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Predictors and Methodological Issues in Tracking Total Body Fat Mass, Trunk Fat, Mass and Abdominal Fat Mass Changes in a Weight Loss Intervention with Overweight and Obese Women

Dissertação apresentada com vista à obtenção do grau de Doutor no Ramo de Motricidade Humana, Especialidade de Saúde e Condição Física

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ABBREVIATIONS

AC - Abdominal circumference

ACC - Abdominal circumference change

AF-ROI - Abdominal fat region of interest (region of interest between L2-L4, excluding lateral subcutaneous fat)

AF-ROIC - Abdominal fat region of interest change

AT - Adipose tissue

BMC – Bone mineral content

BMD – Bone mineral density

BMI - Body mass index

BW - Body weight

BWC - Body weight change

CHD – Cardiac heart disease

CKD - Chronic kidney disease

CT - Computed tomography

CV - Coefficients of variation

%CV - Coefficients of variations

DLW - Doubly labeled water

DXA - Dual energy x-ray absorptiometry

EI - Energy intake

FFAs – Free fatty acids

FFM - Fat-free mass

FM - Fat mass

%FM – Percent fat mass

HC - Hip circumference

HCC - Hip circumference change

ICC - Intraclass coefficient of correlation

IDF - International Diabetes Federation

IPAQ - International physical activity questionnaire

LPL - Lipoprotein lipase

LPTA - Leisure-time physical activity
MPA - Moderate physical activity
MPAC - Moderate physical activity change
MRI - Magnetic resonance imaging
PCOS - Polycystic ovary syndrome
REE - Resting energy expenditure
R - Reliability coefficients
SEE – Standard error of measurement
SD – Standard deviation
SD - Sagittal diameter
SDC - Sagittal diameter change
SIT - Total minutes sit
SITC - Total minutes sit change
TBFM - Total body fat mass
TF-ROI - Trunk fat region of interest
TEM - Technical error of measurement
TBFMC - Total body fat mass change
TF-ROIC - Trunk fat region of interest change
TPA - Total physical activity
TKD -Total calories spent per day
TKDC -Total calories spent per day change
TPAC - Total physical activity change
VPA - Vigorous physical activity
VPAC - Vigorous physical activity change
WAT - White adipose tissue
WC - Waist circumference
WCC - Waist circumference change
WHR – Waist to hip ratio
WK - Total minutes walking
WKC - Total minutes walking change

CHAPTER 1

GENERAL INTRODUCTION

General Introduction

Obesity is a major public health problem among developed and less developed countries. Obesity has been shown to be associated with chronic diseases and health conditions such as heart disease, diabetes, cancer, hypertension, and hiperlipidemia (1-3). The risk associated with obesity is becoming a global health hazard. Until 1999 it was estimated that approximately 64.5% of USA adults over the age of 18y have a body mass index (BMI) ≥ 25 kg.m⁻², with approximately 34.5% having a BMI ≥ 30 kg.m⁻² (4). Between 1999-2000 and 2007-2008, there was an increase of 4.7 percentage points (95% CI, 0.5 to 9.0) for men and a nonsignificant increase of 2.1 percentage points (95% CI, -2.1 to 6.3) for women (5). Abdominal obesity increased in women (6). The increasing prevalence of overweight and obesity has resulted in an estimated expenditure of billions of dollars per year, to treat obesity-related conditions, being this a great part of the healthcare charges (7).

The prevalence of obesity in Europe has significantly increased over the past several decades, a phenomenon that is corroborated by data from several other industrialize countries outside Europe. In the mid-1980s, 15% of the male and 17% of the female population in Europe had a BMI ≥ 30 kg/m² (8), meaning that the rate of obesity has increased by approximately 30% over the past 10 to 15 years (9).

In Portugal, the overall overweight/obesity prevalence increased from 49.6% (in 1995–1998) to 53.6% (in 2003–2005) (10). These data suggest that, although obesity was identified as a public health problem a decade ago, actions that may have been taken to reduce it do not seem to have been very effective. Well-defined public health intervention must target specific population groups where higher levels of obesity prevalence were found: low socioeconomic

level groups and low-education level groups (10). Recently the Portuguese Physical Activity Registry concluded that physical activity must be considered a health promotion issue. The same registry also concluded, based on the data collected, that physical activity may increase as a result of different levels of decision and cooperation of several society departments (11), promoting the reduction of obesity prevalence.

The general purpose of this thesis was to analyse the usefulness of simple anthropometric measurements in predicting weight loss and their sensibility to fat mass changes, particularly abdominal and trunk fat mass changes, and the effects of physical activity on fat mass loss.

The thesis begins with a general introduction (*Chapter 1*) in which we review human body composition's literature related with weight loss and health conditions, as well as exercise recommendations for obesity treatment. Then will be described the usefulness of body composition analysis in issues related with weight loss and the effect of exercise on obesity treatment.

Chapter 2 includes a detailed description of the methodology used in the present thesis. *Chapters 3, 4, and 5* present the original research contributions. In *Chapter 3* was addressed the utility of simple pre-treatment anthropometric measurements to predict body composition changes that occur after body weight change. In *Chapter 4* was analyzed the effect of different types and intensities of physical activity in body composition, preferentially in abdominal fat region of interest after a weight loss intervention program. The ability of simple anthropometric measurements to detect changes in abdominal fat region of interest and total body fat mass during weight loss in overweight and obese women was analyzed in *Chapter 5*.

Based on this original scientific research, *Chapter 6* discusses these findings within the scope of the areas of anthropometric measurements and their ability to predict total body fat mass and central fat mass loss, and the association of physical activity with body composition changes. Finally, in *Chapter 7* is presented a summary of the main findings of this thesis.

Human Adiposity

Anatomy and typology of body fat

Adipose tissue is not a single homogeneous compartment, but rather a tissue with specific regional depots with varying biological functions (12, 13). Moreover, individual adipose tissue compartments have stronger associations with physiological and pathological processes than does total adipose tissue mass (14-17). According to the five-level body composition model, adipose tissue and fat are different components, and their taxonomic separation is important when measuring their mass and metabolic characteristics (18). In the past, adipose tissue has been considered a passive storage energy depot that serves as a long-term reservoir for fuel stored as triglyceride. However, laboratory, clinical, and epidemiological studies over the past decade have redefined and greatly expanded our understanding of the physiological role of adipose tissue (19). We now appreciate that adipose tissue is an endocrine organ with important roles in maintaining whole-body energy homeostasis. For example, when body fat is in excess, especially as visceral adipose tissue, it “leaks” fatty acids into the blood. Those fatty acids may accumulate in the liver and muscle promoting insulin resistance (20).

Adipose tissue contains ~80% fat; the remaining ~20% is water, protein, and minerals (21). Typically, adipose tissue is a specialized loose connective tissue that is extensively laden with adipocytes. The cellular content of adipose tissue is approximately 50% adipocytes, with the remaining 50% being the stromal vasculature fraction of fibroblasts, endothelial cells, macrophages and preadipocytes. In the past, it has been

suggested that the number of human adipocytes were fixed early in life and that a “fixed adipocyte-number” predestined individuals to be lean or obese. However, this is no longer thought to be true (22). Not only does adipocyte hypertrophy occur in humans (23-25), but the

recruitment and the proliferation of preadipocytes is also thought to occur in adult humans (23, 24, 26-28). Adipogenesis is, therefore, an important physiologic process whose function or dysfunction may prevent or promote metabolic disease (29-31). During positive caloric balance, increases storage of energy optimally occurs through the generation of added, functional cells, achieved through adipogenesis from preadipocytes (32). If adipogenesis is impaired after initial adipocyte hypertrophy, then further adipocyte hypertrophy may result in adipocyte dysfunction (31, 33). Some have even suggested (24, 34-36) that an increase in fat cell size might be viewed as failure of adipocytes to adequately proliferate. This may have pathological consequences. It has been known at least since 1970s that during times of positive caloric balance, excessive fat cell enlargement results in adipocyte metabolic and immune abnormalities (37, 38). During times of positive caloric balance, if energy is stored predominantly through lipogenesis and fat cell hypertrophy of existing adipocytes, as opposed to adipogenesis with recruitment and differentiation of new fat cells and fat cells hyperplasia, then this may lead to pathologic adipose tissue responses that contribute to metabolic disease (24, 26, 27, 36, 39-44). However, it is not hypertrophy of individual fat cells alone that has potential adverse clinical consequences. Excessive extension of the adipose tissue organ itself may also contribute to pathogenic processes.

White adipose tissue (WAT) is the common fat found in the enlargement of buttocks and protruding bellies (45). Brown adipose tissue is not nearly as fat as white adipose tissue as its main function is to burn fatty acids for nonshivering heat generation (46). Human babies have this type adipose tissue and it may help to keep them warm. It disappears, however, with age and it is mostly gone by adulthood (47).

As proposed by Shen (48), total body adipose tissue is defined as the sum of adipose tissue, usually excluding bone marrow and adipose tissue in the head, hands, and feet, can be first divided into two main measurable components, subcutaneous and internal adipose tissue.

Subcutaneous adipose tissue is well defined and has clear anatomic demarcations - the layer found between the dermis and the aponeuroses and fasciae of muscles, includes mammary adipose tissue (48). Subcutaneous adipose tissue is divided into two components, the superficial subcutaneous adipose tissue (the layer found between the skin and a fascial plane in the lower trunk and gluteal-thigh area) and the deep subcutaneous adipose tissue, defined as the layer found between the muscle fascia and a fascial plane in the lower trunk and gluteal-thigh areas (48).

Internal adipose tissue is divided into visceral and nonvisceral components. Internal adipose tissue is the total adipose tissue minus subcutaneous ectopic adipose tissue (48). Visceral adipose tissue (adipose tissue within the chest, abdomen, and pelvis) is divided into intrathoracic adipose tissue (intrapericardial and extrapericardial) and intraabdominopelvic adipose tissue. Intraabdominopelvic adipose tissue is divided into intraperitoneal (e.g. omental and mesenteric) and extraperitoneal adipose tissue, which is divided into intraabdominal and intrapelvic adipose tissue. Intraabdominal adipose tissue is divided into preperitoneal and retroperitoneal (e.g., perirenal, pararenal, periaortic, and peripancreatic) adipose tissue. Intrapelvic adipose tissue is divided into parametrial, retropubic, paravesical, retrouterine, pararectal and retrorectal adipose tissue (48).

Nonvisceral internal adipose tissue (internal adipose tissue minus visceral adipose tissue) is divided into intramuscular adipose tissue (adipose tissue within a muscle) and perimuscular adipose tissue (adipose tissue inside the muscle fascia, excluding intramuscular adipose tissue). Perimuscular adipose tissue is divided into intermuscular adipose tissue (adipose tissue between muscles) and parasosseal adipose tissue (adipose tissue in the interface between muscle and bone). There are other nonvisceral adipose tissue as, orbital adipose tissue and aberrant adipose tissue associated with pathological conditions (e.g., lipoma).

Dual-energy absorptiometry (DXA) has the potential to provide overall and regional assessment of body composition in terms of fat, lean mass and bone. DXA quantifies fat, rather than adipose tissue. According to the 5-level body-composition classification system (18), fat is a molecular-level component and adipose tissue is a tissue-level component. Eighty percent of adipose tissue is composed of fat (48). As it measures two-dimensionally, DXA cannot differentiate between visceral and subcutaneous fat directly. In spite of this limitation, DXA has been used to estimate abdominal fat mass by using the standard trunk region or by manually defining a subregion at the abdomen. These subregions correlate strongly with visceral fat and it is assumed that the between-and within-examiner variation is smaller (49, 50).

Simple anthropometric measurements are often used as indirect measurements of abdominal fat. The most widely used is waist circumference (WC), but this indirect measurement cannot differentiate between visceral fat and subcutaneous fat, but it is more strongly correlated with visceral fat than subcutaneous fat and can therefore be used as a marker for visceral fat (51). However, several studies found that these correlations are weaker in obese or older subjects (52-54). In addition, anthropometric measurements cannot differentiate between bone, fat, and lean mass. In our study abdominal fat mass assessed by DXA (determined by a region of interest) will be predicted by anthropometric measurements.

Absolute and relative visceral adipose tissues have been associated with the greatest health risk (55, 56). It is more sensitive to catecholamines (epinephrine, norepinephrine), thus is more stimulated for lipolysis (57). At the same time, visceral adipose tissue is also less responsive to insulin, making it easier to turn on lipolysis and harder to shut it off (58). Subcutaneous adipose tissue seems to be used more for long-term storage of fatty acids incorporated into triglycerides (59). It is less sensitive to the signals that promote lipolysis and more sensitive to signals, such as insulin, that opposes lipolysis (60). This type of adipose tissue tends to be found in the buttocks and extremities as well as around the belly (59).

The 70-kg Reference Man has 15 kg of adipose tissue, representing 21% of body fat mass (21). The percentage is higher in women, the elderly, and overweight subjects. Adipose tissue is anatomically distributed throughout the human body, and the pattern of adipose tissue distribution is influenced by many factors, including sex, age, genotype, diet, physical activity level, hormones, and drugs (61-65). In contrast to adipose tissue, the molecular level or chemical component of fat is usually lipid in the form of triglycerides (18). Although fat is found primarily in adipose tissue, fat also exists in other tissues, especially in pathological conditions such as hepatic steatosis and various forms of lipidoses. The total mass of the two compartments in adults is similar, but not identical (49, 66-69).

