the fatness (Mesa et al., 2006).

Diastolic function was strongly related to exercise capacity. However the variation in LV systolic function within normal range is not associated with the exercise capacity. Increased resting and post exercise left ventricular filling (E/e´) pressures were also associated with a reduction in exercise capacity (Grewal, McCully, Kane, Lam, & Pellikka, 2009).

There was a weak to moderate association observed between the cardiovascular risk factors and aerobic capacity among the children and exercise up to or above the specific threshold level for aerobic fitness helps to decrease the cardio metabolic risk (Tomkinson, 2011).

1.8. Prevention or treatment of childhood obesity

Prevention and treatment of the childhood obesity is necessary to prevent the life long health consequences and reduce mortality among the population and it should commence from a very early phase as the obesity process begins from the early fetal life (Freeman, 2010). There are lots of other intervention method like family based (Karnik & Kanekar, 2012), community based (Tucker, Irwin, Sangster Bouck, He, & Pollett, 2006), and school based intervention (Sahota et al., 2001). This section deals with the previous literature reviews on different types of exercise and diet intervention done for the prevention or treatment of childhood overweight/obesity.

1.8.1. Dietary therapy and/or combined exercise therapy

In a study by Shalitin et al., pre-adolescent boys were randomized in a 12 weeks interventional program in which they were assigned to three intervention groups: exercise (90 min moderate exercise 3 days/week), diet (balanced hypocaloric diet, weekly meetings with dietician) and diet plus exercise groups respectively; and follow up were done after 9 months. The study concluded that diet alone or combined with exercise have a greater influence in BMI, waist circumference, LDL reduction, improved cardiometabolic profiles without a significant difference between them. Exercise alone had less effect on the above factors. There was no significant difference in the outcome variables among the three groups after 9 month (Shalitin et al., 2009).

Nemet et al studied short (3 months) and long term (12 months) beneficial effects of a combined dietary-behavioral-physical activity intervention in obese children and adolescents. The study found a significant weight loss, reduced BMI, reduced body fat, increased habitual physical activity, and improved fitness; as well as reduced total and LDL cholesterol levels among obese children and adolescents. The control group gained weight, increased body fat percentage, did not change their habitual physical activity level and reduced fitness level. The favorable effects on body weight, BMI, body fat, and habitual physical activity were maintained in the intervention group, compared to the control groups after one year of follow up period (Nemet et al., 2005).

A combination of diet and exercise improved insulin resistance (Savoye et al., 2007) and significantly reduced inflammatory markers (CRP and IL-6) among obese children (Balagopal et al., 2007). Even though exercise alone has less effect on the weight loss, it helps to reduces the greater number of cardiovascular risk factors (Shaw, Gennat, O'Rourke, & Del Mar, 2006). Catenacci & Wyatt reported that exercise intervention alone produced an average weight loss between 1-3 kg and combined diet restriction with exercise produced an average increase in weight loss of about 1.5kg (Catenacci & Wyatt, 2007).

1.8.2. Physical activity in childhood obesity

Physical activity prevent the obesity related comorbidities; enhance the psychological health, improve body composition and aerobic fitness level among the children/adolescents (F. Ortega et al., 2008). Based on the first law of thermodynamics (energy can neither be created nor be destroyed but can transfer from one form to other), increasing physical activity might be an effective way to manage childhood obesity (Hill & Wyatt, 2005). However, only limited data are available for the quantity and quality of physical activity to prevent or treat obesity (S. R. Daniels, 2009; Reichert, Baptista Menezes, Wells, Carvalho Dumith, & Hallal, 2009).

Different studies show that the cardiovascular morbidity and mortality reduces when physical activity is at equal or above the recommended guidelines in all ages (Steven N Blair, LaMonte, & Nichaman, 2004); (Bertheussen et al., 2011). Recommendations for the amount of physical activity in which children should engage for health benefits have largely been derived from recommendations for physical activity in adults (Pate et al, 1995). A recent study found that children and adolescents (aged 6-17) should be physically active one hour every day for three days per week which includes moderate and vigorous intensity aerobic activities, muscle and bone-strengthening activities for a healthy life (Oja, Bull, Fogelholm, & Martin, 2010).

Physical activity enhances the endothelial function and intima media thickness. Even a moderate increase in the physical activity is favorably associated with decrease progression of intima media thickness; thus preventing the development of sub-clinical atherosclerotic vascular change in healthy adolescent (Pahkala et al., 2011). The exercise training can reverse the vascular dysfunction associated with obesity in children/adolescents (Watts et al., 2004) by improving blood flow which leads to augmented shear stress and further stimulation of nitric oxide production and enhancing the endothelial function (Watts et al., 2004).

Training for the physiological benefit

Training can be designed in a variety of ways but the training load is characterized by three factors: the frequency of training, the duration of each exercise session and the intensity of the exercise (Smith, 2003). The frequency can be defined as the number of training session in every week. The duration of training means the length of the time spend for each training session. Intensity of training is the qualitative measurement of the training session in relation to time.

The HUNT 3 study illustrated a strong association between all aspects of physical activity (frequency, duration, and intensity) and physical and mental health in young and old adults for both sexes. The physical activity performed at or above the recommended guidelines found to have better effect on physical and mental health indicating that intensity and duration

rather than high frequency are important for better health for young adults (Bertheussen et al., 2011).

Exercise intensity is the most important and mostly studied factors out of the above three factors. The HUNT study investigated the association between the amount and intensity of exercise and cardiovascular mortality in 27,143 men and 28,929 women who were free from known cardiovascular disease at the beginning of follow-up. One high-intensity exercise session per week was associated with 39% and 51% reduction in mortality in both sexes respectively, compared with those who reported no activity at all. Thus intensity of physical activity was found to be important to reduce risk of cardiovascular mortality and no additional benefits were observed after increasing the duration or the frequency of exercise sessions per week (Wisløff et al., 2006).

Ruiz suggested that physical activity at vigorous intensity for more than 40 minutes per day reduced the total body fat and improved the cardiorespiratory fitness to a greater extent compared to moderate and normal physical activity per day. In addition the study reported that children who engaged in 40 minutes vigorous physical activity per day had lowered body fat and improved cardiovascular fitness than did those who engaged in 10 –18 min vigorous physical activity per day. This study concluded that vigorous physical activity was effective to prevent the childhood obesity than the lower intensity while both vigorous and the low to moderate intensity helps to improve the cardiovascular fitness (Ruiz et al., 2006).

Exercise training at the level of lactate threshold significantly reduced BMI, skinfold thickness, waist girth measurement; and improved cardiovascular fitness and running and jumping ability among obese adolescent boys and girls aged between 9-10 years. This study suggested that training at lactate threshold can be used as en effective exercise intensity especially for above age groups to manage obesity (Tan, Yang, & Wang, 2010).

A systematic review and meta- analysis of randomized controlled trials studies illustrated that the higher doses exercise intensity (155-180 min/weeks) accumulated a larger and significant improvement on body weight, whereas the lower doses of exercise (120-150 min/weeks) generated a small and non-significant effects on the body weight. The review further concluded that an aerobic exercise prescription of 155–180 min/weeks at moderate-to-high intensity is more effective for reducing body fat mass in overweight children/adolescents, but effects on body weight and central obesity were unsettled (Atlantis, Barnes, & Singh, 2006).

Intensity of exercise training

There has been a long standing debate concerning the effectiveness of aerobic interval training (AIT) compared to continuous moderate exercise (CME) for the improvement of the cardiovascular health. This part deals with the different studies related to the AIT and CME.

Schjerve et al compared the two types of exercise intensities on the obese adult; high-intensity group performed aerobic interval exercise at 85–95% of maximal heart rate and the moderate

intensity group performed exercise continuously at 60–70% of maximal heart rate. The study resulted that the AIT leads to greater improvement in aerobic capacity, endothelial function and reduction in the cardiovascular risk profile through improved calcium transport, increased PGC- 1∂, reduced diastolic blood pressure, and body weight. However, less improvement was observed among the moderate exercise group (Schjerve et al., 2008).

The similar results were found in the study done by Tjønna, et al among the metabolic syndrome (elevated blood pressure, dyslipidemia, impaired glycemic control, and abdominal obesity) patients with equal maximal oxygen uptake. The AIT group significantly improved the metabolic syndrome score compared to the CME, suggesting that the AIT is superior over CME in pertaining the metabolic syndrome in the adults (Tjønna et al., 2008). Tjønna et al compared the effect of AIT and multi-treatment approach (MTG) (exercise, dietary and psychological advice, twice a month for 12 months) on the cardiovascular risk factors in the obese and overweight adolescence (14.0±0.3yrs). The AIT significantly improved maximal oxygen uptake compared to MTG, both at 3 months and 12 months. High intensity training enhanced endothelial function to a greater extent both at 3 months and 12 months; favorably reduced BMI, percentage of fat, MAP (mean arterial blood pressure), increased peak oxygen pulse, maintained insulin and glucose level compared to MTG. This study suggested that the AIT significantly reduced the cardiovascular risk factors and the continuity of the high intensity training further improve and sustain the cardiovascular health (Tjonna et al., 2009) .

Slordahl et al. concluded that short term of aerobic interval training improved the cardiac dimension (posterior wall thickness and LVM) at rest and the left ventricular systolic function in sub maximal exercise (Slordahl et al., 2004). Other studies done on diseased adult population (N. Pattyn, E. Coeckelberghs, R. Buys, V. Cornelissen, & L. Vanhees, 2014; Wisloff et al., 2007) pointed that the cardiac function improved with high intensity exercise comapred to moderate exercise. The recent study was performed among the overweight/obese adolescent where the adolescents performed AIT twice a week for 13 weeks (4 × 4 minutes intervals at 90% of maximal heart rate, each interval separated by 3 min at 70% of maximal heart rate) and the cardiac function was compared with the lean counterparts. The AIT restored an impaired systolic and diastolic cardiac function almost to the same as lean group, with increased peak velocities and a more efficient ejection fraction and relaxation. This study concluded that the aerobic training favorably enhanced the cardiac function among the obese (Ingul C, 2010).

