CHAPTER 1

Introduction
1.1. Overweight and obesity - definition and classification

As defined by World Health Organization (WHO), overweight and obesity are characterized as abnormal or excessive amount of adipose tissue accumulation that may impair health.\(^1\) Obesity is considered as a chronic metabolic disease of positive energy balance influenced by many factors such as diet, physical inactivity and hereditary factors.\(^2\)

Quetelet index which is now known as Body Mass Index (BMI) is widely used to classify the body weight and to categorize the degree of overweight and obesity.\(^3\) Classification recommended by WHO is followed worldwide to assess the risk of non-communicable diseases. The risk of non-communicable diseases (NCD’s) and death rates due to these diseases has been directly linked to this classification in many populations.\(^4\) The global status report given by WHO in 2010 on NCD’s mentioned the consequences of obesity.\(^5\) BMI is used as a measure of adiposity based on the assumption that a variation of weight for the persons of same height is due to increased fat mass.\(^6\) However, the degree of fatness is not directly associated with body weight of a person as observed across different populations. In spite of its limitations in body fat assessment, BMI is routinely used as an important method in obesity evaluation.\(^7\)

1.2. Classification of obesity in Asian-Indian population

The risk of cardiovascular diseases has been found to be high even with low BMI in Asian population.\(^8\) A WHO expert consultation reviewed the scientific evidence and observed that the risk of obesity related complications increased with BMI more than 23 in this population.\(^9\) The body fat in Asian population was found to be considerably high with lower BMI when compared to other populations.\(^10,11\) The risk of metabolic syndrome has been found to be high
in south-Asian population with proportionately lower levels of body fat; however, few studies attributed these differences to the genetic characteristics in South Asians. The central obesity was found to be 41% in Indians compared to an average of 28% in rest of the countries.\textsuperscript{12,13} The new classification proposed for Asian population recommends considering the BMI range of 23.0 to 26.9 as overweight and obesity as 27.0 to 32.9.\textsuperscript{14} The combined category of “overweight and obese” refers to a BMI of 25 or higher.\textsuperscript{15} Lower thresholds of BMI cut points have been used for some countries in Asia, although the consensus on these guidelines are yet to be arrived.\textsuperscript{16}

1.3. Prevalence of overweight and obesity:

Obesity is now considered as a worldwide problem.\textsuperscript{17} The prevalence rates have been calculated in several countries and most recent global estimates find that roughly 500 million adults are obese.\textsuperscript{18} The global prevalence rate of adult obesity is projected to increase to 1 million by the year 2030.\textsuperscript{19} Estimated prevalence rates of obesity as per WHO were highest in America (62% overweight and 26% obesity) and lowest in South East Asia (14% overweight and 3% obesity).\textsuperscript{20-22} The lowest prevalence rates in largely populated countries like China and India might have underestimated the actual number of obese subjects.\textsuperscript{23} The prevalence of obesity and its associated complications as reported by WHO are increasing in most of the countries.\textsuperscript{24,25} The prevalence of obesity in women was almost double to that in men in many countries.\textsuperscript{26}

Countries like Afghanistan, Bangladesh, Bhutan, India, Nepal, and Pakistan have seen a rapid rise in obesity rates in past two decades.\textsuperscript{27,28} The rate of obesity has doubled in the last 20 years in India with the rate of increase being more in urban population compared to rural
population. Various studies have shown high prevalence of abdominal obesity in India. The incidence and prevalence of obesity in most of the studies was projected based on Body Mass Index values. Advanced imaging methods which are currently available have not been used extensively to study the prevalence rates in India. If the newly proposed Asian-specific cut-off points for the definition of obesity (body mass index >28 kg/m2) are taken into account, the number of adults considered obese may increase in India. Although the accurate estimates of prevalence rates in India are not available, the increase in number of obese individuals has warranted the need for an effective management.

1.4. Causes, risk factors of obesity and disease burden in Indians

Urbanization and modernization are highly associated with several dietary and behavioural risk factors of obesity and its related complications in Indian population. The availability of unhealthy processed foods and low physical activity levels are some of the main contributing factors for obesity. Increased migration of rural population to urban areas combined with lifestyle changes has also contributed to increase obesity rates in India. The increased stress levels among working class and genetic predisposition are also believed to be the causes for an increase in prevalence rate in Indian population.