Catecholamines promote proliferation and impair differentiation (70). Glucocorticoids impair proliferation and promote differentiation (71, 72). Finally, epidermal growth factor impairs proliferation and promotes differentiation (73). This has practical, clinical implications in that glucocorticoids increase the differentiation of existing adipocytes (especially visceral adipocytes) relative to subcutaneous, peripheral adipocytes, while decreasing adipocyte proliferation. The resulting hypertrophy of visceral adipocytes, coupled with a decrease in the recruitment of functional subcutaneous, peripheral adipocytes, is a contributing cause of the T2DM, hypertension and dyslipidemia often found with hypercortisolemia (70, 72).

Apart from species differences, the development of adipose tissue varies according to sex and age. Moreover, it has been known that the ability of humans to increase the number of adipocytes depends on the nature of the diet and the localization of the adipose depots (74). Beside environmental considerations, adipose tissue is also dependent upon genetic predisposition. In Pima Indians there is a high predisposition to have hypertrophic, bloated, pathogenic adipocytes, as opposed to smaller, leaner and more functional fat cells (75), a high concentration of fasting plasma non-esterified fatty acids is a risk factor for development of NIDDM.

Lipid mobilization and the release of free fatty acids (FFA) and glycerol are modulated by the sympathetic nervous system. Catecholamines are the most potent regulators of lipolysis in human adipocytes through stimulatory β_1 and β_2 adrenoreceptors or inhibitory α_2 adrenoreceptors (76). A gene that codes for a third stimulatory β adrenoreceptor, β_3 adrenoreceptor, is functionally active principally in omental adipocytes (77) but also present in mammary fat and subcutaneous fat in vivo (78). The main systems involved in the inhibitory control of lipolysis are insulin/insulin receptor and adenosine/adenosine receptor (79). Regional differences in catecholamine-induced lipolysis and sensitivity to insulin's antilipolytic effects have been extensively described in vitro studies. In both genders and independently of the degree of obesity, femoral and gluteal fat cells exhibit a lower lipolytic response to catecholamines than subcutaneous abdominal adipocytes, the latter showing both increased β_1 and β_2 adrenoreceptor density and sensitivity and reduced α_2 adrenoreceptor affinity and number (79, 80). Abdominal visceral adipocytes, compared with subcutaneous abdominal or femoral adipose cells, are more sensitive to catecholamine-induced lipolysis, equally (or slightly less) sensitive to both α_2 and adenosine receptor-dependent inhibition of lipolysis, and less sensitive to insulin's antilipolytic effects (79).

Exercise is an excellent physiological challenge to promote sympathetic nervous system (SNS) activation; there is no doubt that it contributes to the control of lipid mobilization during exercise. Increased catecholamine levels, promoted by exercise, stimulate both fat cell β_{1-2} - and α_2 -adrenergic receptors (ARs) which stimulate and inhibit lipolysis, respectively (81, 82). Recently, Glisezinski and co-authors (83) revealed that it is plasma adrenaline rather than noradrenaline that is the main adrenergic factor that contributes to the control of exercise-induced lipid mobilization in subcutaneous adipose tissue.

Apart from receptor distribution, it is also likely that regional differences in adipose tissue growth may result from differences in the cells' local environment. A better blood supply may

provide higher levels of humoral factors that are involved in the regulation of adipose tissue growth, and also more substrates for lipid accumulation.

Many studies have been dealing with changes of adipose tissue cellularity throughout life (84-86). Based on such observations, it was early established that there are sensitive periods in adipose tissue development during childhood. Two peaks for accelerated adipose tissue growth were reported: one after birth and the other between 9 and 13 years (87).

Only sparse data are available on site-specific differences in adipose tissue cellularity and growth, in humans. They indicate that intraabdominal fat cells are smaller than subcutaneous cells, while published results on fat cell's size variations among subcutaneous depots are inconclusive or found to be influenced by many factors, such as age, hormonal status, diet, and others (88). It seems that the age-related increases in fat cell size was particularly obvious in the abdominal depot.

Visceral adipose tissue is more harmful to health (89, 90), since it is more sensitive to catecholamines (epinephrine, norepinephrine) it is more easily stimulated for lipolysis (20). Visceral adipose tissue, found more frequently in post-menopausal women, subcutaneous (or peripheral body fat) is common problem for pre-menopausal women (91). After menopause, women may become more expose to visceral adiposity than before (91, 92).

Human Body Fat and Health

Total body fat and health

Beyond the conspicuous presence of excess body fat, many of these disease processes are relatively silent, that is, many individuals with this body type feel fine, with no symptoms of any disease. Most experts agree that overweight people are approaching a state of serious disease, where those in the obese range have arrived (93).

BMI is a widely used, inexpensive method for assessing body fatness, but it can be inaccurate. However, BMI is positively associated with morbidity (94, 95) and has a U- or J-shaped relationship with mortality (96-98). It is commonly held that a high BMI is associated with increased health risk or mortality because of its association with adiposity. Indeed, within a given population, BMI is positively associated with adiposity (99-101). It is noteworthy, however, that this relationship is altered by numerous factors such as age (102), gender (102), race (103), and physical activity patterns (104). For example, smokers frequently weigh less than non-smokers (105) and this can contribute to distortions in studies (106, 107). Whether it is smoking alone or the associated lower weight that contributes to the increased risk, remains open (107).

Obesity triggers a plethora of metabolic disturbances, including insulin resistance, hyperglycemia, hypertriglyceridemia, and reduced levels of high-density lipoprotein (HDL) cholesterol, together referred to as the metabolic syndrome (108). In addition, increasing evidence suggested ethnic differences with respect to the effects of obesity on risk of metabolic diseases, especially type 2 diabetes. Another area of growing interest is the impact of obesity on complications of the metabolic syndrome, including gallstones, gout, polycystic ovary syndrome (PCOS), chronic kidney disease (CKD), and sleep apnea.

Gerald Reaven used the term “Syndrome X” to describe the close interrelationships among obesity, hyperinsulinemia, glucose intolerance, and dyslipidemia (109). In 1989, Kaplan (110) used the term “deadly quartet” to describe the clustering of upper body obesity, hypertriglyceridemia, glucose intolerance, and hypertension. In 1998, the World Health Organization (WHO) coined the phrase “metabolic syndrome” and defined it as insulin resistance and/or impaired glucose regulation with at least two of the following conditions: dyslipidemia (elevated triglycerides or low HDL); high blood pressure; obesity (high waist-to-hip ratio - WHR- or body mass index - BMI); or

microalbuminuria (111). In 2001, the Third Report of the Expert Panel on Detection, Evaluation, and Treatment of High Blood Cholesterol in Adults (Adult Treatment Panel III – ATP) (112) defined the metabolic syndrome as three or more of the following: abdominal obesity (waist circumference > 102 cm in men and > 88 cm in women); hypertriglyceridemia (≥ 150 mg/dL or 1.69 mmol/L); low HDL cholesterol (<40 mg/dL or 1.04 mmol/L in men and <50 mg/dL or 1.29 mmol/L in women); high blood pressure ($\geq 130/85$ mm Hg); and high fasting glucose (≥ 110 mg/dL or 6.1 mmol/L). In 2002, using data from NHANES III, Ford et al. (113) estimated that approximately one quarter of U.S. adults (or 47 million people) have the metabolic syndrome. In 2009, based on the NCEP/ATP III guidelines, Bethene (114) estimated that a little more than one-third of the adults in the United States could be characterized as having metabolic syndrome. The author concluded that metabolic syndrome increased with age but increased even more dramatically as BMI increased. The prevalence of metabolic syndrome varied by race and ethnicity but the pattern was different for males and females. Non-Hispanic black males were less likely than non-Hispanic white males to have metabolic syndrome but non-Hispanic black and Mexican-American females were more likely than non-Hispanic white females to have it. Among the five diagnostic criteria for metabolic syndrome abdominal obesity, hypertension, and hyperglycemia were the most prevalent (114).

In 2005, the International Diabetes Federation (IDF) proposed another definition of metabolic syndrome – central obesity plus any two of the following conditions: hypertension, hypertriglyceridemia, reduced HDL cholesterol, or impaired fasting glucose (115). The IDF definition included gender – and ethnic-specific cut-points for central obesity measured by WC, but justifications for these cut-points remain controversial.

Although the various descriptions of metabolic syndrome differ somewhat, they all include a similar cluster of metabolic disorders and central obesity. Most notably, they all include that the co-occurrence of obesity, hypertension, high cholesterol, and insulin resistance is not due to chance alone, but rather, to a common underlying process (116).

The metabolic syndrome has provided a useful theoretical framework for studying the biological basis for the clustering of obesity and multiple metabolic disorders. Insulin resistance is often considered the common link between obesity and metabolic risk factors (117). However, there is a recent recognition that chronic inflammation by adipocyte-secreted cytokines may be the underlying pathophysiology in the development of insulin resistance and the metabolic syndrome. For this reason, the metabolic syndrome has also been called “the inflammatory syndrome” (118).

Although mechanisms linking obesity to elevated risk of individual components of the syndrome are not yet fully understood, evidence suggests that specific hormones, cytokines, and FFAs secreted by adipose tissue play crucial roles. Demonstration of crosstalk between adipose tissue and other insulin target tissues (e.g. skeletal muscle and liver), has greatly advance our understanding of the link between obesity and insulin resistance (119, 120).

The problem in insulin-resistant states is that gluconeogenesis is not shut down and lipolysis, especially of visceral adipose tissue, is not suppressed. That is, the liver is making too much glucose and the visceral adipose tissue is releasing too many fatty acids flowing directly to the liver. Increasing glucose stimulates the pancreas to produce more and more insulin, and the vicious cycle known as insulin resistance begins. Normal mechanisms of regulation of insulin secretion are lost, and tissue response even to excess insulin is abnormal. The result is an ever increasing blood glucose concentration that stimulates more insulin secretion.

FFAs, the primary oxidative fuel for several tissues including liver and resting skeletal muscle, also play an important role in insulin resistance (121, 122). Excess body fat can lead to fatty

acid spillover from adipose to nondipose tissue, causing peripheral insulin resistance and abnormal glucose metabolism (119, 120, 122).

The relationship between obesity and hypertension is well established. Even within lean populations in developing countries, individuals with greater body mass have substantially elevated blood pressure and higher rates of hypertension (123, 124). Overweight and obesity are the most important modifiable risk factor for hypertension, accounting for more than 66% of the risk in some populations (125). In the Nurses` Health Study (NHS), multivariate analysis showed that BMI values at 18 years of age and midlife were both significantly associated with hypertension (126). There was a significant association between long-term weight loss after 18 years of age and a decreased risk of hypertension, while weight gain after 18 years dramatically increased the risk.

Dyslipidemia is one of the most common metabolic disorders associated with obesity. In many studies, indices of body size and adiposity – including BMI, WHR, subscapular skinfolds, and percent body fat – are strongly correlated with hypertriglyceridemia, hypercholesterolemia, and low HDL cholesterol. Low HDL cholesterol, high triglycerides, and small dense LDL are among the most common features of dyslipidemia related to the metabolic syndrome (127, 128).

Among all lifestyle risk factors for type 2 diabetes overweight and obesity are the most important. Weight gain during adulthood, even at modest levels (e.g., 10 kg), has been associated with increased risk of diabetes. In the NHS (129), compared with those whose weight remained stable (a gain or loss of ≤ 5 kg between the age of 18 and the baseline in 1976), the RRs for diabetes were: 1.9 (95% CI: 1.5 to 2.3) for women with a weight gain of 5.0 to 7.9 kg; 2.7 (95% CI: 2.1 to 3.3) for a weight gain of 8.0 to 10.9 kg; and 12.3 (95% CI: 10.9 to 13.8) for an increase of 20.0 kg or more. In contrast, women who lost more than 5.0 kg reduced their risk for diabetes by 50% or more. Some findings suggest that a reduced insulin

sensitivity, which may be caused by both genetic and environmental factors, underlies the increased risk of type 2 diabetes in U.S. minorities, particularly Asians (130).

The association of overweight and obesity with noncancer outcomes is generally stronger than the association with all cancer or specific cancer sites. However, the International Agency for Research on Cancer (IARC) Working Group on the Evaluation of Cancer-Preventive Strategies published a comprehensive evaluation of the available literature on weight and cancer that considered epidemiologic, clinical, and experimental data (131). Their 2002 report concluded that there is “sufficient evidence” in humans for a cancer-preventive effect of avoidance of weight gain for cancers of the endometrium, female breast (postmenopausal), colon, kidney (renal cell), and esophagus (adenocarcinoma) (131). Recent studies of the impact of weight loss on breast cancer (132, 133), endometrial cancer (134, 135) and prostate cancer (136) suggest that weight loss over the course of adult life may substantially reduce the risk for several cancers (137).

In summary, although the clustering of obesity-related abnormalities has long been recognized, clinical definitions of the metabolic syndrome have only recently been formalized. Despite controversies regarding the precise definition of the syndrome, there is a consensus that excess adiposity, especially central obesity is the driving force behind the metabolic syndrome. Insulin resistance is widely considered the unifying mechanism for obesity-related disorders, but proinflammatory cytokines secreted by adipose tissue also appear to play an important role in causing insulin resistance and inducing a cascade of metabolic disturbances. Excess adiposity is the single most important factor in the development of various metabolic disorders, in particular, hypertension and type 2 diabetes. Numerous epidemiologic studies have shown that BMI and fat distribution independently predict various metabolic disorders. Weight gain has also been identified as powerful predictor of virtually all metabolic conditions,

and there solid evidence that some ethnic groups, especially Asians, are more susceptible to the adverse effects of excess adiposity.