1.9. Aim of the study

Aerobic interval training improved the cardiac function among healthy (Slordahl et al., 2004), diseased adults (N. Pattyn, E. Coeckelberghs, R. Buys, V. A. Cornelissen, & L. Vanhees, 2014; Wisloff et al., 2007) and obese children (Ingul C, 2010). Aerobic interval training is more effective than moderate training for improving cardiac function among coronary artery disease (N. Pattyn et al., 2014) and patients with post infarction heart failure (Wisloff et al., 2007). A previous randomized control trial study on obese adolescent (Ingul C, 2010)

compared the effect of the aerobic training on cardiac function of obese adolescent with lean counterparts. Through literature review it was confirmed that the comparison of the effectiveness of the aerobic training combined diet intervention with moderate training combined diet intervention for treating childhood obesity has to my knowledge not been studied before.

Thus the aims of the study were:

1. To compare the effects of continuous moderate exercise intervention and intensity-controlled aerobic interval training intervention on the cardiac function in obese children/adolescents.
2. To compare the effects of the exercise (moderate exercise and high intensity exercise) combined diet intervention with the diet intervention alone on the systolic and diastolic cardiac function among the age matched obese children and adolescents.

The hypothesis was that aerobic intensity training is superior compared to moderate training.

Materials and methods

2.1. Study Population

In total 29 obese children and adolescents, age 6-16 years and BMI ISO-BMI ≥30 (Cole et al., 2000) were recruited through an advertisement in the local newspaper (Adressa avisen). The age and BMI of the study population were 11.3 ± 2.4 (range, 7-14 years) years and 32.9 ± 3.3 kg/m^2 respectively.

2.1.1. Consent and screening

All adolescents and parents provided written informed consent before inclusion, and the protocol was approved by the Regional ethical committee. All the children went through medical screening before inclusion including anthropometric evaluation and tanner scoring by a pediatrician. Exclusion criteria were congenital heart disease, coronary artery disease, smoking, family history of hypertrophic obstructive cardiomyopathy, hypertension (defined as either systolic and/or diastolic blood pressure ≥95^{th} percentile measured upon three or more occasions) (Falkner & Daniels, 2004), total cholesterol >213 mg/dl or low-density lipoprotein >116 mg/dl, considerable pulmonary disease, diabetes, kidney failure, orthopedic and/or neurological limitations to exercise and ADHD. Subjects who were involving in another research study were also excluded.

2.1.2 Randomization procedure

This study was a randomized controlled trial study to compare the effect of the three types of intervention on the children/adolescents. After the screening, the subjects were randomized according to age, gender and BMI to either of the three intervention groups: diet intervention, moderate exercise (CME) combined diet intervention and aerobic interval training (AIT) combined diet intervention (Figure 2.1). The randomization code was generated using a computer random number generator to select random permuted blocks. The unit of applied clinical research at the Norwegian University of Science and Technology carried out all randomization procedures to secure complete blinded randomization. The compliance of 80% with the training program was set as a criterion for the training groups to complete the study. Figure 2.1 illustrates the total number of children/adolescents randomized in each of the three intervention groups.

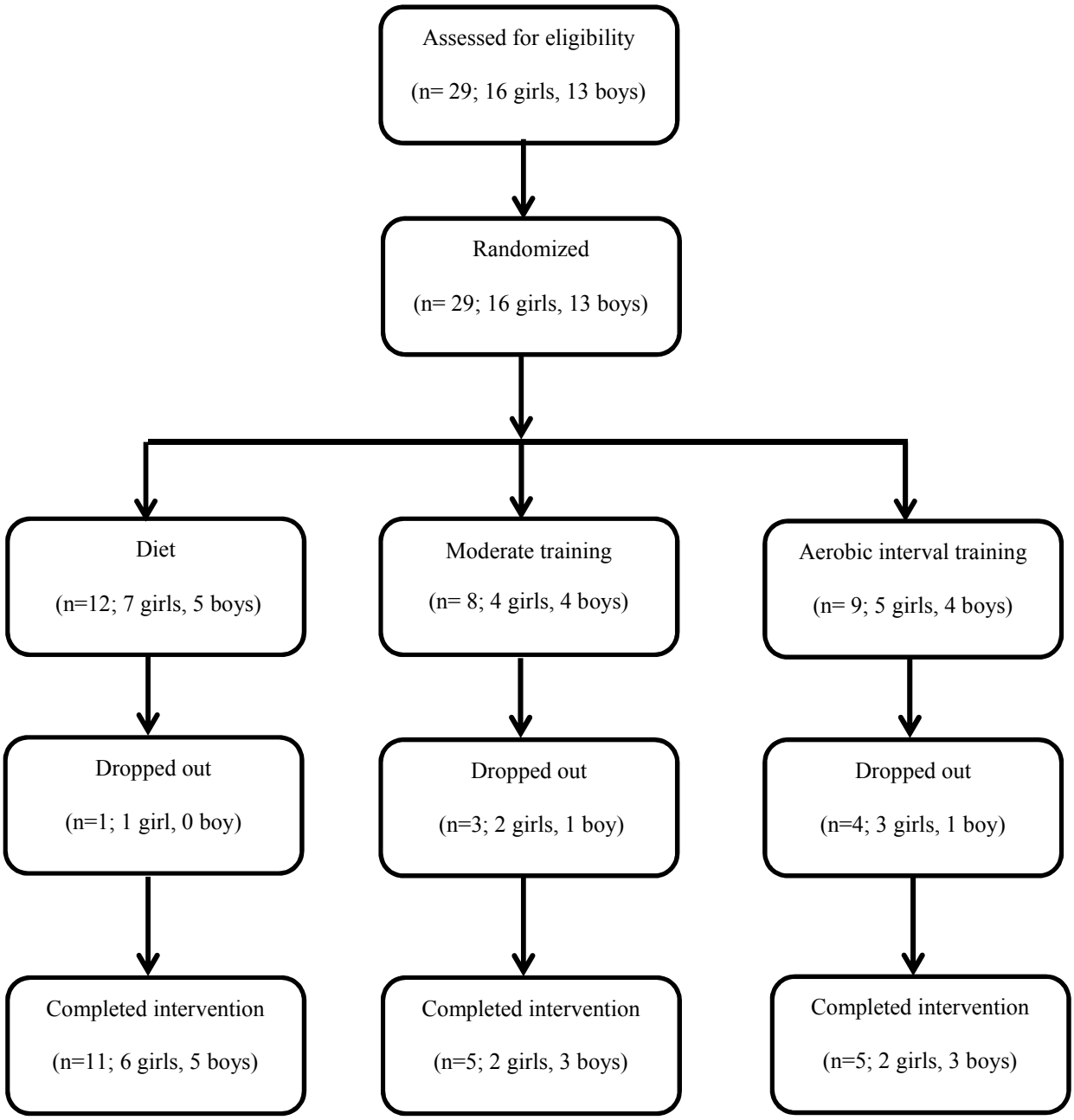

Figure 2.1. Flow chart of the study population (n; number of participants)

All together 29 subjects were contacted and assessed for the eligibility to participate in the study. They were randomized to either of the three study groups (Diet, CME, and AIT) according to age, sex and BMI. Out of 29 subjects, 6 dropped out from the study due to personal reasons. One child stop the study due to relocation and another child did not respond the call for 3 months follow up test. Only 21 subjects were tested after three months of intervention and analyzed in this study. The data was collected in the period between 2012-2013 in the laboratory of Institute of Circulation and Medical Imaging at NTNU in Trondheim, Norway. All the lab work was performed in collaboration with the supervisors.

2.2. Anthropometric measurements and body composition

Weight was measured using digital scale (Seca Clara 803 Digital Scale, US) and height was measured using stadiometer (Seca 213 stadiometer, US). ISO-BMI was calculated as weight (in kilograms) divided by height (in meter square) ^{2} (kg/m^2) using the ISO-BMI calculator on internet[1]. The test date, birth date and gender of the children were entered to calculate the ISO-BMI. Though ISO-BMI is an effective measure to determine obesity among children aged between 2-18 years (Krebs et al., 2007), BMI changes may not particularly reflect the adiposity (Demerath et al., 2006). Some children may have higher weight related to age and gender due to high fat free mass rather than high fat mass. This is especially common among the adolescent boys among whom the lean body mass increases with pubertal changes (Demerath et al., 2006). Thus the body composition was analyzed using the Body Composition Tracking System Analysis (BOD POD) (Life Measurement, Inc, Concord, CA).

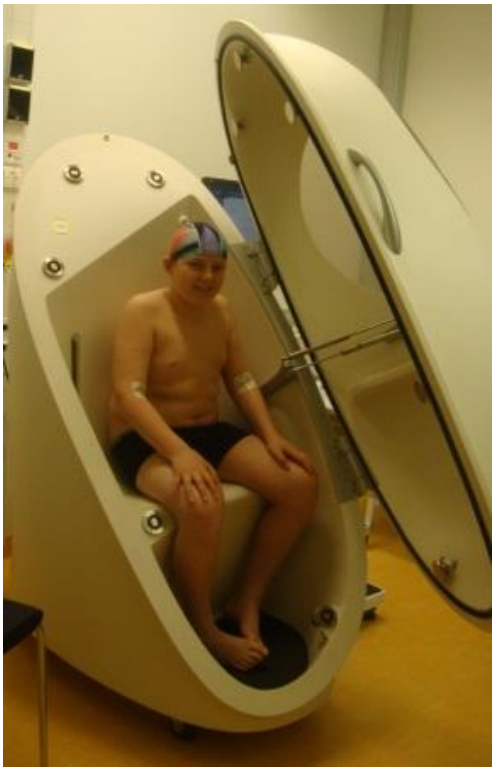

Figure 2.2. A participant being ready for the BOD POD measurement (photo printed with the permission of the participant and his mother).

All the subjects were tested for body composition using BOD POD to assess the total fat mass and fat free mass. The children were oriented about the machine and informed about the test procedure on beforehand. The subjects were informed to remove the clothes and the hair was tucked using the cap to avoid any air trapping and thus false reading. The subjects were then asked to sit quietly inside BOD POD device with their hands placed on the knee (Figure 2.2).

[1] http://xestia.net/tests/isobmi.php

2.3. Diet counseling

Diet counseling was given by a clinical dietician to all the subjects together with their caregivers/parents for 30 minutes every second weeks for the consecutive three months of the intervention period. It was observed that the dietary habits and the portions sizes consumed by the caregiver/parents strongly predict the children's dietary consumption (Johnson et al., 2014). Thus the children together with their parents/caregiver were counseled focusing on sizes of portions and regular mealtimes.

The subjects were given advice to avoid fast foods, sweetened beverages, fruits juice, candies, high fat containing food products and processed meat. They were advised about healthy foods like consuming more vegetables and fruits, drinking a lot of water. They were encouraged to choose healthy eating behavior like regular meal habits, avoid breakfast skipping and avoid snacking.