Obesity has not yet become a major public health priority in developing countries like India whose economy is booming and the living conditions have improved drastically in urban areas. As the country is struggling to tackle and control the diseases affecting the common man due to poor infrastructure and manpower, less attention is drawn towards lifestyle diseases and their prevention programs. Increased focus on creating awareness, initiating the prevention programs and management of obesity may help in reducing the disease burden of non-communicable diseases and improve the health economics.
1.5. Methods of evaluation of obesity: Traditional and new methods

The evaluation of obesity includes the identification of causative factors by comprehensive history taking and subjective examination. The prevention of complications and treatment is imperative for all obese individuals irrespective of the body composition and other clinical outcomes. As achieving the weight loss is considered the primary target or objective in obesity management, achieving fat loss is considered clinically beneficial to improve the health profile and prevent future complications. Many new assessment methods have been proposed in the recent past for accurate assessment of obesity and effective treatment. The objective assessment of obesity is broadly divided into body composition assessment, assessment of exercise capacity, strength and flexibility assessment. The accurate assessment of body fat using body composition assessment methods enables health professionals to plan the individualized treatment program.44,45

Body weight and body mass index are used in the routine clinical assessment as they are simple and inexpensive measures. Association of excess weight with risk of diseases is well accepted. The ideal weight according to the height of an individual for either gender has been suggested. Skeletal muscle mass in a trained individual also leads to increased weight and so the amount of excess body fat cannot be estimated with the ideal weight chart. Although BMI is used to monitor the weight loss and therapeutic effects of interventions, its inability to measure the changes in fat limits its use in research.46

Waist circumference (WC) is a better indicator of body fat than BMI as it is closely associated with cardiovascular disease risk.47 As the prevalence of abdominal adiposity is high in Indian population and the average BMI levels are low in Asian population compared
to other ethnic groups, addition of WC in the obesity evaluation gained the importance.\textsuperscript{48,49} WC measurement has been considered as the most useful tool in health screening of overweight and obese adults. It is a very strong predictor of cardiovascular and metabolic diseases. As excess fat and distribution of fat particularly are associated with several diseases, the circumference measurements which reflect the body fat have been better associated with diseases.\textsuperscript{50,51} WC is a reflector of abdominal fat which includes both subcutaneous and visceral fat.\textsuperscript{52} As there is emerging evidence on visceral fat as a potential risk factor for diseases compared to subcutaneous fat\textsuperscript{53}, research interest is slowly shifting towards the regional visceral fat assessment.

WHO defined cut-off points for WC used in the diagnosis of metabolic syndrome. The risk of cardiovascular diseases appeared to be more in some ethnic groups at lower cut points. International Diabetes Federation classification of central obesity was given for different ethnic populations.\textsuperscript{54} The South-Asian population generally has lower average BMI than other populations. But the prevalence of abdominal obesity was found to be high in these countries which also include India. The gender and ethnicity specific WC cut-off points for South Asian men and women has been reported to be $\geq 90$ cm and $\geq 80$ cm respectively.\textsuperscript{48}

Waist-to-hip ratio is used as an additional measure in anthropometric assessment. The normative ratios proposed based on the gender do not directly measure the amount of body fat.\textsuperscript{55} Waist-to-height ratio is considerably a new method in this field; more evidence is required on its predictive ability.\textsuperscript{56} The knowledge on dangerous complications of body fat is emphasizing the focus on direct assessment of body fat.
1.6. Body fat assessment for cardiovascular risk assessment

The primary goal of a weight-reduction program for obesity is to achieve the fat loss. As obesity is determined by excess fat and not by excess weight, the body composition assessment mainly focuses on body fat estimation. The body fat estimation can be done by simple field methods and also by more accurate imaging methods. The commonly used field methods for fat estimation are skinfold callipers and bioelectrical impedance analysers.\(^57\)