Some evidence also suggest that increasing waist circumference during adulthood is a risk factor for incidence diabetes independent of weight gain {Willett, 1999 #87} as developed in the next sub-chapter. Therefore, it is important to monitor measures of both overall and regional adiposity, such as body weight and waist circumference, in assessing metabolic risk associated with obesity.

Abdominal body fat and health

Currently, the location of the excess adipose tissue in the patient's body is one of the main topics of investigation. Thus, different neuroendocrine responses to stress (139-141), different effects of gonadal and adrenal steroids on metabolism in various adipose tissue depots (140, 142-145) as well as genetic variations in tissue sensitivity (139, 146) have been suggested. All these mechanisms may contribute to the variation in regional fat distribution.

Clinically, it is important to understand if patients have a "pear" shape or an "apple" shape (147-149). In moderate obesity, regional distribution appears to be an important indicator for metabolic and cardiovascular alterations since an inconstant correlation between BMI and these disturbances has been found (150, 151). Over the last two decades, studies have reemphasized the notion put forward in 1947 by Vague (152) that obesity is not a homogeneous condition and that the regional distribution of adipose tissue is important to understanding the relation of obesity to disturbances in glucose and lipid metabolism (80). Many prospective studies have shown that excess fat in the upper part of the body (i.e., central or abdominal), considered by Vague (152) as android or "male-type", more often correlates with increases mortality and risk for disorders such as diabetes, hyperlipidemia,

hypertension, and atherosclerosis of coronary, cerebral, and peripheral vessels more often than “gynoid” (lower body or gluteo-femoral or peripheral depot) female-type of fat distribution (151, 153-156). However, in these studies, the body fat distribution was assessed using anthropometric measurements such as skinfolds and WHR, particularly the latter. Although WHR is simple and convenient for epidemiological studies, and provide a useful estimation of the proportion of abdominal or upper-body fat (157, 158), it does not distinguish between accumulations of deep abdominal (visceral) fat and subcutaneous abdominal fat.

The correlations of abdominal visceral fat mass by CT or MRI scans with total body fat range from 0.4 to 0.8, with higher values obtained when a large range of fatness, from lean to obese, is present in the population (159-162). They tend to be lower in the lean and normal weight subjects than in obese (161). As indicated by Bouchard et al. (80) it is important to recognize that individual differences in abdominal visceral fat remains considerable even when subjects with relatively similar BMI and percent body fat are investigated. We may conclude that the assessment of cardiovascular risk in obese patients solely from the measurement of body weight or total body fatness may be completely misleading (163-165). Most “metabolic obese” normal-weight subjects have some increase in adipose tissue mass and insulin resistance probably due to an increase in visceral fat (166). Thus, subjects with a relatively low BMI, such as “metabolic obese” normal-weight individuals, can have gross increases in abdominal visceral fat (167, 168), and others with a high BMI may have very little intraabdominal fat (163).

For Neil Ruderman (166), it has become apparent that a number of interrelated factors are often associated with and may contribute to the pathogenesis of hyperinsulinemia and insulin resistance in both normal-weight and obese individuals. They include central obesity, low birth weight, inactivity, and family history. Apart from their pathophysiological role, the presence of these factors may also be of value in identifying metabolically obese, normal-weight

individuals. The correlation between BMI and central obesity can vary considerably from one individual to another.

A striking example of how insulin resistance correlates with the amount of visceral fat in these circumstances are the sumo wrestlers of Japan. As demonstrated by Matsuzawa (169), sumo wrestlers, though generally quite obese, have small amounts of visceral fat (but a very large abdominal subcutaneous fat layer) and are quite insulin sensitive. In contrast, retired sumo wrestlers have large amounts of visceral fat, and they are insulin resistant and have a very high prevalence of type 2 diabetes and cardiovascular disease. Different levels of physical activity in the active and retired groups could have contributed to these findings; however, similar correlations have been described in other studies in which exercise was probably not a confounding factor (165).

Intraabdominal fat is associated with an increase in energy intake but is not an absolute requirement. Positive energy balance is a strong determinant of truncal-abdominal fat as shown by Bouchard and colleagues (170) overfeeding experiments in identical twins. The correlations between gains in body weight or total fat mass with those in subcutaneous fat on the trunk reached about 0.7 in their 100-day overfeeding study in 12 pairs of male identical twins. In contrast, these correlations attained only 0.3 with the gains in abdominal visceral fat, corresponding to a common variance of less 10% (80, 170). Thus, positive energy balance does not appear to be a strong determinant of abdominal visceral fat as is the case with other body fat phenotypes (80).

The increase of visceral fat masses with increasing total body may be explained by an increase of fat cell size only up to a certain adipocyte weight (171). However, with further enlargement of intraabdominal fat masses with severe obesity, the number of adipocytes seems to be elevated (172, 173).

The amount of visceral fat increases with age in both genders, and this increase is present in normal weight (BMI, 18.5 to 24.9 kg/m²) as well as in overweight (BMI, 25 to 29.9 kg/m²) and obese subjects (BMI > 30 kg/m²) but more so in men than in women (80, 174, 175). In a study of 130 subjects (62 males and 68 females with a wide range of age and weight), Enzi et al. (175) found that in young females, either lean or obese, the subcutaneous abdominal fat area was predominant over abdominal visceral fat, both measured by CT at the upper renal pole. This fat topography was retained in young and middle-aged females up to about 60 yr of age, at which point there was a change to an android type of fat distribution. This age-related redistribution of fat is due to an absolute as well as relative increment in visceral fat depots, particularly in obese women, which could be related to an increase in androgenic activity in postmenopausal subjects.

From the published data (174, 175), it can be concluded that both subcutaneous and visceral abdominal fat increase with increasing weight in both sexes but while abdominal subcutaneous adipose tissue decreases after the age of 50 yr in obese men, it increases in women up to the age of 60-70 yr, at which point it starts to decline (71).

Several studies have shown that the detrimental influence of abdominal obesity on metabolic processes is mediated by intraabdominal fat depot. For example, the visceral fat area correlated with glucose intolerance on the presence of hyperinsulinemia during an oral glucose tolerance test, suggesting an insulin-resistant state (12, 165, 176). In addition, correlation analyses have shown that the effect of accumulation of deep abdominal fat on glucose tolerance was independent from total adiposity and subcutaneous abdominal adipose tissue and that association was observed between total adiposity and glucose tolerance after control for visceral fat area (12, 165). In their study of a wide range of total body fat in both healthy young (168) and middle-aged (177) men, Park and col. found that the intraabdominal fat area evaluated by CT was associated with a decreased in insulin sensitivity measured by an

euglycemic hyperinsulinemic glucose clamp. In addition to being associated with disturbances in insulin-glucose homeostasis, abdominal obesity has been related to alterations in plasma lipoprotein-lipid levels (164, 178), particularly increased plasma triglyceride and low HDL cholesterol concentrations, as expected from the association of insulin resistance with disturbances in plasma lipid transport and lipoprotein levels (179, 180). Lemieux et al. (181) have indicated that the gender difference in visceral adipose tissue accumulation was an important factor in explaining the gender differences in cardiovascular risk profile. In addition, the adjustment for differences in visceral fat between men and women eliminated most of the sex differences in cardiovascular risk factors. There is evidence supporting the notion that abdominal visceral fat accumulation is an important correlate of the features of the insulin-resistant syndrome (178, 182) but this should not be interpreted as supporting the notion of a cause and effect relationship between these variables (79).

Although the cause-and-effect association has not been definitively established, the available evidence indicates that visceral fat is an important link between the many facets of the metabolic syndrome. However, because of the considerable metabolic heterogeneity still remaining among obese patients with similar levels of visceral adipose tissue, it was proposed that genetic susceptibility plays a major role in modulating the risk associated with a given excess of visceral adipose tissue (183). In this regard, visceral obesity should be considered a factor that exacerbates an individual genetic susceptibility to the components of the metabolic syndrome (184). While there is a consensus that visceral fat has a strong association with cardiovascular risk factors, particularly dyslipidemia and hyperinsulinemia (182), the primary importance of visceral adipose tissue vis-à-vis subcutaneous abdominal obesity with regard to insulin sensitivity of glucose metabolism has been challenged by Abate et al. (185) and Goodpaster et al. (1). These researchers found that abdominal subcutaneous fat, as determined by magnetic resonance imaging and CT, was at least as strong a correlate of insulin sensitivity (evaluated by euglycemic clamp) as visceral fat and retained independent

significance after adjusting for visceral fat (1). In addition, it has been emphasized that the endocrine abnormalities described in obesity, which involve steroid hormones, growth hormone, and insulin, may actually result in abdominal depot accumulation. This might cause the metabolic syndrome in the susceptible individual (60, 186).

Recently, a study with free of cardiovascular disease participants from the Framingham Heart Study (n=1155, mean age 63 years, 54.8% women) who were part of a multidetector computed tomography study underwent quantification of intrathoracic fat, pericardial fat, visceral abdominal fat, coronary artery calcification, and aortic artery calcification, showed that pericardial fat is correlated with multiple measures of adiposity and cardiovascular disease risk factors, but visceral fat mass is a stronger correlate of most metabolic risk factors (90).

Several epidemiologic studies have examined the relationship between overall adiposity, fat distribution, and endothelial function. In a cohort of healthy women, Wexler et al. (187), found similar correlations between plasma concentrations of e-selectin with both BMI and WC. Adhesion molecules were significantly elevated in women with central obesity but low BMI, and markers of endothelial dysfunction appeared to largely mediate the relationship between central body fat, insulin resistance, and incident diabetes.

Studies have suggested that WC or WHR significantly predicts risk of hypertension independent of BMI (188, 189). In a cohort of Japanese Americans, visceral obesity measured by CT was a better predictor of incident hypertension than BMI or WC (190). There was no significant association between subcutaneous fat and hypertension.

In a review of 23 published studies of intervention strategies to promote loss of visceral adipose tissue, measured by magnetic resonance imaging or CT, Smith and Zachwieja (191) concluded that individuals with greater visceral fat mass, either through an increase in body weight or the propensity to store fat in the visceral depot, lose more visceral fat when adjusted

to the loss of body fat, regardless of the intervention applied (caloric restriction, pharmacological therapy, or exercise) because the visceral adipocyte has a higher lipolytic rate also in the steady state.

As previously indicated, visceral fat is more sensitive to weight reduction than subcutaneous adipose tissue because omental and mesenteric adipocytes, the major components of visceral abdominal fat, have been shown to be more metabolically active and sensitive to lipolysis (20). The adipose tissue build-up in the butt area is considered subcutaneous fat and it is harder to get free fatty acids released from this fat during fasting, whereas beer-belly fat is visceral fat, and it is readily available for easy build-up, breakdown, and release of FFA into the blood. Excess visceral fat, which is more sensitive to hormonal signals for fat breakdown, seems to be a constant source of fatty acids that build up in the blood (20). The vascular anatomy and the metabolic activity of visceral fat may be the key factors predisposing to complications of obesity (20).

Only visceral adipose tissue is drained by the portal venous system and has a direct connection with the liver. Mobilization of FFAs is more rapid from visceral than from subcutaneous fat cells because of the higher lipolytic activity in visceral adipocytes, in both nonobese and obese individuals, particularly in the latter, which probably contributes significantly to the FFAs levels in the systemic circulation (60). The visceral fat catecholamine-induced lipolysis is greater in obese men than in women; this is partially due to a large fat cell volume and also to a greater β_3 - and lower α_2 -adrenoreceptor sensitivity (192), which results in higher FFAs mobilization from visceral fat to the portal system in men than in women. On the other hand, the antilipolytic effect of insulin is reduced in omental adipocytes regardless of the presence of obesity. Thus, the enhanced total lipolytic activity probably contributes significantly to the FFAs levels in circulation (191).

Moreover, Goodpaster et al. (1) found that FFAs released by visceral adipose tissue were correlated with visceral fat mass, but relative amounts of FFAs derived from visceral adipose tissue lipolysis were much lower than those derived from subcutaneous adipose tissue. Visceral lipolysis accounts for only 5% to 10% of the portal vein FFAs in lean individuals and 20% to 25% of portal vein FFAs in obese individuals.

Together, current evidence suggested that both visceral fat and subcutaneous fat contributes to insulin resistance (193). Theoretically, visceral fat is more relevant to the development of insulin resistance, but the data on the relative importance of subcutaneous fat and visceral fat are conflicting (193). In epidemiologic studies, WC as a measure of abdominal or upper body obesity reflects the effects of both subcutaneous fat and visceral fat (194). Thus, in practice, distinction between these two fat locations may not be easy or essential.

The decrease in basal plasma FFAs an average of approximately 60% was associated with a reduction of approximately 50% of basal insulin levels and a decrease in basal glucose lower in the nondiabetics (~7%) but higher in the diabetics (~15%). This suggest that basal plasma FFAs exert a physiological important effect supporting up to one half of basal insulin levels in nondiabetic and diabetic subjects and that basal plasma FFAs are responsible for some of the hyperinsulinemia in normoglycemic obese subjects (195).