The subjects who were exercising (AIT and CME) were asked to avoid consuming high calorie food after the training as a substitute of the burned out calorie. The subjects who were randomized to the diet intervention were asked to avoid the vigorous physical activity during the intervention period.

2.4. Test procedures

All the intervention groups (Diet, CME, and AIT) went through following test twice; before the intervention and after three months of intervention. Blood pressure and heart rate were measured together with echocardiography on the same day while the maximal oxygen uptake test was performed on the separate day.

2.4.1. Testing of maximal oxygen uptake (VO_{2max}) and maximal heart rate (HR_{max})

Maximal oxygen uptake of all the subjects was tested on a tread mill (Woodway USA Inc. Waukesha, WI, USA) in which the subjects walked or ran with an individually adjusted speed and/or inclination. Information regarding the test was given and subjects were instructed to exercise to their maximal limits on beforehand. The test started with a warm-up period for 10 min (~60% of HR_{max}) with individually adjusted speed and inclination (3-7 km/hr, 0%-5%) respectively. Following the warm up, the mask was placed on the subject's face for measurement of maximal oxygen using a direct ergospirometry (Jaeger, Oxycon pro, Hoechberg, Germany). Gradually the load of the exercise was increased by increasing either the speed (by 1km/hr) or the inclination (2%) every minute until the patient reached to the maximal limit of the exercise. The subjects were motivated to perform the test to their maximal limit of the exercise until volitional exhaustion.

Heart rate was measured continuously during the test using a Polar RS 400 (Polar Electro OY, Kempele, Finland) and the highest value obtained from the test is termed as the maximal heart rate (HR_{max}). Leveling off of oxygen uptake (VO_2) despite increased work load and respiratory exchange ratio ≥1.05 were used as criteria for reaching true VO_{2max}. The respiratory exchange ratio is defined as the ratio of the volume of CO_2 exhaled per minute to the volume of O_2 inspired during the same time. This criterion was achieved in all the subjects in the study. The mean of the three highest values of last minutes were calculated as achieved VO_{2max} which is expressed as ml/kg/min. Absolute VO_{2max} may not completely remove the body mass difference when the heavy subjects are assessed (Loftin et al., 2001). Thus the allometric scaling was used and the VO_{2max} normalized with body weight ($ml/kg^{0.75}/min$) and lean body mass ($ml/LBM^{0.75}/min$) were calculated to compare children with large body mass.

2.4.2. Echocardiography

Echocardiography was performed by an experienced medical doctor (CBI) with a Vivid 7 scanner (GE Vingmed Ultrasound, Horten, Norway) using a phased-array matrix transducer (M4S). The children were informed about the test procedure on beforehand. They were positioned to left lateral decubitus and connected with three lead electrodes to monitor the resting heart rate. Three cine loops from the three standard apical planes (four-chamber, two-chamber and long-axis) were recorded in gray scale harmonic mode and tissue Doppler mode. The mean acquisition frame rate for gray scale was 51.3 frames per second (range, 34-66/s) and for tissue Doppler was 106.2 frames per second (range, 72-182/s) simultaneously.

Left ventricular (LV) volumes and ejection fraction (EF)

Left ventricular diastolic and systolic volumes were measured using a modified Simpson's biplane method which was found to be more accurate method (Otterstad, Froeland, Sutton, & Holme, 1997). The endocardium of left ventricle was traced from the two dimensional (2D) image of apical four chamber view and apical two chamber view (Figure 2.3) at end diastole and end systole and the mean of the acquired value was calculated.

Ejection fraction (EF) was defined as the percentage of the left ventricular diastolic volume ejected from the aorta at each cardiac cycle. EF% was calculated using following equation:

$$EF\% = \frac{LVEDV - LVESV}{LVEDV} \text{ x } 100$$

where

LVEDV = left ventricular end diastolic volume,

LVESV = left ventricular end systolic volume.

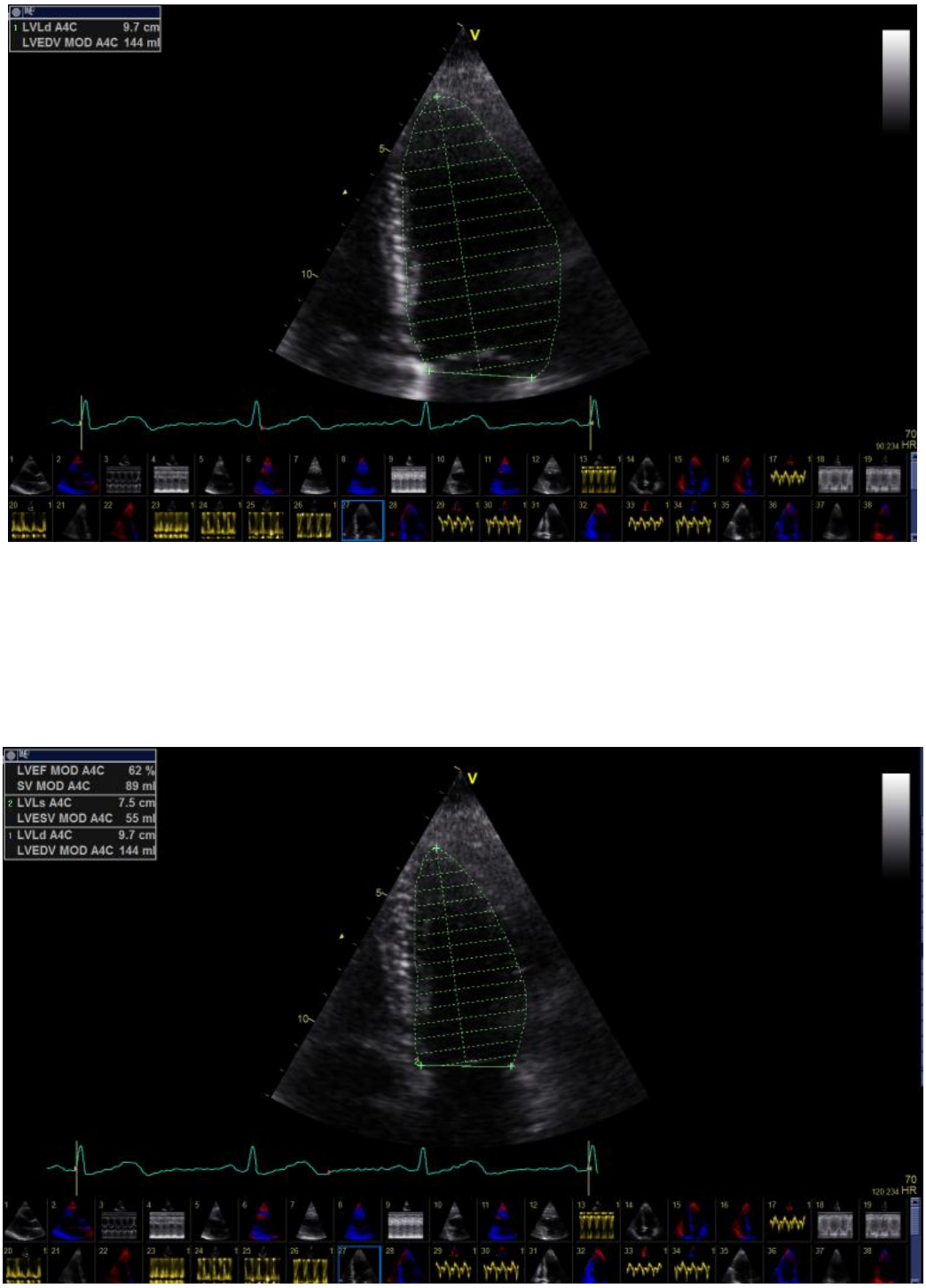

Figure 2.3. Estimation of left ventricular volumes by the Simpson's Bi-plane Method. Picture first: From the 2D apical four chamber view, the ventricular endocardium of left ventricle was traced at end diastole to determine the left ventricular end diastolic volume. Picture second: From the 2D apical four chamber view, the endocardium was traced at end systole to determine the end systolic volume.

Stroke volume and cardiac output

Stroke volume is defined as the amount of blood ejected in each cardiac cycle. It is calculated from the following equation:

$$SV = CSA \times VTI$$

where

SV = stroke volume (ml),

VTI = velocity time integral: distance a column of blood travels with each stroke (cm),

CSA = cross sectional area (cm^2) of left ventricular outflow tract.

Cardiac output is defined as the total amount of blood ejected from the left ventricle in one minute which is calculated from the product of stroke volume and heart rate:

$$CO = \frac{SV \times HR}{1000}$$

where,

CO = cardiac output (L),

SV = stroke volume (ml),

HR = heart rate (BPM),

1000 = conversion of milliliters (ml) to litres (L).

Stroke volume and cardiac output were estimated from pulsed wave Doppler imaging. The left ventricular outflow tract (LVOT) diameter was measured from the parasternal long axis view, and flow velocity was recorded from the apical four chamber view with the sample volume placing in LVOT tract. Stroke volume was determined as the product of the velocity-time integral of the Doppler signal and the maximal cross sectional area of LVOT. Heart rate was registered and cardiac output was obtained as a product of stroke volume and heart rate.

