CHAPTER 5

Discussion
According to World Health Organization, there is a transition in healthcare burden from communicable diseases to non-communicable diseases.\(^{20}\) The increased prevalence of non-communicable diseases is mainly attributed to decreasing level of physical activity and increased prevalence rates of overweight and obesity in both developing and developed countries. The primary prevention measures to counter the obesity and its related complications have gained lot of importance.\(^{43}\) The visceral fat monitoring is helpful in studying the effect of primary prevention measures such as exercise in obesity management.\(^{225}\) In the present study, the effects of aerobic exercise on various physiological, biochemical and body composition assessment methods in healthy overweight and obese population were investigated. We studied the effect of moderate intensity aerobic exercise on EEATT, which is a simple and reliable method for measuring VAT. The effect of 12 weeks moderate intensity aerobic exercise was studied on EEATT in younger and middle-aged Asian-Indian population with no cardio-metabolic complications to note a reduction in our study. Previously, the studies involving the pharmacological\(^ {226}\) and other non-pharmacological interventions\(^ {227}\) also were shown to have similar effect on epicardial fat thickness which were associated with weight loss. The findings in our study now add to the evidence on potential benefits of aerobic exercise in primary prevention of diseases and obesity management.

### 5.1. Effect of aerobic exercise on EEATT in overweight and obese individuals

In the present study, 12 weeks of supervised aerobic exercise program was found to be effective in reducing the total body fat and visceral fat levels in study group compared to control group. EEATT and visceral fat reduction were found to be higher in magnitude when compared to the reduction in anthropometric parameters. EEATT was found to have reduced
by 16.24 percent (0.42 mm) with respect to change in BMI by 3.11 percent and reduction in waist circumference by 2.29 percent. There was minimal increase in EEATT by 0.32 percent (0.04 mm) along with an increase in BMI by 0.24 percent and WC by 0.01 percent in the control group (Table 5). A significant change in the study group was observed in EEATT after 12 weeks of aerobic exercise with an effect size of 0.37 in study group. The findings in the present study are in agreement with the findings in previous studies. Kim et al. conducted non randomized trial and reported the changes in EEATT values to have reduced by 8.61 percent along with a reduction in BMI by 4.3 percent and WC by 4.2 percent in response to 12 weeks aerobic exercise in Japanese obese men. In a study conducted by Kenneth et al., EEATT values were reduced by 11 percent due to lower intensity aerobic exercise in patients undergoing haemodialysis. The magnitude of effect on EEATT was found to be higher in our study compared to that reported by Kim et al. This could be due to the supervised moderate intensity exercise program given in our protocol. The findings in our study suggest that EEATT reduction occurs with aerobic exercise at a higher magnitude with a minimal weight loss and reduction in waist circumference.

The change in EEATT was found to be higher in magnitude compared to the change in anthropometrics with dietary modification in a previous study. EEATT reduction of 32 percent was achieved with a BMI reduction by 19 percent and WC reduction by 23 percent in response to a 6 month low calorie diet as reported by Iacobellis et al, indicating that more weight loss is associated with higher amount of EEATT reduction. It was found in the previous studies that the exercise induced EEATT reduction was higher in magnitude compared to reduction in SAT and was similar to the amount of reduction in VAT. Most
of the earlier studies were conducted in moderate to severe obese individuals of high risk category.

The mean reduction in the EEATT was 0.42 mm with a maximum reduction of 1.6 mm in the study group. However, the minimum reduction of EEATT signifying the clinically beneficial change is not known currently. The change in EEATT showed moderate correlation with change in body weight (r=0.50) and BMI (r=0.53) in both the groups. Our study tested the effect of aerobic exercise alone on EEATT without calorie restriction. The daily energy intake and non-exercise physical activity levels were not monitored during the study period; instead the control group participants were suggested to continue the same lifestyle as prior to the commencement of study. Although the clinical benefits depend upon the method of weight loss and distribution of fat reduction, weight loss as low as 5 percent is associated with reduction in obesity related disorders. The physical activity of more than 150 minutes per week caused modest weight loss of 2-3 kilograms in previous studies. As per the ACSM position stand, less than 3 percent change in the body weight is considered as weight maintenance and more than 5 percent as clinically significant weight change that can be achieved with physical activity.\textsuperscript{229} In our study, the study group participants who were included in the final analysis completed the supervised exercise program for more than 150 minutes per week. Although the weight reduction achieved in our study was less than 3 percent, it had been associated with a reduction in metabolic syndrome from 54.7 percent to 38.8 percent. In the present study, we found that the moderate intensity aerobic exercise for minimum of 150 minutes per week significantly reduces EEATT and visceral fat levels measured by BIA.
5.2. Influence of gender on response to aerobic exercise on EEATT