The problem in insulin-resistant states is that gluconeogenesis is not shut down and lipolysis, especially of visceral adipose tissue, is not suppressed. That is, the liver is making too much glucose and the visceral adipose tissue is releasing too many fatty acids flowing directly to the liver. Increasing glucose stimulates the pancreas to produce more and more insulin, and the vicious cycle known as insulin resistance begins. Normal mechanisms of regulation of insulin secretion are lost, and tissue response even to excess insulin is abnormal. The result is an ever increasing blood glucose concentration that stimulates more insulin secretion.

Lebovitz and Banerji (196) cited several lines of evidence supporting a causal relationship between the amount of visceral fat and insulin resistance. The first line of evidence, albeit inconsistent, suggests that in diverse populations, visceral fat is more strongly associated with insulin resistance than total or subcutaneous fat mass (197, 198). Second, Lemieux et al. (199) found that increases in visceral fat, but not total fat mass, predicted changes in glucose tolerance and insulin secretion in a cohort of women followed for 7 years. Third, Klein and colleagues reported that liposuction of abdominal subcutaneous adipose tissue did not appear to improve insulin action and cardiovascular risk factor in obese subjects (200). Lastly, treatment with peroxisome proliferator-activated receptor (PPAR) agonist (e.g., pioglitazone and rosiglitazone) led to a shift of fat distribution from visceral to subcutaneous adipose depots, and that shift was associated with improvements in hepatic and peripheral tissue sensitivity to insulin (201).

Conversely, several lines of evidence argue against the causal relationship between visceral fat and insulin resistance. Miles and Jensen (202) noted that differences in the amount of subcutaneous account for the most of the between-person variability in abdominal fat mass, while the relative content of visceral fat is similar between lean and obese individuals. In addition, some studies have shown similar correlations between subcutaneous fat and visceral fat and insulin resistance (1).

In women, but not in men, omental adipose tissue has smaller adipocytes and lower lipoprotein lipase (LPL) activity than subcutaneous fat depots since variations in LPL activity parallel differences in fat cell size (80). With progressive obesity, adipose tissue LPL is increased in the depots of fat in parallel with serum insulin. However, when obese subjects lost weight and became less hyperinsulinemic, adipose LPL increased further and the patients who were most obese showed the largest increase in LPL, suggesting that very obese patients are most likely to have abnormal LPL regulation, independent of the influence of insulin. This

probably indicates that adipose tissue LPL activity may represent an adipocyte “set point” that is intended to limit adipocyte shrinkage induced by hypocaloric diet (79), suggesting a genetic regulation of LPL.

The hypothalamic-pituitary axis, particularly in visceral obesity, has been extensively evaluated, and the studies have shown that an increase in cortisol clearance (both absolute and body-weight corrected) results in a significant correlation with intraabdominal fat area, either expressed by WHR or obtained by CT. Thus, obese subjects with intraabdominal fat areas equal or greater than 107 cm² with an increased cardiovascular risk profile presented as expected, a significant higher cortisol clearance than the ones with areas lower than 107 cm² (203). The ratio of visceral/subcutaneous fat areas presented a significant correlation with the volume of distribution of cortisol at steady state (203), probably related to the larger number of glucocorticoid receptors in adipocytes of the intraabdominal fat (145). There is the possibility that the increased number of glucocorticoid receptors could be responsible for a hypersensitivity of the intraabdominal fat adipocytes to cortisol, leading to accumulation of visceral adiposity.

Excess visceral fat mass seems to be so harmful that there are already some studies showing the relation between increased visceral adipose tissue and some types of cancer (204-206). It seems that visceral adipose tissue is an independent risk factor for colorectal neoplasm. However, further large scale studies are needed to clarify the causal relationship between these cancer type and abdominal accumulation of fat (207).

A recent systematic review suggests that central adiposity, rather than general adiposity, may be a predictor for premenopausal breast cancer (208). The same review suggests that central adiposity is not an independent predictor of postmenopausal breast cancer risk beyond the risk attributed to overweight alone (208).

In summary, recent studies have demonstrated that regional distribution of adipose tissue is critical in the clinical assessment of patients, particularly if they are obese. In effect, excess fat in the central (visceral abdominal) vs. peripheral part of the body (gluteofemoral) independent of overall obesity is associated with higher plasma glucose and insulin, hyperlipidemia, and decreased HDL cholesterol concentrations, components of the metabolic syndrome and constituting a cluster of risk factors for atherosclerotic cardiovascular disease, as shown in prospective studies.

Physical Activity and Human Body

Physical activity and total body fat

The role of physical activity in body weight regulation has long been recognized. It has been demonstrated that a reduction in body weight and an increase in physical activity may facilitate the management of body weight and reduce the risk and onset of obesity-related diseases (209).

Because primary prevention of weight gain is more effective than weight loss in reducing obesity rates (210), it is critical to understand the role of physical activity in reducing age-related weight gain. Most evidence on weight gain prevention is derived from epidemiologic studies (211). Cumulative evidence from prospective cohort studies and randomized clinical trials indicates that physical activity and active lifestyle play an important role in weight control, probably mediated through multiple pathways including increasing total energy expenditure (211), reducing fat mass (211), maintaining lean body mass (211) and basal metabolic rate (211), and increasing psychosocial well-being and thus compliance to physical activity regimens (211).

The secular decline in physical activity that coincides with increasing obesity rates has been observed in many societies. Ewing et al. (212) conducted an ecological analysis of the relationship between urban sprawl and physical activity and obesity using data from Behavioral Risk Factor Surveillance System - BRFSS (including 448 counties and 83 metropolitan areas). Residents of sprawling counties were likely to walk less during leisure time, weigh more, and have greater prevalence of hypertension than residents of compact counties. At the metropolitan level, sprawl was similarly associated with minutes walked ($p = .04$) but not with the other variables. This ecologic study reveals that urban form could be significantly associated with some forms of physical activity and some health outcomes.

In many studies, the cross-sectional associations between physical activity and obesity are substantially stronger than those in prospective studies. In a prospective study, Hill et al. (213) estimated that U.S. adults have been gaining an average of 0.45 to 0.90 kg/year over the past decades since the start of the obesity epidemic. In the past three decades, many prospective cohort studies have examined the relationship between physical activity and weight gain. For example, Lee and Paffenbarger (214) concluded that participants in the Harvard Alumni Study who reported levels of physical activity consistent with approx 30 min of moderate-intensity physical activity had a lower body weight when compared with individuals reporting lower levels of physical activity.

At the individual level, numerous cross-sectional studies have examined the relationship between physical activity and obesity. Most have shown an association between higher levels of physical activity and lower body weight. In general, higher-intensity activity was more strongly associated with body weight than moderate-or low-intensity activity. For example, Bernstein et al. (215) demonstrated a clear dose-response relationship between high-intensity activities and lower odds of being obese, but the relationship for moderate-intensity activities was not clear. Other data, however, have shown an inverse association between walking

distance or steps and body weight (216). Chan et al. (217) concluded that accelerometer-measured physical activity has also been associated with lower BMI (218, 219) and body fatness (220). Several cross-sectional analyses found a strong positive association between time spent watching TV and prevalence of obesity (221, 222). A strong positive association between time spent watching TV and BMI was found among middle-aged and older women in the Nurses' Health Study ((NHS) (223). When change in cardiorespiratory fitness is used as a surrogate for change in leisure-time physical activity (LPTA), the data reported by DiPietro et al. (224) demonstrate the inverse association between change in fitness and change in body weight, which also supports the importance of physical activity in the prevention of weight gain in adults. In longitudinal studies the results seems to be conclusive. For example, in a twin study (30-years follow-up) (225) that aimed to determine the association between long-term LPTA, weight gain and WC, 146 twin pairs were comprehensively identified from the large Finnish Cohort. The findings give further evidence that persistent long-term participation in LTPA is associated with a decrease rate of weight gain and smaller WC in adults. The same study reported that a 10cm reduction in WC across the population would produce significant benefits for public health. A longitudinal relationship between changes in physical activity and weight gain during 10 years of follow-up among 5 115 black men and women aged 18-30 years at baseline in the Coronary Artery Risk Development in Young Adults (CARDIA) Study, was seen by Schmitz et al. (226). The author concluded that, after adjustment for secular trends, age, and other covariates, increasing physical activity was significantly associated with less weight gain in the entire group. The benefits of exercise in preventing weight gain were much greater for obese subjects than for those of normal weight at baseline.

Dale schoeller et al. (227), using relatively precise objective measures of energy expenditure based on the doubly labeled water (DLW) method in a prospective study, found that active postobese women maintained their reduced weight better than those who were inactive. The author also concluded that the relation between physical activity and weight gain was not

linear but showed a threshold-like relation for weight control. This threshold corresponded to 80 min/d of moderate-intensity physical activity or 35 min/d of vigorous physical. Recently, the same author concluded from the accumulating data, from the application of the DLW method, a need to place greater emphasis on mechanisms that lead to a mismatch between energy intake and expenditure rather than a continuing emphasis on energy intake or energy expenditure alone (228). Thus, it appears that adequate levels of physical activity do not act alone to control body weight long-term, but rather work in synergy with appropriate levels of energy intake. For example, Jakicic et al. (229) reported that the combination of increased levels of physical activity combined with reduced levels of energy intake were predictive of long-term weight-loss outcomes following an 18-months intervention. Similar findings were reported by McGuire et al. (230) based on data from the National Weight Control Registry. Thus, these data appear to support the importance of maintaining adequate levels of energy balance (energy intake and energy expenditure) to enhance long-term weight loss and prevent weight regain following weight loss.

Several short term weight loss programs (6 months or less), document the effects of exercise and caloric intake in human body composition, and some studies report a high contribution of exercise on weight loss (100, 231, 232). It has been clearly established that effective behavioral weight-loss interventions result in approximately a 10% weight loss compared to initial body weight within 6 months of initiating an intervention (233). These results appear to be achievable with the combination of a reduction in energy intake and an increase in energy expenditure (209). It seems that, the contribution of each of these components (reduction in energy intake and increase in energy expenditure) are not equal, with the majority of weight loss resulting from a reduction in energy intake. However, Ross et al. (100) reported similar weight losses (7.6 kg) between two groups who participated in a 3 months weight loss program based on energy restriction (700 kcal/d) caused by reduction in energy intake, compared with an increase in energy expenditure promoted by physical activity. In response to

a 12-wk intervention, Hagen et al. (234) reported a reduction in body weight in the exercise-plus-diet group (-10.4 and -24%) significantly greater than diet group (-7.8 and -20%), with both groups significantly greater than exercise group and controls. The energy intake ranged from 1000 to 1500 kcal/d. Wing et al. (235) reported a weight loss of 10.4kg (after 6 months) in the exercise-plus-diet group compared with 9.1kg in the diet group. Similar results are documented in a literature review by the National Heart Lung and Blood Institute, confirming the influence of exercise in clinic intervention programs (209). Thus, the National Heart Lung and Blood Institute recommend the combination of a reduction in energy intake and an increase in energy expenditure to maximize weight loss in response to behavioural intervention (209).

Some studies reported that subjects who participated in exercise programs had modest decreases in body weight and body fatness, and this appears to occur in a dose-response manner (236). For Mougios et al. an increase in the total energy expenditure and a high intensity exercise appears to be the most important determinants of successful exercise-induced weight loss (232). For same, the total volume of physical activity, expressed as energy expenditure, may be more important for weight control than the intensity of the physical that is performed. For example, Duncan et al. (237) have demonstrated that when total volume of physical activity is held constant, there is no difference in the effect on body weight across different intensities of physical activity. Similar results have been reported by Jakicic et al. (238), who demonstrated that the magnitude of weight loss was affected by volume of physical activity rather than the intensity of physical activity within a 12 months clinical trial.

Despite the minimal effect of exercise on short-term weight loss, exercise appears to be an important component of long-term interventions. This is supported by the 2005 US Dietary Guidelines (239), the Institute of Medicine (240), and extensive reviews of the literature (241, 242). However, a common conclusion that appears to be supported by cross-sectional data,

prospective observational data, and data from clinical trials is that physical activity equivalent to ≥ 2000 kcal/wk or approx 250 to 300 min/wk is associated with improved long-term weight loss at 12 to 24 months (238, 243, 244) . These results appear to support prevention weight regain following significant weight loss (239). In summary, it appears that physical activity can contribute to a significant increase in energy expenditure, which will facilitate long-term weight control provided that a sufficient dose of physical activity is performed.

The majority of clinical trials have incorporate aerobic forms of physical activity (e.g., brisk walking) into the weight loss interventions; overweight/obese individuals report that walking is the self-selected mode of physical activity for 80 to 90% of activity sessions (238). Although the accumulation of at least 10 000 steps per day, measured using a pedometer, may be associated with improvements in health-related parameters (245), it has been suggested that it may be necessary to progressively increase daily steps to levels above 10 000 steps per day to improve weight loss (246). An additional factor when considering the volume of physical activity is whether this needs to be done in a continuous manner to have an effect on the desired outcomes. In fact, there are numerous studies to support that intermittent exercise performed in multiple bouts of at least 10 minutes in duration can significantly improve desired outcomes. These outcomes can include cardiorespiratory fitness (247, 248) and selected risk factors (249). Despite these findings, additional forms of physical activity have been examined for weight control with mixed results. For example, a review of the scientific literature revealed no apparent improvement in weight loss with the addition of resistance exercise (250). Moreover, Janssen et al. (251) reported no significant improvement in risk factors with the addition of resistance exercise when compared with weight loss resulting from diet alone. However, there is initial evidence, despite these findings, that resistance exercise has been associated with a reduction in all-cause mortality (252). Moreover, resistance exercise will improve muscular strength (253, 254), which may affect physical function of overweight and obese adults (255).