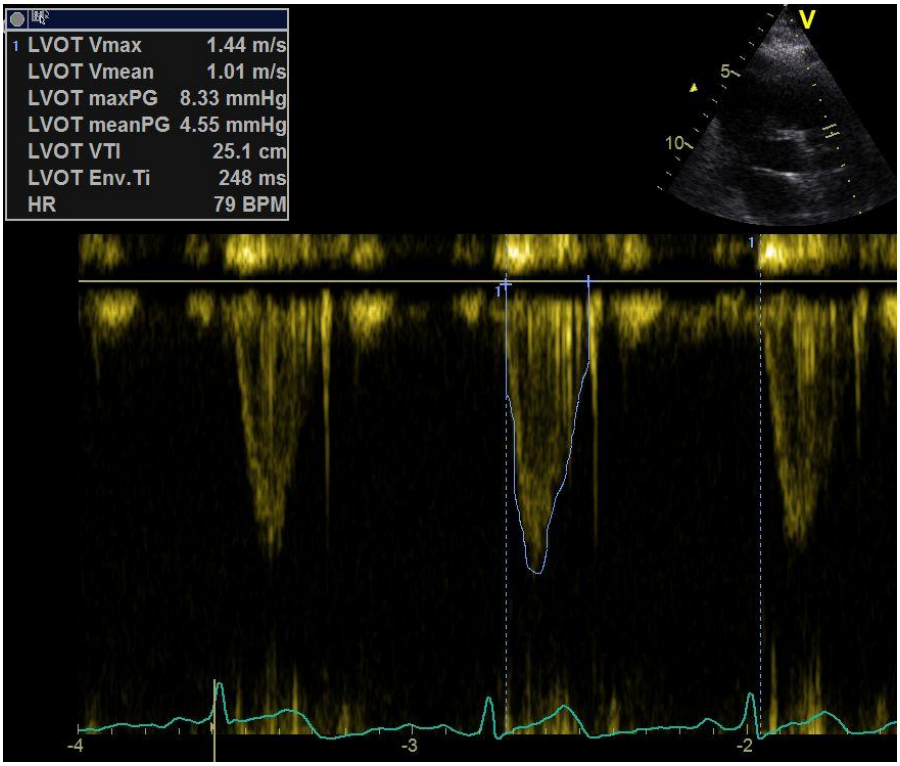

Figure 2.4.: Pulsed wave Doppler trace through the left ventricular outflow tract trace from apical four chamber view. The first view: 2D image of apical four chamber view which shows the sample volume at aortic outflow tract; second picture: pulsed wave Doppler trace of velocity time integral.

Stroke volume among the obese subjects is greater than age matched normal weight peers. Heart rate increased as a consequence of the alteration of the autonomic tone. Thus increased stroke volume and heart rate magnifies the cardiac output (Alpert, 2001). Indexation of stroke volume and cardiac output for body surface area is applicable when the effect of obesity needs to be removed, as a result of which the impact of obesity is obscured. Thus normalization of stroke volume and cardiac output for ideal body surface area or for height to its age-specific allometric power should be practiced (de Simone et al., 1997).

Body surface area (BSA) was calculated using Du Boise formula to normalize cardiac dimensions for differences in body size.

$$\text{BSA } (m^2) = 0.007184 \times \text{Height}(cm)^{0.725} \times \text{Weight}(kg)^{0.425}$$

Stroke volume and cardiac output indexed to BSA was calculated:

$$SVI = \frac{SV}{BSA}$$

where

SV = stroke volume

SVI = stroke volume index

BSA= body surface area

Isovolumic relaxation time (IVRT)

Isovolumic relaxation time (IVRT) is defined as the time interval between aortic valve closure and the mitral valve opening. The pressure in the LV remains constant during IVRT since there is no emptying and/ or filling; and the LV pressure falls rapidly due to the relaxation of ventricles.

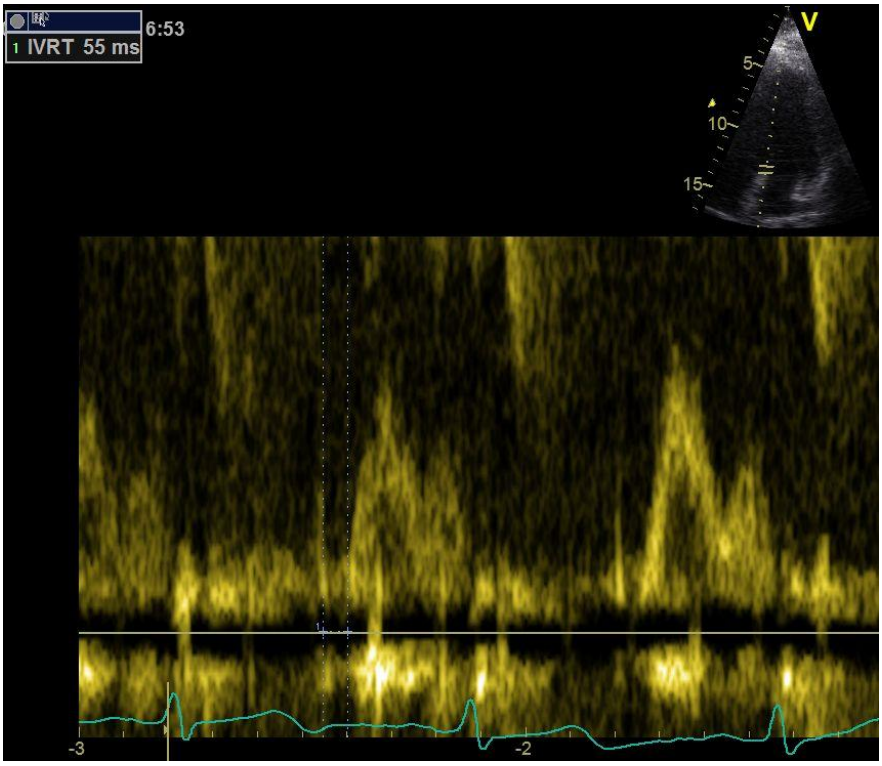

Figure 2.5. Measurement of IVRT using pulsed wave spectral Doppler image of mitral annulus from apical four chamber view. First picture: 2D image of apical four chamber view which shows the sample volume at mitral annulus; second image: pulsed wave image of mitral annulus.

It was measured from pulsed wave Doppler imaging by putting the sample volume first at the LV outflow tract registering the closure of aortic valve and second at the mitral valve leaflets registering the opening of mitral valve.

Mitral Inflow velocity

Following IVRT, the pressure within LV falls below that of left atrium (LA) resulting in mitral valve opening and the beginning of the early rapid mitral filling (E) which subsequently increases the LV pressure and reduce the LA pressure. This rapid change of LV filling pressure and LA emptying contributes 80% of LV filling.

As the early rapid mitral filling progress, at one point the pressure of LV and LA equalize which is termed as diastasis. In this phase, a small amount of blood continues to flow across the mitral valve due to inertia. Following diastasis, LA pressure increase slightly causing a small amount of blood propelling out towards LV which is indicated as the late mitral filling (A). Only 20% of LV filling is contributed by this phase (Anderson, 2002).

Measurement for mitral inflow velocity was determined by pulsed wave Doppler imaging. Doppler imaging was found to be more sensitive marker of diastolic function in subclinical heart disease (Fang et al., 2003; Von Bibra et al., 2005). The mitral inflow curve was obtained by putting the sample volumes at the tips of mitral valve leaflets in four chamber view (Figure 2.6). E was measured as the first peak and A as the second peak in the transmitral inflow trace (Figure 2.6). Deceleration slope is traced starting from the peak of E wave to the zero baselines and deceleration time was obtained by measuring the time interval between the peak E wave velocity and the point of deceleration extrapolated to the zero baseline (Figure 2.6). The E/A flow velocity ratio was calculated and used to estimate the diastolic filling and diastolic function.

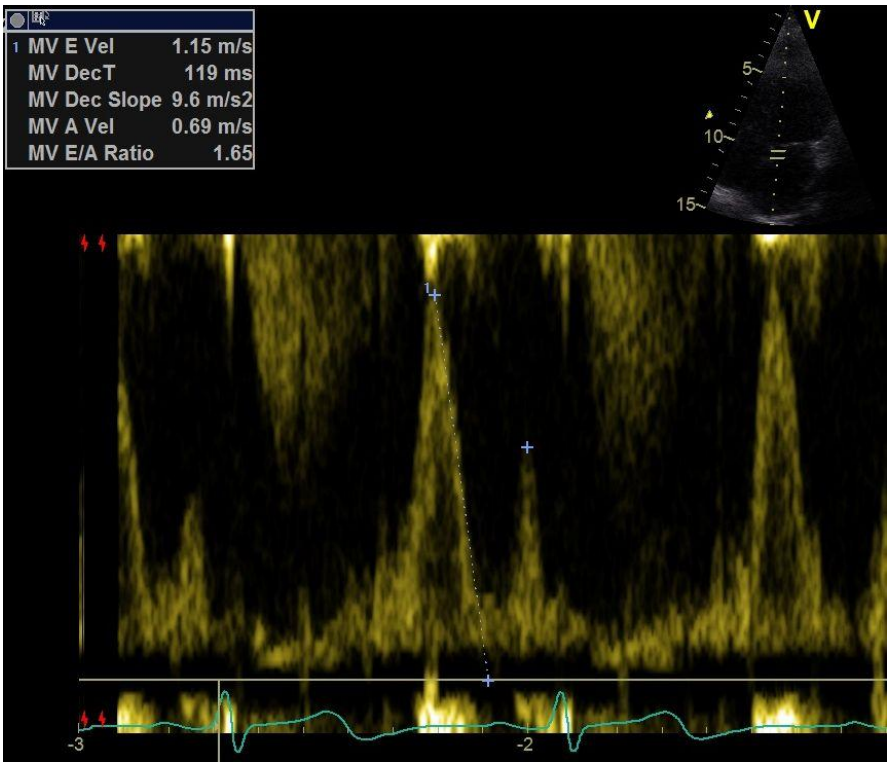

Figure 2.6: The spectral Doppler examination of the Mitral inflow (E, A, DT) from the apical four chamber view, where E is peak early diastolic mitral flow, A is peak late diastolic mitral flow and DT is deceleration time. Here first image shows imaging plane and sample volume position, and second image shows the normal spectral Doppler display.

Tissue Doppler velocity imaging

Tissue Doppler velocity was used to record the myocardial velocity. The three distinct waveforms of myocardial velocity profile includes: peak systolic myocardial velocity (S´), peak early diastolic (e´) myocardial velocity and peak late diastolic (A´) myocardial velocity. The tissue Doppler velocities were obtained using color tissue Doppler imaging. The color Doppler sample volume was placed at medial (septal) and then at lateral corner of the mitral annulus from the apical four chamber views; then at inferior and at anterior wall in the apical 2-chamber view respectively. The mean of the four values were calculated to obtain the values of S´, e´ and A´ respectively.

Image analyses

All the echo images were transferred to the computer and EchoPAC (Version 112, GE Medical Systems) software was used for analyzing images. All the echocardiographic analysis was done by a single observer. The ratio of E/e´ was calculated for a measurement of the left ventricular filling pressure.

2.4.3. Blood pressure

Blood pressure was measured using an automatic blood pressure machine in upright position (SunTech Tango M2 Stress BP Monitor, USA). Blood pressure was measured after 5 minutes rest.

2.5. Training protocols

The subjects who were randomized for exercise intervention performed two intensity types of exercise training for 12 weeks. One group performed 4 x 4 min aerobic intervals training (AIT) and the other group performed continuous moderate exercise (CME).