Skinfold callipers are popularly used to measure total body fat percentage with a predictive equation for both men and women. The gender specific testing sites used in this method predict the body fat percentage by these standard equations. The errors in measurement are common because of difficulty in grasping and holding.\(^58\) Previously, the use of skinfold callipers to assess weight loss was found to be unreliable.\(^59\) Skinfold measurement has been found to be more accurate in normal weight population whereas, accuracy in obese population with BMI >30 has not been found good.\(^60\)

Bioelectrical impedance analysis (BIA) is found to fairly accurate under standard testing conditions. BIA is relatively inexpensive and a widely used method for body fat assessment. The accuracy of BIA depends upon the device and the prediction equation used.\(^61\) BIA is most suitable to be used in BMI range of 16-34 in healthy individuals with electrolyte balance and normal levels of water in the body. The application of body composition technology has certain limitations in morbid obese adult population and obese children.\(^62\) Most BIA instruments use a single frequency at 50 kHz which predominately measures extracellular and intracellular water. The single frequency devices are most common as hand-to-foot devices; other devices are hand-to-hand and foot-to-foot. The other types of BIA
devices are Multi-Frequency BIA (MF-BIA), Bioelectrical Spectroscopy (BIS) and Segmental-BIA. All these devices have certain technological advantages of one over the other based on the measurement of water levels in the body.\textsuperscript{63} Earlier research studies have found that body composition assessment measured by BIA was reproducible and better than skinfold callipers in monitoring the fat loss through a weight reduction program.\textsuperscript{64}

The prevalence of obesity in many countries was under-estimated using weight and BMI as indices of obesity. More acceptable body fat assessment methods are required to monitor and treat obesity. The body fat estimation and monitoring its change with weight loss is an important objective in the primary prevention of metabolic syndrome.\textsuperscript{1} DEXA is the gold standard method in the assessment of obesity. Validation of body composition assessment method is done with DEXA.\textsuperscript{65}

Dual Energy X-ray Absorptiometry (DEXA), Magnetic Resonance Imaging (MRI), hydrostatic (underwater) weighing, and Computerized Tomography (CT) are accurate methods to determine the body composition. These methods are reliable in differentiating the amount of subcutaneous and visceral fat. As visceral fat is considered more dangerous than subcutaneous fat; there is emerging evidence on the use of visceral fat estimation methods in risk evaluation of cardio metabolic diseases.\textsuperscript{66} The imaging methods are highly expensive and cannot be used for obesity assessment and monitoring on regular basis. There is a growing need for development of less expensive, but reliable methods of visceral fat assessment.

Advanced imaging methods can accurately measure the true visceral fat and thus predict the risk of cardiovascular diseases. As these methods are highly expensive and not practically possible for routine clinical use, cheaper and reliable methods have been
introduced. WHO has made several recommendations for the development and validation of new and existing techniques in the assessment of obesity. The accurate estimation of various body fat compartments and regional body fat deposits using advanced imaging methods is the main focus of research as the cardiovascular risk assessment can be made more precise.

1.7. Subcutaneous fat V/s visceral fat in risk assessment:

Adipose tissue is of two types; function of brown tissue is to store excess energy whereas that of white adipose tissue is heat production. It is well established that the fat distribution can influence the predisposition to certain diseases. The fat stored in the body has pathogenic profile and those stored fat in different forms are known as adipose tissue stores. The two main types of adipose tissues are Subcutaneous Adipose Tissue (SAT) and Visceral Adipose Tissue (VAT). SAT is the adipose tissue under the skin and is further divided into superficial and deep SAT. VAT surrounds the organs in the abdominal cavity and mediastinum. VAT deposited surrounding the heart is identified as epicardial and pericardial adipose tissue, stomach as epigastric adipose tissue and that over blood vessels as perivascular adipose tissue.