Some individuals may be less susceptible to an increase in body fat due to an high resting energy expenditure (REE), also called resting metabolic rate (RMR). That is, body mass – represented by organs, fat, and muscle – burns energy at this background level. Someone who loses weight, including fat mass, will have a lower REE after the weight loss. Body organs such as brain, liver, and kidneys, have higher REE than muscle or adipose tissues. The relative scale of REE is approximately: organs (1,000-1,500 KJ/kg per day), skeletal muscle (60-125 kJ/kg per day) (256, 257). Unfortunately, there is no healthy way to increase organ mass to take advantage of this. However, exercise specially resistance training, such as weight-lifting, seems to increase REE through the increment of muscle mass (258). Despite these potential benefits, resistance exercise has not been shown to be more effective for weight loss or the maintenance of weight loss compared with other forms of physical activity.

In 2000, Fogelholm and Kukkonen-Haarjula (259) conducted a systematic review of 16 cohort studies on physical activity and weight gain. The follow-up of these studies ranged from 2 to 21 years. Most of the studies have focused on LTPA measured by various physical activity questionnaires. Several studies found that higher physical activity at baseline predicted less weight gain (260, 261) but this finding was not seen in other studies (262, 263). This data showed that LTPA can play a significant role in the prevention of weight gain; this is mostly likely a result of the increase in energy expenditure resulting from an increase in LTPA. Interestingly, several studies reported a significant inverse association between physical activity at follow-up (rather than at baseline) and long-term weight gain (264, 265), suggesting that weight gain led to changes in physical activity.

In 2005, Wareham et al. (266) conducted a systematic review of 14 cohort studies on physical activity and weight gain published since 2000. The follow-up periods ranged from 3 to 10 years. Twelve studies examined physical activity by means of self-report (223, 267-277) two included an objective measure to assess physical activity (278). This systematic review found

that the more recent studies showed more consistent findings of physical activity and weight gain than the studies reviewed by Fogelholm and Kukkonen-Harjula (259), although the effects were, in general, modest. Two factors may have contributed to the positive findings in more recent studies. First, the studies were much larger than the earlier ones and thus had more power to detect relatively small effects. Second, the more recent studies were better designed because investigators were able to examine the association between longitudinal changes in physical activity and body weight rather than simply the association between baseline physical activity and subsequent instruments; recent studies have used more detailed and validated physical activity questionnaires to assess activity levels.

In 2009 Jakicic (279) reported, in a review of the literature, that physical activity has been shown to have a modest effect on body weight that is typically <3% of initial body weight, but has an additive effect when combined with dietary restriction (279). Moreover, for the author, physical activity has been shown to be an important behavioral factor for enhancing long-term weight loss and minimizing weight regain; however, this may require relatively high doses of physical activity that approach 300 min/week (279).

Müller et al. (280), in a recent review, concluded that there is evidence for the long-term effectiveness of physical activity interventions in healthy adults. The author also concluded that increases in physical activity can meet recommended targets necessary for meaningful health benefits. Comprehensive and high-quality interventions, using additional exercise prescriptions and booster strategies achieved most substantial long-term increases in physical activity behaviour.

In summary, it has been demonstrated that a reduction in body weight and an increase in physical activity may facilitate the management of body weight and reduce the risk and onset of obesity-related diseases. The secular decline in physical activity that coincides with increasing obesity rates has been observed in many societies. Numerous cross-sectional

studies have examined the relationship between physical activity and obesity. Most have shown an association between higher levels of physical activity and lower body weight. In general, higher-intensity activity was more strongly associated with body weight than moderate-or low-intensity activity. Longitudinal studies, after adjustment for secular trends, age, and other covariates, demonstrated that increasing physical activity was significantly associated with less weight gain. Several short term weight loss programs, document the effects of exercise and caloric intake in human body composition, and some studies report a high contribution of exercise on weight loss. Some studies reported that subjects who participated in exercise programs had decreases in body weight and body fatness, and this appears to occur in a dose-response manner. However, it is important to analyse if this occurs with specific body regions, as the abdominal area, to which reductions are associated with health benefits. There is not enough evidence to determine whether an increase in physical activity is associated with a corresponding reduction in abdominal obesity, in a dose-response manner.

Physical activity and abdominal body fat

The literature describes a predisposition to lose fat mass in trunk region including abdominal area, studying the influence of structured exercise on this fat depletion (281, 282) and analysing also daily physical activity effects on this fat depot.

Although many cross-sectional studies have shown an inverse association between physical activity and waist circumference, few longitudinal studies have examined the impact of physical on waist gain. Sternfeld et al. (283) examined the relationship between physical activity and changes in body weight and WC among 3 064 healthy women aged 42 to 52 years. Over 3 years of follow-up, mean weight increased by 2.1 kg (SD \pm 5.4). Increases in both

sports/exercise and daily routine physical activity, such as walking or biking, were associated with smaller gains in weight and WC over time. In 2008, Lovejoy et al. (284) observed in a 4 years longitudinal study that the reduction in both basal and physical activity energy expenditure at menopause, along with observed reductions in dietary protein and fiber intakes, may significantly increase risk postmenopausal women's risk for weight gain.

Several cross-sectional analyses also found an inverse association between physical activity and WC or WHR (285, 286). For example, Chan et al. (217) found an inverse association between pedometer-determined steps per day and BMI ($r=-0.40$, $P < 0.0001$) in all participants and WC in females only ($r= -0.43$, $P < 0.0001$). In 2010, Dugan et al. analysed the relationship between physical activity and intra-abdominal fat mass in 369 white and black midlife women from the Chicago site of the Study of Women's Health Across the Nation (SWAN). Associations did not differ between white and black women. This study demonstrates a significant negative association between physical activity and intra-abdominal independent of multiple covariates in midlife women. Molenaar et al. in 2009 (287), found that a higher level of physical activity was associated similarly with lower subcutaneous and visceral abdominal fat mass volumes in both sexes, extending the results from prior small-sectional studies (100).

The genetic effect was 56% for visceral fat area after adjustment for age, sex, and total fat mass in the Quebec Family Study (288), it is possible that central adiposity, low birth weight, and inactivity, in concert and independently, contribute to the development of insulin resistance in both normal-weight and obese individuals.

In a review of the effects of diet-and exercise-induced weight loss on visceral adipose tissue distribution in both men and women, Ross (99) mentioned that a diet-induced loss of approximately 12 kg corresponds to a 30-35% reduction in visceral fat mass. Regarding the effects of exercise per se on visceral fat, there appears to be a relative resistance to visceral adipose tissue reduction in obese women, whereas as previously mentioned (191), exercise-

induced weight loss is associated with significant reductions in visceral fat in men. In conclusion, it can be postulated that the improvement in insulin sensitivity by regular exercise in individuals with visceral obesity and insulin resistance is associated with a disproportionate loss of visceral fat. It is possible that visceral obesity, which often accompanies decreased fitness, contributes to the association between inactivity and insulin resistance. Since regular exercise ameliorates the entire cluster of metabolic and homeostatic abnormalities found in patients with insulin resistance and in addition tends to reverse the abnormal body composition and fat distribution found in these individuals, it can be an indication that the apparent effectiveness of regular exercise in decreasing the incidence of coronary heart disease and type 2 diabetes is due to its effects on insulin action and central adiposity.

The purpose of the study presented by Kay and co-authors (281) was to systematically review the relationship between physical activity and abdominal fat. With database searches performed on MEDLINE, CINAHL, SPORT DISCUS and PUBMED, from 1985 to 2005 with keywords "exercise", "abdominal fat" and "visceral fat", the authors concluded that there are limited evidence from a number of studies suggesting a beneficial influence of physical activity on the reduction of abdominal and visceral fat in overweight and obese subjects when imaging techniques are used to quantify changes in abdominal adiposity. This highlights the importance of more rigorous studies to test some of the claimed hypothesis.

A review by Wareham et al. (266) showed that four of five studies identified a significant association between physical activity and waist gain (224, 277, 283, 289) the other one did not (290).

Ohkawara and co-workers (291) studied the dose-response effect of physical activity in abdominal fat mass loss. The purpose of their study was to systematically review the current literature to establish whether reduction of visceral fat by aerobic exercise has a dose-response relationship. In conclusion, the authors suggested that at least 10 METs ×

h/w in aerobic exercise, such as brisk walking, light jogging or stationary ergometer usage, are required for visceral fat reduction. Additionally, there is a dose-response relationship between aerobic exercise and visceral fat reduction in obese subjects without metabolic-related disorders.

Thomas et al. (292), authors of a meta-analysis, which included fourteen randomised controlled trials, compared exercise against no-exercise treatments in 377 type 2 diabetes' patients. The intervention ranged from eight weeks to twelve months of duration. When compared with the control, the exercise group has improved significantly the glycaemic control with a decrease in glycated haemoglobin levels of 0.6. There was a reduction in visceral adipose tissue (-45.5 cm²) and subcutaneous adipose tissue with exercise. The authors concluded that, in people with type 2 diabetes exercise significantly improves glycaemic control and reduces visceral adipose tissue and plasma triglycerides, but not plasma cholesterol, even without weight loss (293).

In summary, abdominal adiposity has been strongly associated with metabolic diseases, cardiovascular diseases and mortality. Results from prospective studies suggest that increasing physical activity (especially weight training) and reducing sedentary behaviour can offset age-related waist gain. Longitudinal studies demonstrated that increases in both sports/exercise and daily routine physical activity, such as walking or biking, were associated with smaller gains in weight and waist circumference over time. The literature describes a predisposition to lose fat mass in trunk region including abdominal area and several cross-sectional analyses found an inverse association between physical activity and waist circumference or waist to hip ratio. Additionally, there is a dose-response relationship between aerobic exercise and visceral fat reduction in obese subjects. These studies demonstrate a significant negative association between

physical activity and intra-abdominal independent of multiple covariates in midlife women. It can be postulated that the improvement in insulin sensitivity by regular exercise in individuals with visceral obesity and insulin resistance is associated with a disproportionate loss of visceral fat. Additionally, meta-analysis confirmed that there is a dose-response relationship between aerobic exercise and visceral fat reduction in obese subjects without metabolic-related disorders, and observed also that in people with type 2 diabetes, exercise significantly improves glycaemic control and reduces visceral adipose tissue and plasma triglycerides.

Human Body Composition Methodology

Accurate assessment of body composition is essential to obesity research. The past several decades have witnessed major conceptual and technological advances in the measurement of body composition. Conceptually, Heymsfield and his work group (18) organized the human body into four different levels: atomic (e.g., oxygen, carbon, and hydrogen), molecular (i.e., water, lipid, protein, minerals, and glycogen), cellular (e.g., body cell mass and extracellular solids and fluids), and tissue (e.g., adipose tissue, skeletal muscle, bone, and visceral organs). Based on this framework, many multicompartiment models have been facilitated by the advent of DXA.

More recently developed high-tech imaging options, such as computed tomography (CT) and magnetic resonance imaging (MRI), are being used with increasing frequency to measure body composition at tissue and organ levels. Although these methods offer excellent accuracy and reproducibility, several factors, including cost, technical complexity, and lack of portability, prohibit their routine use in large epidemiologic studies (294). While DXA is becoming more

widely available and accessible for use in relatively large field studies, CT and MRI are often used in small-scale studies that requires a high degree of accuracy or as reference methods.

Despite technological advances in methods of body composition assessment, the simplicity and low cost of anthropometric measures, particularly of weight and height, make them the most commonly used variables in obesity epidemiologic research. WC as a measure of abdominal or central obesity has attracted particular attention because of its inclusion as a key criterion or prerequisite for diagnosis of the metabolic syndrome (112, 295).

Dual energy X-Ray absorptiometry

DXA scanning was initially developed for measuring bone mineral density and diagnosing osteoporosis. It is now rapidly becoming one of the most frequently used methods for estimating human body composition in clinical studies (296). DXA can provide estimates of the three components of the whole body (fat free mass, fat mass, and bone mineral) as well as specific regions, such as arms, legs and trunk. The procedure is relatively simple and quick. It is based on the principle that two x-ray beams of very low but differing energy passing through the body are attenuated differentially by bone mineral, soft tissue, fat tissue, and FFM. Because DXA provides highly reproducible and accurate measures of body fat and lean body mass, it is becoming an accepted reference method for assessing body composition (297, 298). DXA exposes subjects to extremely low levels of radiation, which makes it safe for use in a wide range of populations, including children (299). But it is not safe for pregnant women, and most currently available systems cannot accommodate morbidly obese subjects. The instruments itself is expensive and immobile-factors that preclude its widespread use in large epidemiologic studies of morbidity and mortality (296).