The AIT group performed 10 min warm up at ~60% of maximal heart rate (HR_{max}) initially. Warm up is followed by training at 85%-95% of HR_{max} in each of 4 x 4 minutes, with 3 minutes active breaks (~60 % HR_{max}) in between intervals. The exercise session was terminated by a 5 min cool-down period (~60 % HR_{max}). The total exercise duration for the AIT was 40 minutes. The CME group walked/ran continuously for approximately 47 min at 70% HR_{max} to equalize the training volume between the groups.

Figure 2.7: Children training in the treadmill in the training lab in ISB (printed on the permission of the children and their parents).

All of them exercised twice per week for 12 weeks in the training lab (24 sessions in the lab supervised by exercise physiologist) and once per week by themselves (12 sessions). The mean lab training for all the subjects was 18 sessions and the training was performed on treadmill (Woodway USA Inc. Waukesha, WI, USA). All the participants performed training on their own once per week for 12 weeks under the supervision of parents. The children in AIT were instructed to perform the exercise at 16-18 Borg RPE (rate of perceived exertion) scale and moderate training to 12-14 on the Borg scale to meet the training intensity.

Continuous supervision and motivation were given to the subjects during each training session by the exercise physiologist. The exercise log book was used to record the heart rate, speed and inclination and was maintained all the time. The training speed and/or inclination were adjusted according to subject's voluntary decision to reach the target heart rate in every session. A polar RS 400 (Polar Electro OY, Kempele, Finland) was used to monitor the heart rate during the training session. An 80% of attendance for the training was achieved for all the subjects.

2.6. Statistical analysis

Means and standard deviations (mean ± standard deviation) for all variables were calculated using descriptive statistics. All values were expressed as mean ± standard deviation. All the data were checked for normal distribution using quantile-quantile (Q-Q) plots. The results of the Q-Q plots were interpreted by examining the shape of the plots and the closeness of the plot to its best linear fit. The data which closely fits to the linear line is considered as normally

distributed data. All the variables were normally distributed and use of the parametric test was employed.

Paired Student's t-test was used to compare the mean value at baseline and at three months test. One-way ANOVA test was done to compare the difference in the baseline characteristics between the groups. The significant level was set as $p \leq 0.05$. Microsoft Excel 2010 and SPSS version 21 statistical software (SPSS Inc, Chicago, Illinois) were used for all analyses. Graph pad Prism version 6 (GraphPad Software Inc., San Diego, CA, USA) was used to make figures and graphs.

Results

The mean age for diet, CME and AIT were 11.6 ± 2.6 (range, 7-14 years; 6 girls, 5 boys), 11 ± 2.4 (range, 8-14 years; 2 girls, 3 boys), 11.0 ± 2.5 (range, 8-14 years; 2 girls, 3 boys) respectively. Among 21 obese children, 11 (7 boys, 10 girls) were obese (ISO-BMI ≥30) and 4 (4 boys, 0 girl) were severely obese (ISO-BMI ≥ 35). 7 boys were on their pre-pubertal phase and 5 boys had started developing some features of pubertal development. However none of them reach to the sexual maturity. One girl was on pre-pubertal phase, 3 had started developing the secondary sexual characteristics and 6 girls were reaching their pubertal maturity. Almost 50% of the obese children/adolescents had prehypertension at baseline (Table 3.1).

Table 3.1. Number of boys and girls in blood pressure percentile.

	Systolic BP		Diastolic BP	
	Boys	Girls	Boys	Girls
No. of children having BP≤ 90th percentile	4	7	8	10
No. of children having 90-95th percentile	7	3	3	-
	11	10	11	10
Total	21		21	

The baseline value of maximal oxygen uptake was significantly different between diet, CME and AIT (33.7±5.4 vs. 25.5 ±7.9 vs. 36.2±2.9 ml/kg/min, respectively; p= 0.04) (Table 3.3). There was no significant difference in the baseline heart rate and blood pressure between the groups (Figure 3.2). No baseline echocardiographic variables differences were observed between the groups. When the exercise intervention (CME+AIT) was compared with the diet intervention, a significant difference was observed in deceleration time (p= 0.01) at baseline.

3.1. Anthropometry and body composition

The mean ISO-BMI for the study population was 32.9 ± 3.3 kg/m^2 at baseline and 32.4 ± 3.7 kg/m^2 (p= 0.03) at three months test respectively. Following table (Table 3.2) shows the anthropometric and the body composition variables of the study population.

Table 3.2. Anthropometry and body composition of the study population.

	Diet (n=11)			CME (n=5)			AIT (n=5)		
	Baseline	3 month	p-value	Baseline	3 month	p-value	Baseline	3 month	p-value
Weight (kg)	75.3±20.6	75.9±22.4	0.59	75.9±25.3	77.2±25.3	0.53	63.8±8.7	68.9±18.5	0.39
Height (cm)	158±14.5	160.4±15.2	0.002	154.2±14.9	157±14.4	0.009	151.0±8.0	153.5±9.0	0.01
ISO-BMI (kg/m^2)	32.8±3.1	32.2±3.3	0.13	34.8±4.3	34.3±5.4	0.41	31.2±2.2	31.0±2.2	0.23
FM (%)	41.9±6.7	41.0±6.4	0.43	44.2±6.1	43.6±6.5	0.37	39.5±4.2	36.0±6.8	0.10
LBM (kg)	37.6±9.8	38.7±11.1	0.12	40.5±9.5	42.1±9.4	0.04	36.7±3.3	38.5±3.9	0.07

Data are presented as mean±standard deviation. Abbreviations: kg, kilograms; cm, centimeter; ISO-BMI, Body Mass Index; FM, Fat Mass; LBM, Lean Body Mass.

Height increased significantly and there was a tendency to increase in weight after intervention among all the groups (Table 3.2). Total fat mass decreased by 3.5% (p=0.10) among the AIT (Table 3.2). ISO-BMI tended towards reduction for all groups after three months of intervention. Diet intervention decreased ISO-BMI from 32.8±3.1 to 32.2±3.3 kg/m^2 (p=0.13), the CME decreased ISO-BMI from 34.8±4.3 to 34.3±5.4 kg/m^2 (p=0.41) and the AIT decreased ISO-BMI from 31.2±2.2 to 31.0±2.2 kg/m^2 (p=0.23) (Table 3.1). The lean body mass increased significantly among the CME by 1.6 kg (p=0.04), almost significantly increased among the AIT by 1.8 kg (p= 0.07) and no change was observed among diet intervention (Table 3.2).

3.2. Resting heart rate and blood pressure

Resting heart rate remained unchanged among diet intervention and the CME; and significantly decreased among the AIT by 10 BPM (p=0.05) (Figure 3.1).

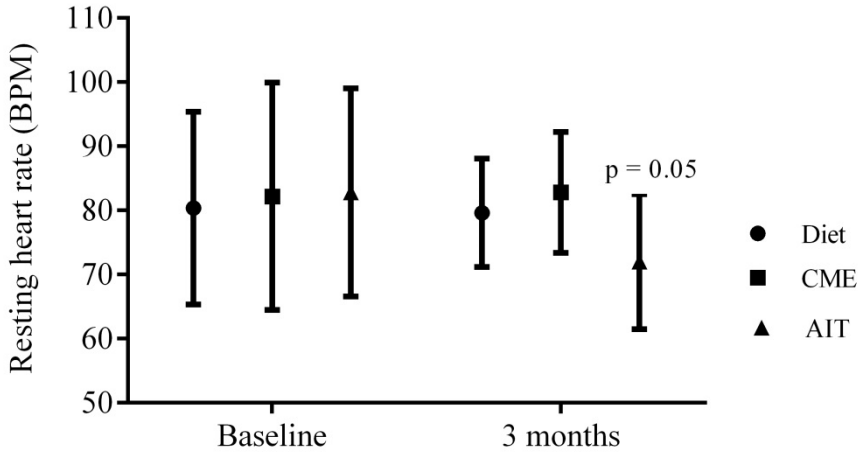

Figure 3.1. Effect of three months intervention on resting heart rate. Significantly better within the groups from baseline to three months test ($p < 0.05$).

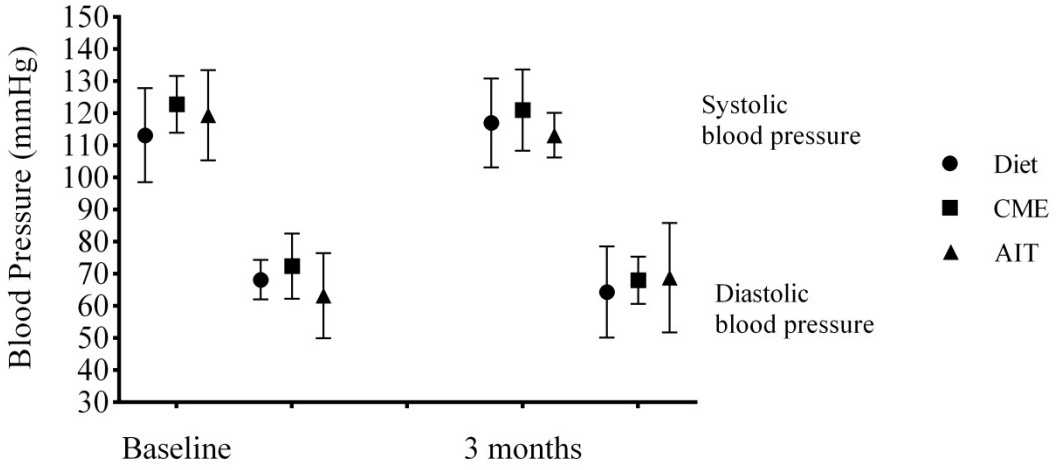

Figure 3.2. Effect of three months intervention on the upright systolic and diastolic blood pressure. Significantly better within the groups from baseline to three months test ($p < 0.05$).

The systolic blood pressure had a tendency towards reduction among the AIT by 6 mmHg (p=0.21) after intervention. However no change was observed among other intervention (Figure 3.2). The diastolic blood pressure decrease among the diet and CME by 3mmHg (p=0.54) and 4 mmHg (P=0.59) respectively but none of them reached to the statistical significance.