VAT has been found to be more pro-inflammatory and metabolically active compared to the SAT. VAT has been correlated with diseases such as type-2 diabetes and atherosclerosis and has been found to be very important clinically to predict the cardiovascular and metabolic risk profile. Visceral fat is known to release bioactive molecules and hormones such as Adiponectin, Leptin, Tumour Necrosis Factor (TNF-alpha), Resistin and Interleukin-6 (IL-6). Adiponectin has inverse relationship with visceral fat whereas all other major substances have pro-inflammatory role in the development of coronary artery diseases (CAD).
VAT quantification is also very important to study the effects of treatment methods used in obesity management; it may well serve as a therapeutic endpoint. The visceral fat accumulation was also found to correlate well with cardiovascular disease risk factors even in non-obese population. Increased visceral fat was seen in 40% of the non-obese subjects with risk of coronary artery disease as well. This infers that disease risk increases with increase in the visceral fat gain rather than the body weight gain alone. The obesity evaluation and treatment may largely focus on visceral fat estimation and achieving the clinical benefits with visceral fat reduction.\textsuperscript{72} As the VAT has been identified as more dangerous than SAT, the research interest further expanded to quantification and substantiation of the amount of loss of these two, in response to weight loss programs.

1.8. Epicardial fat as a visceral fat: New marker and predictor of disease risk

The knowledge on adverse effects of VAT in the human body has created new research interest in the area of primary and secondary prevention of diseases. Recently, the adipose tissue within the thoracic cavity has been found to play a greater role in development and progression of diseases. Three different types of intra thoracic fat have been identified according to the location: pericardial fat, epicardial fat and perivascular fat.\textsuperscript{73,74} Epicardial fat is a true intra-thoracic visceral fat surrounding the heart, normally present in humans. It was earlier mentioned in the literature as “pericardial” and “paracardial” fat.\textsuperscript{75,76} The proximity of epicardial fat to the coronary arteries, particularly when it is in excess amount, is now known to increase the risk of cardio metabolic diseases in obese population.\textsuperscript{77} Even though, its role as an independent risk factor or as a surrogate marker of diseases is not known, there is a growing interest on its pathogenic profile and clinical implications. It is not mere ectopic fat, but rather a lipid storing depot and a source of inflammatory markers and called as Epicardial
Adipose Tissue (EAT).\textsuperscript{78,79} EAT quantification is now known to reflect the amount of VAT in the human body.

\textbf{1.9. Clinical implications of Epicardial Adipose Tissue:}

EAT functions like any other visceral adipose tissue in the body as a storing depot for the excess lipids\textsuperscript{80}. The knowledge about pathogenic profile of visceral adiposity has shifted the focus of weight reduction programs from mere weight loss to more important regional fat loss. EATT measurement has been found to be a reliable indicator of metabolic syndrome. It is also found to be an independent risk factor of coronary artery disease in both obese and non-obese population. EATT has been extensively studied for its pathogenic profile, relationship with the progression and severity of CAD and as an important outcome of obesity management.

\textbf{1.10. Measurement of Epicardial Adipose Tissue:}

Imaging of epicardial fat is done to measure the visceral fat and also to identify the risk of incidental findings to predict the risk of CVD along with other risk factors. Recent literature suggests that imaging of epicardial fat also helps in identifying the normal weight individuals with excess visceral fat in the body; this may particularly help in early identification of normal weight obese individuals at risk. Since the quantification of whole body visceral fat is cumbersome, imaging of cardiac adiposity has gained importance for risk evaluation.\textsuperscript{81} The weight loss was associated with substantial amount of total loss of body fat and also proportionately more amount of epicardial fat loss in healthy obese.\textsuperscript{82} The evidence indicates the possible regression of epicardial fat thickness and improvement in the risk profile with weight loss interventions. Thus, the imaging of epicardial fat has been proposed as indicator of visceral fat, metabolic syndrome and also an effective therapeutic target.\textsuperscript{83}
Magnetic Resonance Imaging (MRI) is considered as a gold standard method for epicardial measurement\(^4\). It can differentiate the pericardial fat from epicardial fat and it can accurately measure the entire volume in all the regions. MRI accurately measures the thickness in the grooves and areas where maximum deposition occurs.\(^4\) Cardiac MRI is not routinely done to measure the epicardial fat as a measure of visceral fat since it is highly expensive and cumbersome. There is a great demand for MRI in tertiary hospitals for diagnosis of several diseases; the appointments are given round the clock with the available facility in most of the hospitals. The routine obesity assessment with MRI is not feasible with the available facilities and measurement of epicardial fat volume with MRI is technically challenging. Epicardial fat modulation with weight loss has not been studied using MRI scan.