DXA produces very precise estimates of body composition. Kiebzak et al. (300) scanned 20 subjects once a day for four consecutive days with a Lunar DXA-L densitometer and manufacturer-supplied software. Coefficients of variations (%CV) were 0.62 for total body bone mineral density, 1.89 for total percentage fat, 0.63 for total body tissue mass, 2.0 for fat mass, 1.11 for lean mass, 1.10 for bone mineral content, and 1.09 for total bone calcium. Regional measurements (arm, leg, trunk, pelvis, and spine) were less precise than total body measurements, with CVs in the range of 1% to 5%. These data indicate that DXA produces highly precise short-term measurements of total and regional body composition. The long-term (3-month) reproducibility of DXA measurements (Hologic QDR 4500A absorptiometry) have generally provided highly consistent estimates of percent body fat (296). However, differences in calibration between instruments from different manufacturers, as well as differences between various models and computer software from a single manufacturer, can lead to variability in DXA estimates (301).

Heymsfield research group proposed (18) DXA for their system of organizing in vivo body composition methods because this body composition technique is capable of estimating whole body and regional bone mineral, fat, and fat-free soft tissue. These authors considered that DXA is a body composition technique from molecular level. As described by Minderico and colleagues (302), X-ray attenuation in human tissues at typical DXA energies is mainly related to the type and proportion of elements present and to photon energy. Elements with low atomic numbers (e.g. H and C) minimally attenuate photons, while elements with higher atomic numbers (e.g. Ca and P) strongly attenuate photons. As photon energy increases, there is less photon attenuation. Therefore, DXA uses first elemental analysis for further processing other levels of body composition such as the molecular. There are other authors considering that DXA should be included in the atomic level, providing estimates for the three components of the whole body. As described by Mazess et al., DXA body composition approach assumes that

the body consists of three components that can be distinguished by their X-ray attenuation properties: fat, bone mineral and fat-free or 'lean' soft tissue (303).

Some studies have described the theoretical basis for the use of DXA in estimating soft tissue composition and bone mineral (304, 305), considering some main assumptions. Thus, calibrated DXA systems can provide estimates of fat and lean for soft tissue pixels. In theory, DXA can only solve a two-component mixture. Within any pixel, the proportions of only two components can be solved by the differential absorption of two photon energies. Soft tissues, consisting largely of water and organic compounds, reduce photon flux to a much lesser extent than bone mineral, whereas pixels containing bone are relatively easily distinguished from those with no bone present.

DXA is capable of good precision for the measurement of body fat, fat-free mass and bone mineral, and this has been well documented (298, 306). This attribute makes it a potentially valuable tool for longitudinal studies in the clinical settings. For an accurate estimation of body composition changes in DXA it is important to consider the comparison of body mass with DXA sum parts at baseline and after intervention as a quality control measure.

Accuracy of dual energy X-Ray absorptiometry

The accuracy of DXA has been further confirmed by small experiments in which exogenous fat was added to either central or peripheral body regions during the DXA imaging process (295).

DXA measures of appendicular fat mass are strongly associated with CT-fat mass ($r=0.91-0.99$) (307-309). There is also a tight association between total fat mass, as measured by the four-compartment model, and fan-beam DXA ($r=0.98$) (308).

Wang et al. (310) concluded that DXA-estimated percentage of body fat mass was strongly associated with five-component model percentage of body fat mass (24.4 +/- 12.0% versus

24.9 +/- 11.1%, $r = 0.983$, $P < 0.001$) (310). This study supports the underlying physical concept and accuracy of the DXA method for estimating percentage of body fat mass.

Andreoli et al. (311) suggested that DXA has the potential to provide overall and regional assessment of body composition in terms of fat, lean mass and bone. Silva et al. (312) in a adolescent athletes study aimed in assessing the accuracy of air displacement and DXA percent body fat estimations in comparison with a reference five-compartment model used as the reference method, concluded that the two techniques were not precise for individual percent body fat prediction.

The ability of researchers and health professionals to accurately estimate changes in body composition is critical in determining the effectiveness of medical nutritional therapy and changes that occur with weight management programs. The accuracy of estimating fat, lean and bone mineral changes with significant weight gain or loss is an important methodological issue. There are few studies in obese humans that have examined the ability of DXA to detect changes in fat mass or skeletal muscle as compared to criterion methods such as the four-compartment model or CT. For changes in fatness, Evans et al. (313) compared DXA with a multicomponent model in different weight loss interventions and found mean percent fat agreement to vary between DXA and a multicomponent model from 0.3% to 2.0% within the range of sampling error. Tylavsky et al. (314) estimated similar changes in soft tissue using both pencil and fan beam DXA. In obese premenopausal women, although DXA consistently overestimated fat mass (~10%) and underestimated fat-free mass (~7%) before and after a 14% diet-induced weight loss intervention, it did report comparable mean decreases in fat (11.5 vs 10.9 kg) and fat-free (1.6 vs 2.0 kg) in comparison with the four-compartment model (315). The authors concluded that DXA provides unbiased estimates of fat loss in response to caloric restriction. However, those estimates were not better than those derived using a simple equation with BMI (mean difference vs four compartment model: 0.6 ± 2.1 vs -0.3 ± 2.1 ,

DXA vs BMI, respectively). Similarly, a study by Tylavsky et al. (316) has reported that in response to a 7% weight loss in women, changes in the thigh fat mass and lean mass, as measured by TC, were correlated with changes, as measured by fan-beam DXA (fat: $r = 0.67$, lean mass: $r = 0.55$), and pencil-beam DXA (fat: $r = 0.66$, lean mass: $r = 0.60$) (316). However, both fan-beam and pencil-beam DXA tended to underestimate changes in lean tissue mass (-24.9g and -11.8g vs -44.7g) and overestimate changes in fat mass (-112.1g and -48.5 g vs -45.7g) the thigh, as compared with CT. Thus, some studies, with obese persons, suggest that DXA underestimates changes in lean tissue mass and overestimates changes in fat mass compared with criterion measures, such as the four-compartment model or CT (313, 315, 316).

Minderico et al. (302) in a study comparing DXA with other methods concluded that, although these methods are widely used in clinical settings, applying them interchangeably to detect changes in body composition may not produce accurate results. Therefore, in the clinical settings DXA is recommended to assess body composition changes in weight loss programs.

The results from a study (317) with postmenopausal women indicate that a four-component model and DXA provide comparable estimates of body composition changes. However, the wide limits of agreement between four-component model (the criterion method) and the comparison method indicate that these methods are not interchangeable on an individual basis.

Some researchers have examined the ability of DXA to measure changes in fat by adding pads of lard to the abdomen of a given individual. Two studies have reported that DXA underestimates the fat content in the lard pads when placed in the trunk region by 40% to 50%, but accurately detected more than 90% of the fat content from the same lard pads when placed in the thigh region (308, 318). It has been suggested that this may have been due to a limitation of older software to accurately assess body composition (319). However, this is unlikely to be the sole explanation, as this observation was also reported in one of the

aforementioned studies (308) that used a more recent software version. More likely, this is probably due to the increased sagittal thickness of the individual with the addition of the fat pads. It was also documented that thigh tissue thicknesses can cause beam hardening and an underestimation of fat mass (308, 320).

It is essential to show this agreement between body scale mass and the sum of DXA parts as a part of the quality control of DXA data, Lohman and colleagues (321) have detected lack of agreement in the mean difference and standard deviation of the difference. Mean agreement should be within 1 kg with a standard deviation less than 2 kg at baseline, and again after intervention (322). The author suggested that all future investigators should include this comparison in both DXA validation studies and studies with DXA body composition changes.

Hydration status may be a confounder in DXA body composition estimates.

Reviewing the literature with water and multi-compartment models, Lohman et al. (321) concluded that, the water content of fat-free mass in healthy adults is between 72 and 74.5% with a standard deviation of 3% (2-4% for most investigations). Given this level of variation, questions have been raised about the effects of hydration level on DXA estimates of lean and fat tissue (305). The theoretical work of Pietrobelli et al. (304) and both empirical works of Going et al. (323) and Evans et al. (313) indicate that an increase or decrease in hydration levels of 5% biases DXA estimates of percent fat only by 1 to 2.5% (321). Thus, hydration level is not a major source of variation in DXA body composition estimates in the normal healthy population.

For any method to be accepted as a reference, it is necessary to know the differences between machines from different manufacturers (324) and from the same manufacturer (325). Concern has also been reported about the consistency of results between machines of the same model (326, 327). Software upgrades that appear from time to time often include changes in the algorithms used for body composition calculation, which can affect the measurements for an

individual (319, 324). Both inter and intra-manufacturer comparisons are clearly important for investigators upgrading their machines, particularly during the course of longitudinal studies, and in the context of multicentre trials.

Reliability of dual energy X-Ray absorptiometry

It is important to evaluate precision of body composition, measured by DXA, in short-term (within and between days) and in long term (during months within individuals). Repeatedly scanning subjects and calculating an intra-individual standard deviations are the procedures to analyse the short-term precision of total body composition.

Cordero-MacIntyre et al. (297) analyzed dual-energy X-ray absorptiometry (DXA) measurements using two versions of software (Hologic V8.1a and V8.21) to compare the short- and long-term precisions of the measurements. For the estimation of precision, duplicate scans obtained on the same day for nine women were analyzed using both versions of the software. The correlations between duplicate scans ranged from 0.886 to 0.998 and were similar between software versions. The CVs for fat were 1.2%, for software V8.21 compared to 1.3% for V8.1a. Systematic differences were found between software versions with higher values for fat for software version V8.21. The 3-mo, long-term reproducibility of body composition estimates from DXA was only slightly less than short-term reproducibility for both software versions (CV range from 1.3% for bone mineral content weight to 11.0% for arm fat). Software V8.21 yielded smaller percentage mean differences between scale and DXA-estimated weights (-2.4% and -7.2% at baseline and -2.9% and -7.6% at 3 mo, respectively) and higher fat and lean weights (49.12 and 47.1 kg and 49.6 and 44.6 kg, respectively) than V8.1a. Reproducibility of all variables was comparable between software versions.

Recently, Hink et al. (328) evaluated 52 men and women, aged 34.8 (s.d. 8.4; range 20.1-50.5) years, BMI (25.8 kg/m²); range 16.7-42.7 kg/m². Two consecutive total body scans (with re-positioning) were conducted. Precision error was CV 0.82% for total fat mass and 0.86% for percentage fat. Precision was better for gynoid (root mean square 0.397 kg; CV 0.96%) than for android fat distribution (root mean square 0.780 kg, CV 2.32%). There was good agreement between consecutive measurements for all measurements (slope (s.e.) 0.993-1.002; all R²=0.99). The author concluded that DXA provided excellent precision for total body composition measurements.

Regional estimations by dual energy X-Ray absorptiometry

Although originally designed to measure bone mineral content, DXA is commonly used to assess total and regional fat and fat-free mass in vivo (329, 330). DXA measures of appendicular or total skeletal mass are highly associated with the corresponding values obtained by CT or MRI ($r = 0.86 - 0.98$) (307-309, 331, 332). Similarly, DXA measures of appendicular fat mass are strongly associated with CT – fat mass ($r = 0.91 - 0.99$) (307, 308). DXA has also been used to measure abdominal adiposity. Within the abdominal region, DXA measures of total abdominal fat correlate very well with measures by CT ($r = 0.87-0.98$) (49, 333), in both black and caucasian men and women (333). However, DXA can assess body composition only two-dimensionally. Thus, it is unable to differentiate subcutaneous fat from visceral fat. Although DXA estimates of abdominal visceral fat have been validated against a single-slice CT scan (49). The DXA estimates of trunk and abdominal fat mass were strongly correlated with total abdominal fat ($r=0.94$ to 0.97) and abdominal visceral fat ($r=0.86$ to 0.90) as assessed by CT. However, the association between DXA measures of abdominal fat ($r=0.51-0.90$) (49, 50, 333) and CT – or MRI- measured visceral fat tend to be weaker than total abdominal fat.

In the health ABC Study of elderly men and women, Snijer et al. (333) compared the measurements of visceral fat from DXA and CT. Total body fat and trunk fat were measured by DXA with a Hologic QDR 1500. Visceral fat and total abdominal fat were measured with a 10 mm CT scan at the L4-L5 levels. The study showed a strong correlation between total abdominal fat measured by DXA (subregion) and CT (ranging from 0.87 in white men to 0.98 in black women). The DXA subregion underestimated total abdominal fat by 10% compared with the CT scan. This study supports the value of DXA as a good alternative to CT for predicting total abdominal fat in an elderly population.

DXA allows for the separation of the body into regions of interest including the abdominal, often defined as the fat mass located between lumbar vertebral bodies L1 and L4 (334, 335). Some studies support the possibility of estimating abdominal fat using a region of interest selected by conventional whole body dual-energy X-ray absorptiometry (DXA) (336, 337). Park et al. (337) observed that DXA regions of interest (L2-4, L2-upper iliac) were associated with total visceral adipose tissue as well as MRI-derived visceral adipose tissue area at L4-5 in non-obese men. The authors concluded that fat distribution estimates of DXA regions of interest may be useful in the early detection abdominal/visceral obesity.

In addition, a few reports describe the capability of DXA to estimate changes in abdominal region (318, 336, 338). Glickman et al. (336) developed a study which indicate that DXA measures of total abdominal fat mass are in total agreement with total adipose tissue mass measured by a volumetric CT scanning technique. The DXA's L1-L4 region of interest technique is both reliable and reproducible for assessment of abdominal adipose tissue. For DXA to be used in longitudinal or interventions studies, it must also be sensitive to changes in the abdominal region. Some studies confirm the ability of DXA to determine changes in abdominal fat by placing packets of porcine fat over the abdomen. Gilckman et al. (336) observed only 78% of the total packed fat that was added. Although this was an improvement relatively to

others reports in which DXA detected only 52 and 55% of the additional fat placed over the abdominal region, these differences may be explained by the different DXA scanners and software that were used. Moreover, this kind of equipment is not always available in clinical approaches, so it is important to observe if DXA region of interest estimates changes may be predicted by simple anthropometric measurements, showing their usefulness in the early detection of women with intra-abdominal obesity and its alterations.