3.3. Cardiac functions

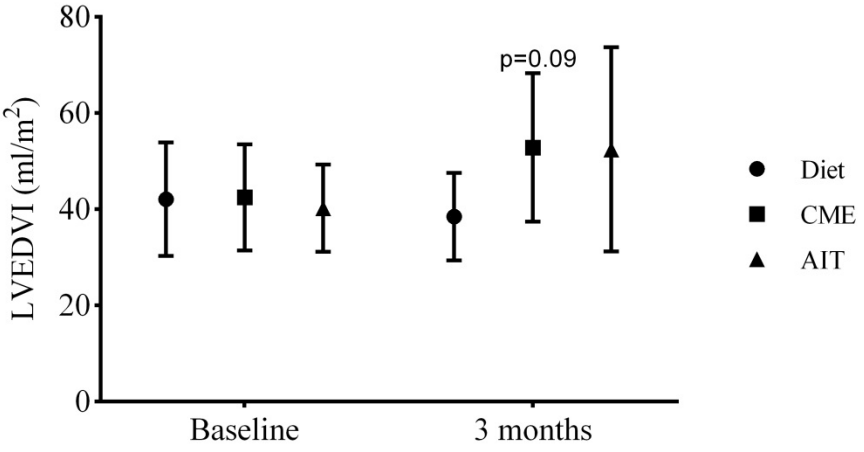

Figure 3.3. Effect of three interventions on the left ventricular end diastolic volume index. LVEDVI, Left ventricular end diastolic volume index. Significantly different within the intervention groups from baseline to three months.

Table 3.3. Comparison of systolic functions and left ventricular volumes among groups.

Supine value	Diet (n=11)		CME (n=5)		AIT (n=5)	
	Baseline	3 months	Baseline	3 months	Baseline	3 months
Resting heart rate BPM	80.3±15.0	79.6±8.4	82.2±17.7	82.8±9.4	82.8±16.2	72.0±10.5*
S' cm/s	8.8±1.2	9.0±1.1	9.9±1.6	9.6±1.1	8.6±2.3	8.1±2.6
Stroke volume, ml	68.4±19.1	69.0±20.7	66.6±9.4	64.8±12.4	64.6±8.7	63.4±7.6
SVI	37.3±7.6	37±7.2	39.1±6.9	36.7±3.0	42.3±3.7	41.2±4.9
CO, L/min	5.4±1.3	5.4±1.3	5.4±0.9	5.3±0.6	5.6±1.0	4.9±0.8
COI, L/min/m^2	2.99±0.6	2.95±0.45	3.13±0.54	2.97±0.4	3.5±0.8	2.9±0.4
$V_{max\ LVOT,}$ m/s	1.21±0.16	1.22±0.14	1.12±0.25	1.09±0.12	1.16±0.12	1.09±0.16
EF(%)	51.8±6.4	54.2±6.1	53.4±5.9	53.0±5.3	50.2±1.3	58.4±6.1*
LVEDV, ml	77.2±23.3	70.3±17.8	71.6±11.6	91.6±22.5**	73.8±27.1	89.6±28.9
LVEDVI, ml/m^2	42.1±11.8	38.5±9.09	42.5±11.2	52.9±15.4**	40.3±9.1	52.5±21.0
LVESV, ml	37.6±14.3	32.2±9.4	33.2±6.4	43.2±12.3	36.4±12.6	39.4±16.9

Data are presented as mean±SD. *Significantly better from baseline to three months within the groups ($p<0.05$), ** Difference within the groups ($p<0.1$) from baseline to three months. Abbreviations: S', peak systolic tissue velocity; SV, Stroke Volume; SVI, Stroke Volume Index; CO, Cardiac Output; $V_{max\ LVOT,}$ maximal velocity in the left ventricular outflow tract; LVEDV, Left Ventricular End Diastolic Volume; LVEDVI, Left Ventricular End Diastolic Volume Index; LVESV, Left Ventricular End Systolic Volume.

Left ventricular end-diastolic volume (LVEDV) as well as LVEDV indexed to body surface area (LVEDVI) increased almost significantly in the CME by 27.9% ($p=0.07$) and 24.5% ($p=0.09$) respectively (Figure 3.3). The AIT group tended to improve LVEDV and LVEDVI by 21.4% (LVEDV, $p=0.2$) and 30.5% (LVEDVI, $p=0.2$) respectively (Table 3.3). However none of them reached the statistical significance. Ejection fraction increased only significantly in the AIT group by 16.3% ($p=0.05$) (Table 3.3).

Table 3.4. Diastolic Doppler and tissue Doppler imaging variables.

Supine value	Diet (n=11)			CME (n=5)			AIT (n=5)		
	Baseline	3 months	p-value	Baseline	3 months	p-value	Baseline	3 months	p-value
E, cm/s	104±18.6	99.2±12.6	0.40	93.2±7.8	93.2±9.1	0.95	90.4±13.4	99.2±15.0	0.31
e', cm/s	15.9±2.3	15.9±3.1	0.99	16.9±1.8	17.4±2.9	0.48	15.3±3.0	14.7±1.8	0.59
E/e'	6.5±1.2	6.3±1.5	0.60	5.7±0.4	5.1±0.5	0.13	6.5±1.5	6.8±1.4	0.41
E/A	1.7±0.4	1.6±0.3	0.70	1.6±0.2	1.6±0.4	0.77	1.5±0.4	1.6±0.6	0.80
A, cm/s	63.1±12.1	61.6±8.7	0.77	60.0±8.7	61.0±15.6	0.84	60.4±8.3	63.8±12.9	0.61
DT, ms	189.6±34.6	173.4±35.2	0.20	171±36.9	138.2±38.4	0.28	162.2±42.8	141.0±43.2	0.20
IVRT, ms	48.5±11.3	35.9±13.0*	0.006	45.8±11.1	39.2±11.9	0.18	35.2±5.5	31.0±4.4	0.38

Data are presented as mean±SD. * Significantly better within the groups from baseline to three months ($p<0.05$). Abbreviations: E, peak early diastolic mitral flow; A, peak late diastolic mitral flow; DT, deceleration time; e', peak early diastolic tissue velocity; IVRT, isovolumic relaxation time.

Even though the AIT increased peak early diastolic mitral flow (E) by 8.8 cm/s ($p<0.31$), it did not reach statistical significance (Table 3.4). Both isovolumic relaxation time and deceleration time improved in all groups, but only IVRT was significantly different after intervention (decreased 26%) among the diet intervention ($p=0.006$) (Table 3.4).

3.4. Diet versus exercise

Diet group decreased ISO-BMI from 32.8±3.1 to 32.2±3.3 kg/m^2 (p=0.13) from baseline to three months and exercise group (CME+ AIT) decreased ISO-BMI from 33.1±3.7 to 32.6±4.3 (p=0.17) respectively. There was a tendency towards the reduction in resting heart rate by 5 BPM (p=0.22), systolic blood pressure by 4 mmHg (p=0.3), total fat by 1.9% (p=0.06) and increment of fat free mass by 1.7% (p=0.003) among the exercise groups after intervention. Only LBM reached the statistical significance.

Table 3.5. Comparison of left ventricular volumes and systolic functions between diet and exercise groups.

Supine value	Diet (n=11)		Exercise (n=10)	
	Baseline	3 months	Baseline	3 months
S' cm/s	8.8 ±1.2	9.0 ±1.1	9.3±1.9	8.8±1.9
Stroke volume, ml	68.4±19.1	69.0±20.7	65.6±8.6	64.1±9.9
SVI	37.3±7.6	37±7.2	40.5±5.6	38.7±4.4
CO, L/min	5.4±1.3	5.4±1.3	5.5±0.9	5.1±0.7
COI, L/min/m^2	2.99±0.6	2.95±0.45	3.3±0.7	3.0±0.4
$V_{max\ LVOT,}$ m/s	1.21±0.16	1.22±0.14	1.14±0.19	1.09±0.13
EF (%)	51.8±6.4	54.2±6.1	51.8±4.4	55.7±6.1
LVEDV, ml	77.2±23.3	70.3±17.8	72.7±19.7	90.6±24.4*
LVEDVI, ml/m^2	42.1±11.8	38.5±9.09	41.5±9.6	52.7±16.9*
LVESV, ml	37.6±14.3	32.2±9.4	34.8±9.6	41.3±14.1

Data are presented as mean±SD.*Significantly better within groups from baseline to three months (p<0.05), ** Difference within groups from baseline to three months (p<0.1). Abbreviations: S, peak systolic tissue velocity); SV, Stroke Volume; SVI, Stroke Volume Index; CO, Cardiac Output; $V_{max\ LVOT,}$ maximal velocity in the left ventricular outflow tract; LVEDV, Left Ventricular End Diastolic Volume; LVEDVI, Left Ventricular End Diastolic Volume Index; LVESV, Left Ventricular End Systolic Volume.

Ejection fraction had a tendency towards improvement by 3.9% (p=0.17) but the statistical significance could not reached. The left ventricular end diastolic volume and left ventricular end diastolic volume when normalized with the body surface area increased by 24.6% (p=0.02) and 26.9% (p=0.03) after three months of exercise intervention (Table 3.5).

Even though the exercise intervention increased peak early diastolic mitral flow (E) by 4.3 cm/s (p<0.33), it did not reach statistical significance (Table 3.6). IVRT reduced by 25.9% (p=0.006) in diet intervention; and almost significantly reduced by 11.1% (p=0.08) in exercise intervention (Table 3.6).

Table 3.6. Diastolic Doppler and tissue Doppler imaging variables.

Supine value	Diet(n=11)		Exercise(n=10)	
	Baseline	3MND	Baseline	3MND
E, cm/s	104±18.6	99.2±12.6	91.8±10.4	96.1±12.2
e', cm/s	15.9±2.3	15.9±3.1	16.1±2.5	16.0±2.7
E/e'	6.5±1.2	6.3±1.5	6.1±1.1	5.9±1.3
E/A	1.7±0.4	1.6±0.3	1.5±0.3	1.6±0.5
A, cm/s	63.1±12.1	61.6±8.7	60.2±8.1	62.4±13.8
DT, ms	189.6±34.6	173.4±35.2	147.1±37.4	139.5±38.6
IVRT, ms	48.5±11.3	35.9±13.0*	40.5±9.9	36.0±6.2**

Data are presented as mean±standard deviation.*Significantly different within group from baseline to three months ($p<0.05$), ** Difference within groups from baseline to three months ($p<0.1$). Abbreviations: E, peak early diastolic mitral flow; A, peak late diastolic mitral flow; DT, deceleration time; e', peak early diastolic tissue velocity; IVRT, isovolumic relaxation time.