Computerized Tomography scanning of epicardial fat is relatively less expensive compared to MRI. The method of measurement has been validated for MDCT scan and also single slice measurement. The epicardial fat measurement is an additional tool along with cardiac calcium scoring in CAD patients. The technical feasibility and hazards of exposure with radiation dose in asymptomatic subjects has limited its use for routine epicardial measurement. The epicardial fat volume measurement is also technically challenging even though it is highly accurate and reliable. There have been limited studies using CT scan for measuring epicardial fat thickness.\(^5\)

1.11 Echocardiographic measurement of EAT

Echocardiography is an inexpensive and simple method to measure epicardial fat. Iacobellis et al first proposed the method for measuring epicardial fat. Echocardiography also called as transthoracic echocardiogram is done by a cardiologist or trained sonographer. The
standard two and three dimensional ultrasound is used in the diagnosis of heart diseases with colour Doppler echocardiography that help in the diagnosis of valvular heart diseases. Two-dimensional ultrasound can measure the epicardial thickness when recorded for at least 10 cardiac cycles with optimal cursor beam. The video recordings of the epicardial fat measurement is stored and further measured with minimal errors and reliably interpreted by experienced sonographer. The epicardial fat usually appears as echo-free space between the wall of right ventricle and pericardium when present in lower quantity and hyper-echoic space when present in higher quantity. The epicardial fat measurement at this location is found to be not influenced by the hypertrophy of right ventricle.86,87

Echocardiographic measurement of epicardial fat has been used in several research studies to study the prevalence of abdominal obesity and metabolic syndrome86-88. It has been found to correlate with coronary artery flow89, stenosis and progression of coronary artery disease.90 Echocardiographic measurements of epicardial fat were also found to be high in obese adolescents and children.91 Currently, the use of echocardiography in measuring the epicardial fat as a marker of visceral fat and metabolic syndrome in obese individuals is not routine. It may also be a useful tool in non-obese population with increased visceral fat. As abdominal obesity and increased visceral fat levels with relatively lower BMIs are seen in Asian-Indian population49, echocardiography will be a useful tool for monitoring the visceral fat in the body. Echocardiographic evaluation of epicardial fat has been introduced as a reliable marker of visceral fat and the current research in the obesity management is focused on establishing echocardiographic epicardial fat estimation as a therapeutic target.92
1.12. Management of obesity with focus on VAT reduction

The risk of having excess visceral fat in the body has been known since two decades. It has been used as a research outcome and therapy target in various studies. There is sufficient evidence on effects of various treatment methods on visceral fat. The visceral fat reduction occurs in morbid obese subjects after bariatric surgery. Some pharmacological agents were also successfully used in the treatment of visceral fat and abdominal adiposity as part of prevention of cardiovascular diseases. The diet and physical activity are two most important methods used in primary and secondary prevention of obesity, metabolic syndrome and their complications. The reduction of intake of calories or increasing the physical activity not only helps in weight reduction, but also helps in visceral fat reduction. The dietary restriction alone or/and physical activity have been found to be very effective on the amount of visceral adipose tissue and also its pathogenic profile. The aerobic exercise, resistance exercise and combination of aerobic and resistance training have been found to have positive effects on VAT in the earlier studies. The dose-response relationship of exercise and visceral fat has also been established. Most of the researchers have used expensive imaging methods to study the effects of aerobic exercise in their studies. There is a growing need for non-invasive, inexpensive, valid and reliable clinical tool to estimate visceral fat since the incidence of obesity related morbidity and mortality rates are increasing worldwide. Echocardiographic epicardial adipose tissue thickness (EEATT) measurement is one such easy and affordable method for visceral fat estimation. It has already been proven as a potential therapeutic target and has also been associated with clinical progression of the disease. If the errors in measurement can be prevented by following the standard procedure, this method may be well used in routine clinical assessment of visceral fat and obesity. It is of
great interest to know if EEATT can be used for evaluating the visceral fat reduction through various therapeutic interventions, particularly in the prevention of obesity.