Many studies have evaluated the relationship between DXA estimates of percent body fat and fat distribution and metabolic and cardiovascular risk factors (296). In general, DXA estimates of body fatness correlate well with measures of insulin resistance, glucose intolerance, and blood lipids. However, the correlation between DXA measures and adverse cardiovascular risk factors in adults and children are no higher than those provided by simpler anthropometric measures, such as BMI, WC, and skinfold thicknesses (339, 340). Whether DXA estimates of body fat predict long-term risk of chronic disease or mortality has yet to be determined.

Anthropometry

Anthropometry is a simple reliable method for quantifying body size and proportions by measuring body length, and includes measures such as weight, stature, girth, skinfolds, and body circumferences. Not only total body fat, but also regional fat and skeletal muscle, can be predicted from anthropometrics (341). Standardized methods are available to measure weight, height and the other anthropometric variables (341). These approaches are especially important for national surveys that monitor obesity trends over time, but in clinical settings these methods are important too. Anthropometric measures have been employed extensively to determine the association between obesity and related morbidity (94, 95, 152, 156, 342) and mortality (94, 96). It is generally assumed that the associations between anthropometric measures and health risk are explained by the corresponding ability of anthropometry to

predict body composition – in particular, body fat distribution independent of gender, age, and ethnicity.

In epidemiologic studies on determinants of obesity, weight gain is the most commonly used outcome variable. Changes in weight are typically defined as the difference in weight assessed between two time points (the interval ranging from several months to decades). Studies on health consequences, weight gain during the period from late adolescence (18 to 20 years old) to middle age (30 to 55 years old) is of great interest. Many people gain the greatest amount of weight during this period, and for most, the added weight reflects increases in body fat. In the Nurses' Health Study (NHS), it was calculated weight change between age 18 years and baseline (1976), and classified women into five categories according to the amount of weight gained (4 to 10 kg; 10.1 to 19.9 kg; 20 to 39.9 kg; ≥ 40 kg). There was a dose-response relationship between the amount of weight gained and risk of coronary heart disease (343) and mortality (344).

Although both height and weight are biologically meaningful variables in epidemiologic studies, they do not represent body fatness. Nonetheless, the combination of these two variables can create useful, albeit not perfect, indexes of obesity. The most commonly used obesity index is BMI. BMI is used in clinical settings for the identification of individuals at increased health risk. In 1835, Quetelet, a Belgium mathematician and astronomer, observed that in adults, body weight was proportional to the square of the height (weight/height²) (345). In 1972, Keys et al. (346) examined various weight-height indexes and found that BMI had the highest correlations with adiposity assessed by skinfold and body density measurements. Benn (347) advocated the use of an empirically fit value for value for the exponent of height (p) based on specific population studies to create an index uncorrelated with height. The validity of the Benn index (weight/height ^{p}) has not been found to be superior to that of BMI (in which $P=2$). Gallagher et al. (348) examined the relationship between BMI

and total body fat mass in 504 white and 202 black men and women 20 to 94 years of age. The analysis was based on a four-compartment body composition model and it was used an equation. BMI was strongly correlated with both absolute body fat and percent body fat. The correlations were somewhat stronger for women than for men, and the correlations with absolute body fat were somewhat stronger than those for percent body fat. This study demonstrated that BMI is an excellent indicator of body fatness in different age, sex, and racial groups. Based on the associations among BMI, morbidity, and mortality, BMI categories for normal weight (18.5-24.9 kg/m²), overweight (25.0-29.9kg/m²), and obese (\geq 30.0 kg/m²) have been established for the Caucasian population (349).

Several other studies have shown a strong correlation between BMI and percent body fat assessed by DXA. Blew et al. (350) found a high correlation between two variables ($r= 0.81$) in 317 postmenopausal women. Evans et al. (351) found similar high correlations between percent body fat and BMI in both black and white women, although race modified the prediction of percent body fat by BMI. Prediction equations have been developed to estimate percent of body fat based on BMI for both children and adults (352, 353) but these equations are not widely used.

Many studies have assessed the validity of BMI as a measure of body fatness to predict biochemical markers of obesity and cardiovascular risk. Circulating concentrations of adipocyte-secreted hormones, such as leptin and adiponectin, can be used as surrogate markers of body fat. Jurimae et al. (354) evaluated relationship between leptin levels and body fat assessed by anthropometry and DXA. Among overweight and obese women (BMI > 27 kg/m²), BMI and percent body fat measured by DXA were similarly correlated with leptin concentrations (0.03 vs. 0.79). These correlations were much weaker among women with a BMI \leq 27 kg/m². In numerous studies, BMI has been inversely correlated with concentrations

of adiponectin, a newly discovered adipocyte-derived hormone that is reduced in obese and diabetic subjects (355).

The relationship between BMI and cardiovascular risk factors, such as blood pressure, high-density lipoprotein (HDL) cholesterol, fasting glucose, and triglycerides is well established. Spiegelman et al. (356) compared the associations of BMI, absolute fat mass, percent body fat, and regional fat distribution with fasting blood glucose and blood pressure in 1551 men and women between the ages of 15 and 79 years. Percent body fat and absolute fat mass were assessed by densitometry. This outcome may explain a strong association between BMI and cardiovascular morbidity and mortality observed in many epidemiologic studies. BMI is positively associated with morbidity (94, 95) and has a U-or- J-shaped relationship with mortality (94, 96). It is commonly held that a high BMI is associated with increased health risk or mortality because of its association with adiposity. It was been proposed that the mortality rate associated with a given BMI is higher in men than in women (98).

In 2010, Nguyen et al. (357) presented the results of the differences in the 10-year CHD risk with increasing severity of obesity in men and women participating in the latest National Health and Nutrition Examination Survey. Data from a representative sample of 12,500 U.S. participants in the National Health and Nutrition Examination Survey from 1999 to 2006 were reviewed. The Framingham risk score was calculated for men and women according to a BMI of <25.0, 25.0-29.9, 30.0-34.9, and ≥ 35.0 kg/m². The prevalence of those with hypertension increased with an increasing BMI, from 24% for a BMI <25.0 kg/m² to 54% for a BMI of ≥ 35.0 kg/m². The prevalence of an abnormal total cholesterol level (>200 mg/dL) increased from 40% for a BMI <25.0 kg/m² to 48% for a BMI of ≥ 35.0 kg/m². The 10-year CHD risk for men increased from 3.1% for a BMI <25.0 kg/m² to a peak of 5.6% for a BMI of 30.0-34.9 kg/m². The 10-year CHD risk for women increased from .8% for a BMI <25.0 kg/m² to a peak of 1.5% for a BMI of ≥ 35.0 kg/m². Both diabetes and hypertension were independent risk factors for an

increasing CHD risk. The authors concluded that 10-year CHD risk, calculated using the Framingham risk score, substantially increased with an increasing BMI.

Sun et al. (358) compared correlations of DXA measurements of total fat mass and fat mass percent in the whole body and trunk, BMI, and WC with obesity-related biologic factors, including blood pressure and levels of plasma lipids, C-reactive protein, and fasting insulin and glucose, among 8,773 adults in the National Health and Nutrition Examination Survey (1999-2004). Overall, the magnitudes of correlations of BMI and WC with the obesity-related biologic factors were similar to those of fat mass or fat mass percent in the whole body and trunk, respectively. These observations were largely consistent across different age, gender, and ethnic groups. In addition, in both men and women, BMI and WC demonstrated similar abilities to distinguish between participants with and without the metabolic syndrome in comparison with corresponding DXA measurements. These data indicate that the validity of simple anthropometric measures such as BMI and WC is comparable to that of DXA measurements of fat mass and fat mass percent, as evaluated by their associations with obesity-related biomarkers and prevalence of metabolic syndrome.

Given the same BMI, the relative compositions of fat mass versus lean body mass appear to depend on age, sex, and ethnicity (359). It is well known that for the same BMI, percent body fat is higher in women than in men (348). The sex differences in body composition are established during adolescence and sexual maturation, when males develop more lean body mass, especially bone mass and skeletal muscle (296).

According to NHANES data (4), mean BMI gradually increases during young and middle-aged adult life, reaching peak values at 50 to 59 years of age, then declining slightly after 60 (360). Other authors have drawn similar conclusions regarding the influence of age and gender, but have also notice an effect of ethnicity (296). Wagner and Heyward (361) conducted a detailed comparative review on measures of body composition in blacks and whites. Because of the

difference in body structure, blacks tend to have lower adiposity and percent body fat than do whites for a given BMI. There is consistent evidence that the percent body fat is higher in Asians than in whites with the same BMI (362). Deurenberg et al. (363) found that the percent body fat in Asians was 3 to 5 percentage points higher than that in whites with the same BMI. The high fat at low BMIs in Asians is probably related to their build, which is characterized by shorter legs and a smaller frame. Mortality studies in Asian populations (364) show a similar J-shaped pattern with increasing BMI and mortality, wherein the nadir of the curve lies around 22 to 26 kg/m², a finding that is quite comparable to those in caucasian populations (97, 98). Thus, although it is clear that adiposity and health risk tend to increase with increasing BMI independent of age, gender, and race, the magnitude of the increment in adiposity and health risk with increasing BMI is influenced by these factors, and are therefore important to consider when examining these relationships.

Although often overlooked, BMI is also a significant predictor of regional fat depots such as visceral or abdominal subcutaneous fat. Studies generally report weaker correlations coefficients for abdominal subcutaneous fat and BMI ($r=0.52 - 0.94$) (16, 141, 159, 365-367) as compared to WC. However, BMI is a significant predictor of regional fat depots such as visceral or abdominal subcutaneous fat, independent of WC (365).

Abdominal obesity is commonly assessed using WC, and it is now established that WC is associated with morbidity and mortality independent of BMI (342). Despite a growing literature establishing WC as an independent predictor of morbidity and mortality (368), absent is a consensus as to the ideal placement of WC when measuring abdominal obesity. Common landmarks include the visible narrowing of the waist, last rib, top of the iliac crest, or the midpoint between the last rib and the iliac crest. However, review of the literature reveals that WC measures have been taken anywhere within a region bordered by the sternum to the iliac crest in the upright or supine position. Fortunately, WC at different measurement sites

tend to be highly correlated, and Seidell et al. (369) report that the associations between WC and serum lipids were not significantly altered by measurement site. However, Wang et al. demonstrated that there is a substantial difference (~4.5 cm) in the absolute WC measured at the minimal WC versus the iliac crest in 62 women with a wide range in age (36 ± 18.7 -76 yr) and adiposity (BMI: $26 \pm 8.9 - 43 \text{ kg/m}^2$) (209). Owing to these differences in measurement site and methodology, it is often difficult to compare WC measures across studies or to create meaningful guidelines.

The association between WC and health risk may be explained by its corresponding association with abdominal subcutaneous and/or visceral fat. Indeed, WC is a strong predictor of both visceral fat ($r=0.64-0.89$) (16, 159, 365-367) and abdominal subcutaneous fat ($r=0.53-0.89$) (16, 159, 365-367). Because visceral fat is a strong correlate of morbidity (370-372) and mortality (368), considerable attention has been given to the ability of WC to predict visceral fat. Although it is clear that WC circumference is the single best anthropometric predictor of visceral fat, substantial inter-individual variation in visceral fat deposition exist for a given WC. Previous studies report that error associated with estimates for visceral fat using WC is approx 25 to 35% (296-298, 333). The substantial inter-individual variation is explained in large measure by corresponding variation in the relationship between visceral and subcutaneous fat. In other words, the relationship between visceral and subcutaneous fat varies substantially among individuals (141, 366, 367).

There is some evidence that WC may be superior to WHR as a surrogate measure for central obesity. Clasey et al. (49) examined the utility of anthropometric measures and DXA to predict total abdominal fat and abdominal visceral fat measure by CT scan in 76 white adults 20 to 80 years of age. In both men and women, WC and abdominal sagittal diameter were strongly associated with total abdominal fat ($r = 0.87$ to 0.93) and abdominal visceral fat ($r= 0.86$ to 0.90). WHR was less predictive of total abdominal fat or abdominal visceral fat than WC.

Although WC is a well-accepted measure of abdominal fat, the biological meaning of HC is less clear because a large hip may reflect more accumulation of subcutaneous fat, greater gluteal muscle mass, or larger bone structure (pelvic width) (373).

Several studies have suggested that waist and hip circumference may have opposite effects on metabolic and cardiovascular risk factors. In the Quebec Family Study, Seidell et al. (374) found that increased hip circumference (HC) was associated with decreased visceral fat and increased subcutaneous abdominal fat, especially in men. A large WC adjusted for BMI and HC was significantly associated with low HDL-cholesterol concentrations ($P < 0.05$) and high fasting triglycerides, insulin, and glucose concentrations ($P < 0.01$). HC adjusted for BMI and WC was associated with these risk factors in the opposite direction.