3.5. Exercise testing variables

Table 3.7. Maximal oxygen uptake values at the baseline and after three months intervention.

	Diet (n=11)			CME (n=5)			AIT (n=5)		
	Baseline	3 months	p-value	Baseline	3 months	p-value	Baseline	3 months	p-value
VO_{2max} L/min	2.4±0.6	2.4±0.6	0.94	2.1±0.9	2.2±0.8	0.42	2.2±0.3	2.3±0.6	0.77
mL/kg/min	33.7±5.4	34.4±6.9	0.51	25.5±7.9	26.5±4.3	0.65	36.2±2.9	37.6±9.5	0.74
mL/kg$^{0.75}$/min	89.8±32.5	89.9±33.4	0.27	76.5±24.8	79.9±16.5	0.57	101.2±8.9	104.4±25.8	0.74
mL/LBM$^{0.75}$/min	152.8±27.4	160.6±25.6	0.35	127.9±38.2	129.3±41.7	0.65	148.6±13.5	146.9±31.9	0.87
HR_{max} BPM	197.9±10.3	192.6±13.4	0.11	177.0 ±8.1	177.3±5.5	0.95	192.5±8.7	186.5±11.0	0.31

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Data are presented as mean±SD. Abbreviations: VO_{2max}, Maximal oxygen uptake; HR_{max}, maximal heart rate; BPM, beats per minute; LBM, Lean Body Mass.

Maximal oxygen uptake did not improve significantly in any of the three groups after intervention (Table 3.7). There was a tendency towards reduction in the HRmax among diet and AIT. However, significant difference was not observed (Table 3.7).

Discussion

The main findings of this study are:

1. Aerobic interval training combined with diet intervention was superior compared to continuous moderate exercise combined with diet intervention for improving more cardiovascular risk factors such as resting heart rate, systolic blood pressure, fat mass and fat free mass.
2. Moderate exercise almost significantly improved left ventricular end diastolic volume and left ventricular end diastolic volume index. Aerobic training significantly improved ejection fraction. However the superiority of the aerobic interval training over the moderate training for the improvement of cardiac function was not observed due to small sample size.
3. Exercise combined with diet intervention improved the cardiovascular risk profile more than the diet intervention alone. Left ventricular end diastolic and left ventricular end diastolic volume index improved significantly among the exercise combined with diet intervention and IVRT improved significantly among the diet intervention. However other possible significant difference was not observed.

4.1. Anthropometry and body composition

The weight among the three intervention groups slightly increased and height increased significantly after intervention (Table 3.2). There was a tendency for a reduced BMI after intervention in all three groups (Table 3.2). Since the growth and development spurts up in adolescence due to hormonal changes, weight loss cannot be considered as a measure of effectiveness of the intervention. The girls put on more fat mass and the boys have more lean body mass as they reach puberty (Stephen R Daniels et al., 1995). The weight stagnation rather than weight reduction should be target treatment for the obese adolescent.

In this study, there was a tendency towards reduction of the total fat mass by 3.5% ($p=0.23$) among the AIT and was almost unchanged among diet and the CME intervention (Table 3.2). The contributing factors for fat metabolism during endurance training includes greater blood flow within the exercising muscles, enhanced fat mobilizing and fat-metabolizing enzymes, enhanced mitochondrial respiration and decreased catecholamine synthesis for the same work output (Horowitz & Klein, 2000). Although moderate training may induce a higher fat metabolism percentage, the total fat metabolism is not higher when compared with high intensity training. High intensity training yields greater energy expenditure with higher amount of fat metabolism per minute (Bahr & Sejersted, 1991). Higher intensity training (more than 90%) burn fat (triglycerides and free fatty acids) to yield energy for the post exercise oxidation process even after one hour of recovery of training (Medbo & Jebens, 2002). This means that fat expenditure persist for longer duration after high intensity training compared to moderate training. In addition the energy deficit among the high intensity

increases with the combined diet therapy. All of these processes might contribute to the reduction in fat mass percentage among the high intensity intervention. The children/adolescents in moderate exercise intervention might have consumed a large amount of calories despite of the diet counseling which might led to less reduction of fat mass percentage. On the other hand the high intensity intervention might control their diet habit which led to the reduction of the fat mass percentage.

This result is in line with the findings by Tjønna et al., (Tjonna et al., 2009) who reported that exercise training decreased fat mass substantially more than diet therapy and; as well as Gutin et al.(Gutin et al., 2002) who confirmed that the AIT is superior compared to moderate training in reducing the body fat.

The lean body mass increased in both exercise intervention (AIT, p=0.07; CME, p=0.04) and remained unchanged in diet intervention (p=0.12) (Table 3.2). The possible changes in the caloric intake after diet counseling and preservation of the lean body mass due to exercise might contribute in the improvement in the lean body mass. A study done on adult overweight population depicts that exercise alone causes less weight loss with less effect on fat free mass (FFM), while dietary restriction causes more weight loss with more effect on FFM. The similar weight loss achieved when dietary restriction is combined with exercise causes less loss of FFM (Ross et al., 2000). It was also explained previously that exercise combined with diet therapy have greater effect on reducing body weight, fat mass and cardiovascular risk factor compared to exercise alone (Shalitin et al., 2009; Shaw et al., 2006). However exercise alone causes beneficial effect on the improvement of cardiovascular risk profiles (Shaw et al., 2006). Improving the cardiovascular risk profile, reducing body fat mass and improving lean body mass should be considered as target outcomes of the intervention rather than reducing weight among the children and adolescence (Shaw et al., 2006).

The present study supports that high intensity training combined with diet intervention is effective to maintain the appropriate body composition than diet intervention alone or moderate exercise intervention. If improvement of the body composition is the expected outcome, then high intensity exercise combined with diet intervention should be considered while treating overweight and obese individual.

4.2. Blood pressure and resting heart rate

The systolic blood pressure was reduced by 6 mmHg (p=0.21) and the resting heart rate was reduced by 10 BPM (p=0.05) among the AIT group (Figure 3.2). Blood pressure in the aorta is regulated by several mechanisms and the most rapid to change are peripheral resistance and cardiac output. However blood volume, viscosity of the blood and the elasticity of the large arteries can also be changed (Guyenet, 2006). Exercise on a regular basis can affect the peripheral vascular system resulting in enhanced perfusion and flow (Cornelissen & Fagard, 2005). Underlying mechanisms for a decrease in resting heart rate includes an altered autonomic balance with an increase of parasympathetic nerve activity (Guyenet, 2006).

However, a recent study demonstrated changes in the heart's pacemaker in response to training and the downregulation of an important protein (HCN4) which is responsible for controlling the rhythm of the sinus node and thereby responsible for lowering heart rate (D'Souza et al., 2014). Other possible explanations might be a reduced intrinsic rate of contraction of the atria, a reduced drive from peripheral chemoreceptors as well as a down regulation of β-adrenergic receptors in the myocardium (Rowell, O'Leary, & Kellogg, 1996).

In this study the possible mechanism including reduction in sympathetic nervous system activity and increment of parasympathetic nervous system among the AIT may contribute the reduction of blood pressure and resting heart rate. Aerobic interval training was observed to restore the impaired hemodynamics values of obese adolescents to the same level with the lean counterparts (Ingul C, 2010). The aerobic exercise together with the caloric restriction and behavioral changes produced even greater decrease in the systolic blood pressure and resting heart rate (Rocchini et al., 1988). The result from the present study is in line with these results that high intensity exercise combined with diet counseling is appropriate for reducing systolic blood pressure and resting heart rate among obese (Figure 3.1 & Figure 3.2).

4.3. Cardiac function

The data of the myocardial function among the obese children/adolescents in this study were in line with data from Ingul et al (Ingul C, 2010) who showed cardiac dysfunction among the obese adolescents. The obese adolescents require subsequently a higher cardiac output to supply the oxygen to the excess adipose tissue (P. Poirier et al., 2006). The elevation in cardiac output among the obese children/adolescents can be due to a higher resting heart rate or higher stroke volume (Messerli Fh & et al., 1981). In this study, the baseline stroke volume and the resting heart rate among the children/adolescents were higher compared to those observed among the lean groups obtained by Ingul et al (Ingul C, 2010) but the stroke volume when normalized with body mass were lower. Endurance training increases the plasma volume, red blood cell volume, the amount of blood ejected during systole, augments LV filling during diastole and accelerate the heart rate (Convertino, 1991). The cardiac contractility increases due to enhanced β-adrenergic receptor after exercise and end systolic volume reduces (Rowell et al., 1996). Together these physiological responses lead to an increase in stroke volume and thus cardiac output (Convertino, 1991).

Despite the fact that exercise increases the stroke volume (Helgerud et al., 2007) it did not improve after the intervention in this study. In contrary, the AIT further reduced the cardiac output. Since the stroke volume remained unchanged and the resting heart rate decreased by 10 BPM among the AIT after training, this could be the main reason for the reduced cardiac output. Neither stroke volume nor resting heart rate was changed among the moderate exercise intervention and diet intervention; as a consequence of which the cardiac output remained unchanged in both groups. A technical error in the VTI tracing and LVOT measurement may erroneously affect the three months result. Failure to trace the VTI along the modal velocity for the atrioventricular valve, the failure in the acquisition of the pulsed

wave Doppler image and failure in sampling the mitral annulus may affect the possible outcome of the intervention. The error may occur in the ventricular cross sectional area measurement which includes the measurement of diameter during the wrong phase of cardiac cycle and inconsistent annular measurement might causes the false values than the expected.

The obese adolescents have reduced LVEDV related to their body weight, which is probably due to the consequence of sedentary lifestyle. This reduced LVEDV is compensated by higher resting heart rate. As a result of higher resting heart rate, the diastolic duration reduce which subsequently reduce LVEDV. It has earlier been shown that aerobic interval training normalized LVEDVI among obese children/adolescents to the same level compared with the lean counterparts (Ingul C, 2010). In this study, LVEDV and LVEDVI have a tendency towards improvement in both exercise intervention (Table 3.3). Improvement in the venous return after exercise contributes to the improvement in the LVEDV and LVEDVI.