Although the reduction of EEATT was statistically significant in both genders, the response to aerobic exercise was found to be slightly better on EEATT and visceral fat levels in men as compared to women (Table 10 & 11). It has been well established that visceral adipose tissue quantity is more in men compared to women below 45 years of age or before menopause. The baseline EEATT and VAT levels were found to be high in males and that could have been one of the reasons for better responses in males. Some of the previous studies have shown that VAT responds better to aerobic exercise compared to SAT. The exact mechanism for higher reduction of EEATT in males compared to females is out of scope to this study.

5.3. The measured Epicardial adipose tissue thickness - Lower cut-off values in Asian-Indian population

As observed in our study, the baseline mean EEATT measurements of Asian-Indian population were less compared to other ethnic populations (Table 3). The median EEATT values reported in Asian-Indian population were also found be low compared to European and Caucasian population, published in a recent study. The cut-off values for EEATT as an indicator of metabolic syndrome in Asian-Indian population is not known. As the reasons for lower EEAT values are not known, the questions remain about its role in CAD and metabolic syndrome in Indian population. However, a study on exercise induced changes in EEAT in obese Indian individuals may help in learning its clinical applicability in obesity management. In the present study, there was significant reduction in EEAT values although the measured values before intervention were low comparatively.
5.4. The influence of baseline EEATT values on the magnitude of its change with aerobic exercise

The subgroup analysis showed that aerobic exercise caused greater reduction in EEATT when the baseline values were more than 2.5mm (Table 8). The mean reduction of 0.72 mm was achieved with baseline EEATT more than 7.5 mm in study conducted by Kim et al in older Japanese men with metabolic syndrome. The present study adds to the existing evidence that aerobic exercise induces the reduction in EEATT irrespective of its proportion before the intervention and thus causing potential clinical benefits.

5.5. The possible mechanism of aerobic exercise influencing VAT or EEATT

Although there is evidence on the effect of aerobic exercise on body fatness and more specifically the visceral adipose tissue, the mechanism of its effect on regional adipose tissues such as EAT is not well known. The mechanisms related to visceral fat reduction in subjects with metabolic related diseases was found to be different from those without metabolic related diseases. There is limited understanding about the clinical implications of VAT reduction, the significance of reduction in quantity of VAT translating to improvement in CVD risk. The results in the present study also support the fact that VAT is used more quickly as an energy resource than subcutaneous fat during aerobic exercise-induced weight loss. Ross and Janssen suggested that physical activity with or without weight loss was associated with a reduction in visceral adipose tissue. Although there is insufficient evidence to understand the reasons for preferential VAT reduction with aerobic exercise in obese individuals, some of the probable mechanisms were explained for VAT reduction including secretion of lipolytic hormones, facilitating greater post-exercise energy expenditure and fat oxidation favouring a greater negative energy balance. As the EAT is an indicator of VAT, we presume the same mechanisms could have caused the higher proportion of EAT reduction in our study.
5.6. Visceral Adipose tissue measurement in obesity management

The VAT measurement using precise and reliable methods has become an important part of interventional studies in obesity management as there is evidence on its unfavorable risk profile. The use of expensive imaging methods is limited to only few research studies and may not be practically feasible for routine clinical use. The predictive ability of VAT with EEATT measurement was found to be better than WC in an earlier study.\textsuperscript{152} Although, the sensitivity and specificity of EEATT is not known, it was observed that the VAT and EEATT changes were almost similar in magnitude. EEATT correlated with WC, visceral fat levels and body fat percentage measured with BIA in our study. The present study reconfirms the finding that EEATT is a better indicator of abdominal visceral fat in the body than other anthropometric parameters. However, it is yet to be determined the diagnostic value of EEATT as a surrogate marker of visceral adiposity in Indian population.