1.13. Role of Physical activity promotion and exercise in management of obesity

The promotion of physical activity is the most important strategy in prevention and control of NCD’s. WHO has initiated the national and global action plan for lifestyle modifications for the years between 2013 and 2020 to effectively manage these diseases in developing countries like India. Improvement physical activity levels in obese individuals are associated with reduced health risks, enhanced physical and social wellbeing. Individually tailored and supervised aerobic exercise has been found to be effective in achieving weight loss and prevention of cardiovascular complications of obesity. Exercise forms the mainstay of treatment in prevention of childhood and adult obesity which is well known as potential cause of coronary artery disease. Aerobic exercise training and resistance exercise training have been found to be effective in obesity related body fat reduction, prevention of complications and improvement of health related quality of life. Exercise regimens may or may not reduce the body weight, but it is shown to promote fat catabolism and muscle anabolism. The role of aerobic and resistance exercises in the reduction of visceral adiposity has been studied extensively.

Aerobic exercise is physical exercise of relatively low intensity supported by aerobic metabolism for extended periods of time. The aerobic exercise is given in continuous or interval forms and both methods have been found to have certain advantages. Moderate intensity exercise is defined as exercise intensity more than 50% of VO2max or more than 60% of heart rate maximum or 11-13 on RPE scale. Structured aerobic exercise has
been found to be more effective than unsupervised exercise programs in the management of obesity. Treadmills, stationary bicycle and elliptical trainers are used to prescribe evidence based aerobic exercise programs to achieve weight loss after evaluating the exercise capacity. American College of Sports Medicine (ACSM) has given specific guidelines for prescribing aerobic exercise to overweight and obese population. Current data suggest that most physiological adaptations occur within the first few weeks of exercise training and 12 weeks of training helps in improvement of health related outcomes.\textsuperscript{104-106}

1.14. Echocardiographic Epicardial Adipose Tissue Thickness as a therapeutic target in obesity management

Several researchers have used EEATT as an outcome measure in the interventions used for visceral fat reduction and in obesity management. The surgical, pharmacological and lifestyle interventions have been proved to be beneficial in the reduction of this dangerous adipose tissue and thus EEATT has been found to be a simple and reliable marker to monitor the visceral fat reduction in obesity management.\textsuperscript{107,108} The further research on this cost-effective indicator of obesity may help in widespread clinical use in obesity management.

1.15. Does exercise influence EEATT?

The aerobic exercise is well known to have positive effects on body fat and risk factors of CVD in obese population. The effect of different types of exercise and the relationship with the dose of exercise on regional fat deposits has been the area of research focus recently.\textsuperscript{100,109} The lifestyle modification has been found to have positive effects on EATT. However, there are limited studies on amount of physical activity required to reduce the regional body fat depots such as EAT.
1.16. Need for the Study

The prevalence of obesity and its related complications are increasing in India. The prevalence of central obesity which is now known as the cause for increased risk of cardiovascular and metabolic diseases is also increasing in Asian-Indian population. There is an emerging need for simple and accurate screening methods for obesity management in Indian population. Although EEATT has been proposed as a reliable indicator of VAT in human body and therapeutic target in obesity management, it has not been used in routine clinical practice. The research on EEATT has been limited to Caucasian and European population. There is need for a study on EATT values and its relationship with body composition and lipid profile in Asian-Indian obese population.

Although exercise is considered as an integral part of obesity management, the effect of aerobic exercise on visceral adipose tissue such as EEATT is not well known. The substantial change in EEATT in relationship with changes in body composition and cardio metabolic parameters is not well understood. There is also paucity of literature on effects of supervised aerobic exercise program on EEATT in healthy overweight and obese Asian-Indians. There is a need for randomized controlled trials to study the effect of aerobic exercise on EEATT in obese Asian-Indian population.
1.17. Objectives of the study

1. To study the effect of 12 weeks of moderate intensity aerobic exercise on epicardial adipose tissue thickness and body composition in healthy overweight and obese individuals.

2. To study the effect of 12 weeks of moderate intensity aerobic exercise on blood lipids, fasting blood sugar, highly sensitive C-reactive protein and aerobic capacity in healthy overweight and obese individuals.

3. To study the correlation between epicardial adipose tissue thickness values with anthropometric parameters and aerobic capacity in healthy overweight and obese males and females.