Ejection fraction is highly affected by left ventricular size and hemodynamics status, causing limitation to estimate ejection fraction as the measure of systolic function. If afterload of the left ventricle is reduced, then there will be an increase in ejection fraction (LEWIS & SANDLER, 1971). Afterload reduced among the AIT due to the tendency towards the reduction in systolic blood pressure which causes improvement in the ejection fraction after intervention. The increased LVESV among moderate exercise intervention may be possibly due to the increase in arterial pressure during ejection fraction. This and in addition with the increased LVEDV and the unchanged stroke volume among the moderate exercise intervention might lead to the unchanged ejection fraction after intervention. Other parameters such as left ventricular end-diastolic dimension, left ventricular end diastolic length, LV end systolic length and the LV-end systolic dimension should be assessed because these parameters directly affect the ejection fraction (Drazner et al., 2004; LEWIS & SANDLER, 1971).

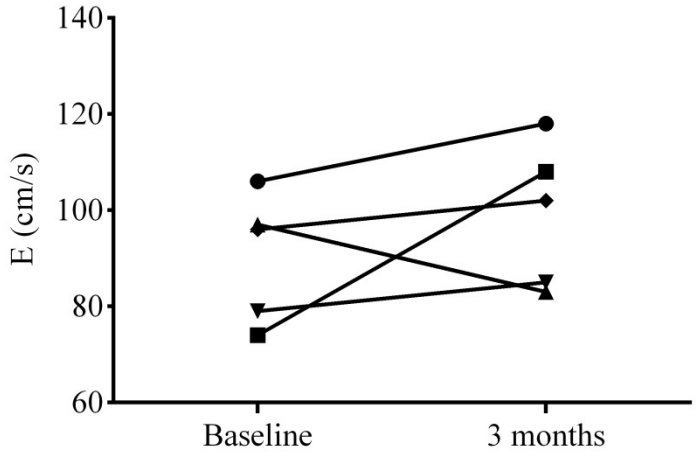

Figure 4.1. The figure shows the changes in the peak early mitral flow velocity within each of the children/ adolescents in the interval training groups. E; peak early diastolic mitral inflow velocity which is expressed in centimeter/second (cm/s). n = 5.

In this study, significant change in diastolic function was not observed among the intervention groups (Table 3.4). Peak early diastolic mitral flow velocity (E) tended to increase among 4 children (p= 0.31) (Figure 4.1) and the E wave deceleration time tended to decrease among the AIT (Table 3.4) suggesting the enhancement of the early mitral filling velocity after intervention. The venous return increased among the AIT suggested through increased LVEDV which increases the early mitral filling velocity.

Ingul et al confirmed that 13 weeks of the aerobic interval training decreased the deceleration time and IVRT; and improved the early diastolic tissue velocity; thus restoring the impaired diastolic function to the same level compared to the lean counterparts (Ingul C, 2010).

IVRT and deceleration time improved in all three groups suggesting improvement in cardiac relaxation after intervention (Table 3.4). The diet intervention significantly reduced the IVRT (p=0.02). There was a tendency towards reduction of IVRT among the exercise groups. The complex cellular factors like decrease in the cytosolic calcium level, increased phosphorylation of troponin I (Zhang, Zhao, Mandveno, & Potter, 1995), inherent viscoelastic properties of the myocardium and the greater systolic load (Leite-Moreira, Correia-Pinto, & Gillebert, 1999) may contribute to the reduction in the IVRT. The reason behind the reduced IVRT among the AIT might be due to the reduced systolic blood pressure. However the group difference was not observed.

Early diastolic tissue Doppler velocity (e') increases with increase in preload (Hsiao et al., 2005). Decrease in e' reflected the prolonged relaxation. The AIT tended to reduce e' even though shortening of the IVRT and the deceleration time and increase in LVEDV were observed. Diastolic pressure can influence the results. Earlier studies on continuous moderate training and aerobic training on cardiac function among healthy (Slordahl et al., 2004), diseased (Dubach et al., 1997; N. Pattyn et al., 2014) and post infarction patients (Wisloff et al., 2007) showed that aerobic training was superior compared to moderate training to reverse the cardiac dysfunction. However these comparisons were done among the adult population only. A study done on obese children concluded that initially impaired cardiac systolic and diastolic function indices were restored after 13 weeks of training among obese adolescent (Ingul C, 2010). However, only AIT was studied and not CME.

4.4. Exercise testing variables

There was a tendency of a reduction of the maximal heart rate significantly in the diet intervention (197.9 to 192.6 BPM, $p < 0.11$) and the AIT (192.5 to 186.5, $p< 0.95$)(Table 3.3). Training induces a reduction of the heart rate during submaximal exercise. It depicts the cardiac adaptation of the exercise on the heart. The baseline cardiorespiratory fitness was 32.5(±6.2) ml/kg/min, which is almost equivalent to the cardiac fitness of a 70 years old person (Weiss, Spina, Holloszy, & Ehsani, 2006). Furthermore, this value is far less than the mean peak oxygen uptake value of healthy adolescent girls (49.2 ml/kg/min) and boys (59.5 ml/kg/min) from the Young Hunt Study (Nes, Østhus, Welde, Aspenes, & Wisløff, 2013).

The three months intervention program could not restore aerobic capacity in all three groups (Table 3.3). Most of the clinical trial studies have found an improvement in the submaximal oxygen uptake rather than improvement in the maximal oxygen uptake among the children. The possible explanation for this may be that it is difficult to obtain the true maximal efforts during the laboratory settings for the children. The excess body weight among the obese may affect their performance while testing for VO_{2max} (Rowland, 1990). It was also observed that VO_{2max} increased slightly among the boys with the stage of maturity and tended to decrease among the girls with the stage of maturity (Mota et al., 2002). In the present study, most of the girls were reaching their pubertal maturity and most of the boys were on their early stage of pubertal changes. This pubertal maturity was not assessed to confirm the effect of the intervention on the aerobic capacity, which could affect the result of the present study.

It has been confirmed that the AIT is superior compared to the CME in improving the maximal oxygen uptake both in diseased (N Pattyn et al., 2014; Tjønna et al., 2008; Wisloff et al., 2007) and healthy adult (Helgerud et al., 2007; Slordahl et al., 2004). Ingul et al found that the AIT significantly improved aerobic capacity among the obese adolescent after 13 weeks intervention (Ingul C, 2010).

Stroke volume is a limiting factor for the aerobic capacity (Bassett & Howley, 2000) and interval training allows rest period in between the high intensities minutes; boosting up their energy for the performance during higher intensities minutes to their maximal limits, thus challenging the pumping ability of the heart. This effect could not be obtained with continuous moderate training. However in this study, stroke volume was not improved among the intervention groups. There was a trend towards increase in both exercise groups, but not significant (Table 3.2). The maximal oxygen uptake when normalized to the body mass and lean body mass (VO_{2max} expressed as milliliters per kilograms to the 0.75^{th} per minute) remained unchanged after intervention.

When the individual values of the high intensity intervention were assessed, 4 children/adolescents in the AIT (n=5) had improved their maximal oxygen uptake after three months of intervention. In contrast, the moderate exercise intervention and the diet intervention did not show the improvement. Thus it can be concluded that the intensity of exercise rather than the duration of training matters for the better cardiorespiratory fitness among the children.

The stroke volume was not improved among the intervention groups. Because of this reason, the aerobic capacity may not be improved in the present study. The sample size in each group was few to find a significant improvement in aerobic capacity. In addition some of the values were missing which may affect the overall outcome.

Though obesity and aerobic capacity are two strong and independent factors for mortality (S. N. Blair & Brodney, 1999), the bond seems to be stronger with aerobic capacity (Gaesser, 1999). Thus improvement in aerobic capacity rather than reducing the weight should be kept in mind while managing obesity.

4.5. Effectiveness of the training modalities

Initially the subjects had aversion towards the exercise program. However they were gradually motivated towards the training which was depicted through the informal conversation with the participants during the training session. The aptitude for training was also increased as the training session progress which was evidenced from their increasing training speed required to reach the target heart rate. Out of 29, 8 of the subjects were dropped out and all of them were from the exercise intervention. This indicates that it was really difficult to resume the children in the planned training program. However the cause of the drop out was unknown. Each training session was also difficult to run in a planned way for some of the children since the children got easily distracted. Since some of the participants continue the habits like grabbing the side bars though requesting not to do it; interrupting the training due to different reasons might affect the effectiveness of the training. This means that the indoor settings may not be a good place for obese children for training. Some of the children who were doing moderate training verbalized that continuous running at the same speed bored them. Some of the exercising children initially did not follow the instruction from the trainer which might affect their exercise initially. However most of them resume their exercise capacity later. Thus the effective motivational strategies should be implemented for training the children/adolescents.

Conclusion

From this study it is observed that both continuous moderate exercise and aerobic interval training improved left ventricular end diastolic volume and left ventricular end diastolic volume indexed to body surface area. The high intensity exercise intervention improved ejection fraction and resting heart rate. The lean body mass was improved among both exercise intervention. Thus it is indicated that high intensity exercise with diet intervention improved more cardiovascular risk factors than the moderate exercise intervention with diet and diet intervention alone. However, it was not confirmed which training intensity was more effective in improving the cardiac function. A larger study with more severe obese children/adolescents should be employed to find out more about the effect of exercise and diet intervention on the cardiac function.

Limitations and strengths

The small sample sizes in each intervention group affect the results of the study. A significant difference among lot of variables was not observed although several variables were almost significant. The drop out was high with about 28% of the participants.

In addition the caloric and macronutrients changes during the intervention program were not assessed which could impact the result of this study. The children in the diet intervention were requested to avoid vigorous physical activity during the three months of intervention, which however was difficult. The sustainability of intervention effect was not assessed. The pubertal growth was not considered while analyzing the data which could have impacted on the cardiac function. Thus, the results and analyses of this study must be interpreted with caution.

However, well-controlled and highly defined exercise intensity intervention regimen is the most important aspect of this study. Further, there were no injuries of the subjects during the study and the training program was therefore considered safe.

Future directions

The study found almost significant improvement in some of the variables although the sample size in each of the intervention groups were few. Thus it was noted that if the sample size in each of the intervention groups were high, more significant changes could be observed in cardiac function indices. Thus in future a long study with a larger sample size in each intervention group need to be recruited to observe the significant difference within and between the groups.

The involvement of the parents in the exercise program may help the children/adolescents to resume the exercise program. A well-planned motivational strategy is needed to improve the children's performance and to prevent the drop out rate.

Most impotantly, a larger sample size including different degrees of obesity should be recruited in future studies to investigate the optimal type of training, as well as the optimal training frequency and intensity to improve the cardiac function among the obese children/adolescents.

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