5.7. Effect of aerobic exercise on lipids, FBS and HSCRP

EEATT values have been found to be higher in obese population with dyslipidaemia and hypertension in various ethnic groups. The baseline metabolic parameters were not abnormally high in all the participants.\textsuperscript{107,148} In the present study, the reduction in EEATT in the study group was associated with an improvement in the lipid profile and fasting blood sugar levels. Although the body fat loss may not be a determinant factor for an improvement in lipid profile, concomitant fat loss may amplify the beneficial effects of aerobic exercise on lipid metabolism\textsuperscript{235}. The improvement in the metabolic parameters with or without weight loss is clinically proven to be beneficial for overweight and obese individuals. The weight loss is considered to be very important for an improvement in the cardio-metabolic risk profile.\textsuperscript{236} There was significant reduction in mean values of TC, LDL-C and TG in the study group after
12 weeks of aerobic exercise along with minimal increase in mean HDL-C values (Table 6). Similar findings were observed in hyperlipidemic and normolipidemic individuals in a study conducted by Halbert et al.\textsuperscript{237} The oxidation of fatty acids from adipose tissue, muscles and liver during and after the aerobic exercise, increased clearance of VLDL-C by skeletal muscle, accelerated removal of fatty acids with exercise are the possible mechanisms for an improvement in the lipid profile.\textsuperscript{195,238}

HS-CRP is an inflammatory marker which increases with increased visceral adipose tissue.\textsuperscript{239} The inflammatory substances also increase with acute inflammation in the body. The diseases with high grade inflammation were not included in the present study. The changes in HS-CRP values were minimal, but statistically significant in study group compared to the control group in our study (Table 7). This is in agreement with the previous findings that only longer duration exercises more than 6 months cause clinically significant reduction in HS-CRP values\textsuperscript{197}. The weight loss in obesity and visceral fat reduction correlated well with the reduction in HS-CRP values in the previous studies. As HS-CRP is reported to be a useful marker of CAD and exercise is known to have anti-atherogenic effect\textsuperscript{240}, the modest reduction achieved may be considered significant. The improvement in biochemical parameters along with an improvement in body composition in the present study implies that exercise causes physiological changes in the body leading to visceral fat reduction and further improving the cardio-metabolic risk profile.

5.8. Effect of aerobic exercise on cardiorespiratory fitness

The relationship between EATT and aerobic capacity has been first studied by Kim et al. The obese individuals with higher EEATT values were found to have lower aerobic...
capacity.\textsuperscript{241} The mechanism by which EEATT influences the aerobic capacity is not known. The moderate intensity exercise of minimum 12 weeks causes physiological changes in the body leading to an improvement in the aerobic capacity.\textsuperscript{242} In the present study, it was found that there is a significant improvement in aerobic capacity which is associated with reduced EEATT values and improvement in metabolic parameters (Table 5 & 6). All the participants in the study group who were considered previously sedentary had an improvement in the cardiorespiratory fitness which was indicated by signification improvement in their peak $V_o_2$ values following 12 weeks of aerobic exercise training. The adherence to the supervised exercise was more than 80 percent in the study group. Although, the baseline EEATT values showed weak negative correlation with baseline $V_o_2$ peak values, there was significant improvement in aerobic capacity along with an improvement in body composition and reduction in EEATT.

5.9. The relationship of EEATT with gender, age and anthropometric parameters

The influence of age and gender on deposition of EAT is not well understood and the literature available is mostly limited to cadaver studies. There is a lack of clear evidence on the gender differences, even though it was much clearer about the age as an influencing factor on EATT. EATT was found to have direct relationship with BMI at baseline, but the influence of age and gender in different ethnic groups is yet to be investigated (Table 12). The baseline parameters obtained in our study showed that EAT values were higher in men compared to women; additionally the thickness is further influenced by age when BMI is same. The VAT tends to increase with the age and is generally more in males compared to females. EAT, which is considered as a true visceral fat was also found to be higher in males as compared to females. As echocardiography has been found to be a reliable method for measuring EATT,
the findings in our study indicate that increased EEATT in Indian males may well be a cardiovascular disease risk factor at a much younger age.

The present study attempted to find the relationship between anthropometric parameters and EEATT values in Asian-Indian population. The body weight was not found to be linearly related to EEAT values, and is in agreement with those of previous studies. Recently, EEATT values have been found to be higher in Asian population at relatively lower BMI. The evidence suggests that EAT is closely related to CAD, better than weight and BMI. In the present study, we found that EEATT is related to waist circumference, which is a marker of central obesity, but showed moderate correlation with weight and BMI.

5.10. Bio-impedance analysis and EEATT

Body fat analyzers are comparatively inexpensive and simple methods used to measure the body fat percentage. As the accuracy of these machines depend on several factors like hydration, the accuracy of the various commercial devices have not been studied. The usage of these devices to measure the visceral fat levels in research studies has been limited. The visceral fat levels measured by BIA device used in the present study showed good correlation with EEATT values, and the reliability of EEATT as an indicator of visceral fat has been well established. The total body fat percentage only showed moderate correlation with EEATT (Table 12), supporting the evidence that EEATT may be a better indicator of visceral fat than the subcutaneous fat and total body fat. As the Asian Indians tend to have more visceral fat compared to other populations and risk of cardiovascular diseases has been linked to this dangerous fat, the measurement of EEATT in the weight management may be crucial for its prevention.
5.11. Clinical implications

The results in our study adds evidence to the existing literature on potential benefits of aerobic exercise in reduction of visceral fat in the body. Our study also emphasizes the need for assessment of VAT in obesity management, particularly in Asian-Indian population. Several new guidelines for obesity management have been recently developed with specific recommendations to achieve weight loss with an improvement in cardio-metabolic profile. As aerobic exercise is proved to have beneficial effects on EEATT which is an indicator of VAT along with metabolic parameters, we recommend the moderate intensity supervised exercise as an effective means for reducing dangerous VAT in asymptomatic adults. The aerobic exercise of 1500 to 2500 MET minutes per week has been found to be effective in reversing the cardio-metabolic profile and reduce the risk of cardiovascular diseases in obese but otherwise healthy middle aged men and women.

5.12. Strengths of this study

The results in present study support the evidence suggesting EEATT as an indicator of visceral fat and therapeutic target in obesity management. Even though there is emerging evidence on clinical applications of EEATT in Caucasian and European population, there is scarcity of literature in Asian-Indian population. Several therapeutic interventions have been successfully used in research studies to find the magnitude of EEATT reduction in moderate to severe obese individuals. This study was first to investigate the clinical applicability of EEATT in primary prevention population. The pattern of distribution of body fat, the proportionate loss of EATT in response to therapy, association with other influencing factors such as age, gender and ethnicity are poorly understood. We attempted to investigate these influences on EEATT reduction in the sub-group analysis.
To the best of our knowledge, this was first randomized controlled trial to study the effect of aerobic exercise on EATT in both men and women, also in Asian-Indian population. The sonographer was blinded to the allocation of group and all the measurements were repeated by the same tester. Our study included primary prevention population with no known diseases. Our important objective of visceral fat reduction was achieved by exercise induced minimal weight loss in a relatively large sample based study with 12 weeks of supervised exercise intervention.

5.13. Limitations of this study

Although the energy expenditure during the exercise sessions was known, the dietary intake in calories was not recorded. The energy expenditure due to any increased physical activity levels when they were not exercising was also not recorded during the study period. Our study did not include the individuals with normal BMI with increased visceral fat. Also, the effect of aerobic exercise on normal and morbid obese individuals, those with higher EEATT values was not studied.

5.14. Recommendations for future research

The dose-response relation between aerobic exercise and EEATT can be further studied. The effect of resistance exercises and in combination with aerobic exercise can be studied in future. Future research may be focused on studying the sensitivity and specificity of EEATT measurements in visceral fat monitoring. High quality research studies are required to establish the clinical applicability of EEATT in obesity management.