Recommended WC cut-offs were 40 in. (102 cm) for men and 35 in. (88 cm) for women (corresponding cut-points for WHR of 0.95 for men and 0.88 for women) (375). However, these cut-points are arbitrary, as the relationship between increased WC and elevated metabolic and cardiovascular risk appears to be linear.

The IDF proposed a new definition of metabolic syndrome that includes central obesity as a prerequisite for diagnosis along with gender- and ethnicity-specific cut-points for WC (295). However, these varying cut-points, which remain controversial, complicate the definition and the clinical diagnosis of metabolic syndrome in different populations.

WC is commonly used to assess change in abdominal obesity. Changes in WC are associated with changes in visceral fat in response to diet and/or exercise weight loss (67, 367, 376). It is reported that a 1-cm reduction in WC corresponds to a 4% reduction in visceral fat; however, there was a substantial amount of variance (standard deviation = 4%) in this relationship. The variation in this association is in part due to changes in subcutaneous fat and/or lean mass that mask the ability of WC to accurately distinguish changes in abdominal tissues.

One of the main interests on estimating changes in total body composition relates to the effect of intervention in obese or overweight persons. There are considerable errors in all body composition measures and these errors may be larger for predicted values than for observed values. Therefore, anthropometrics applied through predictive equations are unlikely to provide accurate measures of changes in total body composition. The observed changes in total body composition with weight loss in overweight and obese persons, calculated from body density, may be inaccurate if a two-compartment model is used due to changes in density of fat free mass (377).

It is of general agreement that efforts to estimate the changes in body composition with weight loss in obese people should be based on equations that use circumferences rather than skinfolds thickness as predictor variables, as changes in circumferences are larger (with a possible exception for subscapular skinfold thickness) (378, 379).

Studies that have evaluated predictive equations for estimating changes in body composition have generally given disappointing results, although they were based on two-compartment models (377, 380, 381). The difficulties of evaluating changes in body composition were reported by Ballor and Katch (380) who showed that, in obese women with a mean loss of 2.7% body fat, none of the ten common predictive equations accurately estimated the changes. Moreover, the accuracy and precision of anthropometric data is largely dependent upon the skill of the examiner, therefore, examiner-dependent (294, 341, 382).

Accuracy of anthropometry

The accuracy and reliability of anthropometric measures can be affected by equipment, technician skill, subject factors, and the precision of the equation selected to estimate the

measure of interest (383). Acceptable errors for estimating relative body fatness (%BF) and fat free mass are $\leq 3.5\%$ and ≤ 2.8 kg (for women) and ≤ 3.5 kg (for men), respectively (384).

The instruments need to be carefully and periodically maintained and calibrated to guarantee their accuracy. The tape measure should be made with a flexible material that does not stretch with use. Plastic-coated tapes can be used if an anthropometric tape is not available. The known precision of the skeletal anthropometers (0.05 cm to 0.50 cm) and range of measurements (0 to 210 cm), depend on the type of the skeletal anthropometer (384).

However, accurate measurement of bony diameters in heavily-muscled or obese individuals may be difficult as the underlying muscle and fat tissues must be firmly compressed. Bony anatomical landmarks may not be readily identified and palpated, leading to error in locating the measurement site. Like the skinfold method, it is more difficult to obtain consistent measurements of circumference for obese compared to lean individuals (384). However, circumferences are preferred to skinfolds when measuring obese clients because regardless of their size, circumferences of obese individuals can be measured; whereas the maximum aperture of the skinfolds calliper may not be large enough to allow measurement.

Moreover, circumferences require less technician skill, and the difference between technicians is smaller compared differences in skinfold measurements (384). It is important to be aware of the possibility that the accuracy of circumferences measurements may be affected by fluid retention and subcutaneous edema, particularly in women experiencing large weight gains during certain stages of their menstrual cycles.

Among various anthropometric variables, weight and height are measured with the highest precision (reproducibility) and accuracy (little deviance from the true value), and the least amount of technical error (385). Because measurements of waist and hip circumferences have greater between-technician variability, these measurements are best carried out by one person. Between- technician variability is even greater for skinfolds measurements. Marks et

al. (386) evaluated reliability for eight anthropometric measures in 95 male and 134 female subjects from NHANES II. Among the anthropometric measurements, the highest inter-observer reliabilities were for weight, height, sitting height, and arm circumference ($R \geq 0.97$); the reliabilities for triceps and subscapular skinfolds were lower but acceptable ($R = 0.81$ to 0.95).

Reliability of anthropometry

Compared to the skinfold method, technician skill is not a major source of measurement error, provided that standardized procedures are closely followed for locating measurements sites, positioning of the tape measure, and applying tension during the circumferences measurement. Variability in circumferences measurements taken by different technicians is relatively small (0.2 cm to 1.0 cm), with some sites differing more than others (384).

In a research developed by Ferrario in 1995 (387), which aimed to estimate the reliability of skinfold and girth measurements – commonly used in epidemiological and clinical studies as measures of body fat distribution – the results confirmed previous findings, which indicate that the reliability of girth measurements is greater than for skinfold measurements.

The variability found is caused by: using a plastic-coated tape measure with a spring-loaded handle which enables to reproduce the tension on the end of the tape measure; differences in location of the anatomical sites; and the technique of grasping the circumference. Skilled technicians can obtain similar values, even when measuring circumferences of obese individuals (379). Trunk circumferences, particularly those of the abdomen, are difficult to measure in individuals who are markedly overweight or obese, but high precision may be obtained (379, 388).

In order to assess the extent of intra- and inter-interviewer variability both in anthropometric measurements and in estimates of body composition, Klipstein and colleagues (389) developed a study with 17 interviewers trained in the anthropometric measurement technique. This study included 10 healthy volunteers (4 men and 6 women). To ensure participation of all interviewers the study was carried out on three different days. On each of these days interviewers got randomly allocated to the subjects being present. Each interviewer took 12 body measurements (weight, height, sitting height, circumferences of waist, hip, and midarm, skinfolds (biceps, triceps, subscapular, and suprailiac), (chest breath and depth) per subject on two occasions. From these measurements, BMI, WHR, percentage of body fat, fat mass, fat free mass and metric index were determined. For all anthropometric variables variance components, reliability coefficients (R) and coefficients of variation (CV) were estimated and systematic differences of measurements between interviewers were assessed. Although the absolute variation in measures due to interviewers was small, systematic differences among interviewers were clearly evident in all measurements and estimates in this group of subjects, except for sitting height. The author concluded that, anthropometric measures and estimates of body composition obtained in the current study show the feasibility of detailed anthropometric data collection by multiple interviewers in large-scale epidemiological studies.

Human Body Composition Methodology – Conclusion

Accurate measurement of the amount of and distribution of body fat is critical to obesity research. The past several decades have witnessed major advances in the field of body composition research. Compared to the traditional two-compartment body composition model, multicompartments models have improved the ability to accurately estimate body fatness. DXA is rapidly becoming accessible and established as the reference body composition method and as an alternative to traditional methods, such as underwater weighing and

hydrometry. DXA can provide estimates of the three components of the whole body (fat free mass, fat mass, and bone mineral) as well as specific regions, such as arms, legs and trunk. In the clinical settings DXA is recommended to assess body composition changes in weight loss programs. DXA provided excellent precision for total body composition measurements. Within the abdominal region, DXA measures of total abdominal fat correlate very well with measures by CT. DXA allows for the separation of the body into regions of interest including the abdominal, often defined as the fat mass located between lumbar vertebral bodies L1 and L4. Fat distribution estimates of DXA regions of interest may be useful in the early detection abdominal/visceral obesity.

Despite these technological advances, anthropometric measures, particularly of weight and height, remain the least expensive and most widely used methods for assessing adiposity in epidemiologic studies. BMI is a reasonable indicator of body fatness in different age, sex, and racial groups. Several other studies have shown a strong correlation between BMI and percent body fat assessed by DXA. The relationship between BMI and cardiovascular risk factors, such as blood pressure, high-density lipoprotein cholesterol, fasting glucose, and triglycerides is well established. The validity of simple anthropometric measures such as BMI and WC is comparable to that of DXA measurements of fat mass and fat mass percent, as evaluated by their associations with obesity-related biomarkers and prevalence of metabolic syndrome.

Although it is clear that WC is the single best anthropometric predictor of visceral fat, substantial inter-individual variation in visceral fat deposition exist for a given WC. Changes in WC are associated with changes in visceral fat in response to diet and/or exercise weight loss.

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CHAPTER 2

METHODS

Methods

A brief description of the methods used throughout the present dissertation is presented in this chapter. First, the sample will be described, then the intervention used with the participating overweight and obese women, followed by the body composition methods that were used at baseline and at the end of intervention. Finally, the statistical analysis used will be described.

Sample

Subjects were recruited from the greater Lisbon area, to participate in 16-month weight management program, through newspaper and other media advertisements, email messages, and study flyers. Inclusion criteria were the following: 1) female, 2) > 24 years old, 3) premenopausal, 4) currently not pregnant nor trying to become pregnant, 5) body mass index (BMI) >24.9 kg/m², and 6) free from any major diseases. After several orientation sessions, 152 females signed up for the program. During the run-in phase, four women decided not to participate (reporting time and scheduling conflicts), four others did not comply with testing requirements, three women became pregnant or were attempting to become pregnant, and one subject was diagnosed with hyperthyroidism, leaving a total of 140 subjects who started the intervention.

An initial visit with the study physician ensured that subjects met all medical inclusion criteria. All women agreed to refrain from participating in any other weight loss program and gave written informed consent prior to participation in the study. The Faculty of Human Movement's Ethics Committee approved the present study.

In *Chapter 3*, the sample was composed of 126 women, because after the intervention, 152 women were evaluated, but only 126 performed all the body composition necessary methods. In *Chapter 4*, the sample used includes 121 women. Despite the fact that at four months after the intervention 152 women were evaluated, only 121 women performed all body composition assessment methods. In *Chapter 5*, the sample consists of 121 women considering that all completed body composition assessment methods at baseline and after weight loss.

Intervention

As described by Teixeira et al. (1), subjects in the first phase attended 15 treatment sessions in groups of 32 to 35 women, for 4 months. Average attendance to the treatment sessions was 83%. Sessions lasted 120 minutes and included educational content and practical application classroom exercises in the areas of physical activity and exercise, diet and eating behaviour, and behaviour modification. Physical activity topics included learning the energy cost associated with common physical activities, increasing daily walking and lifestyle physical activity, planning and implementing a structured exercise plan, setting appropriate goals, using logs and pedometers for selfmonitoring, and choosing the right type of exercises. Examples of covered nutrition topics were the caloric, fat, and fiber content, and the energy density of common foods, the role of breakfast and meal frequency for weight control, reducing portion size, strategies to reduce fat content in the diet, preventing binge and emotional eating, planning for special occasions, and reducing hunger by increasing meal satiety (e.g., increasing fiber content). Cognitive and behavioural skills such as self-monitoring, selfefficacy enhancement, dealing with lapses and relapses, enhancing body image, using contingency management strategies, and eliciting social support were also part of the curriculum. Subjects were instructed and encouraged to make small but enduring reductions in caloric intake and to

increase energy expenditure to induce a daily energy deficit of approximately 300 kcal. Although weight was monitored weekly, subjects were advised that long-term (i.e., after 1-2 years), not necessarily rapid weight reduction, was the primary target. In the first session, participants were informed that reaching a minimum of 3% weight loss at 4 months was an appropriate goal in this program and were subsequently instructed to individually calculate the number of kilograms that corresponded to their specific body weight.

In a second phase of the program (i.e. after 4 months), participants were randomized to a control and two maintenance groups for 12 months, consisting of monthly 120-minute group meetings. These were designed to support participants in their behaviour change experiences and to overcome individual roadblocks to increase physical activity and improve dietary habits. Participants in the two intervention groups were asked to participate in a minimum of 4 and a maximum of 6 physical activity sessions weekly. Additionally, women in one of the two groups were asked to attend two weekend exercise sessions, including aerobic and strength exercises. Compliance was monitored on the basis of daily logs of physical activity. Average attendance to this phase was 68%. For the present analysis, data were pooled across groups.

Body Composition Measurements

Measurements of body composition using each technique were conducted according to standard procedures. Subjects came to the laboratory, after a 12-hours fast, and 24-hours without exercise, alcohol or stimulant beverages. All measurements were carried out in the same morning. In brief, the procedures were as follows.

Dual energy X-RAY absorptiometry

To estimate total body fat mass (TBFM), absolute and relative (%TBFM), trunk fat region of interest (TF-ROI) and abdominal fat region of interest (AF-ROI- region of interest between L₂-L₄, excluding lateral subcutaneous fat) (2) were made a total body scanner (QDR-1500, Hologic, Waltham, USA, pencil beam mode, software version 5.67 enhanced whole-body analyses) that measured the attenuation of x-rays pulsed between 70 and 140 kV synchronously with the line frequency for each pixel of the scanned image. Following the protocol for DXA described by the manufacturer, a step phantom with six fields of acrylic and aluminum of varying thickness and known absorptive properties was scanned alongside each subject to serve as an external standard for the analysis of different tissue composition. The same lab technician positioned the subjects, performed the scans and executed the analysis according to the operator's manual using the standard analysis protocol. Based on ten subjects, the coefficient of variation in our laboratory for fat mass (FM) is 2.9 %.

Anthropometry

All subjects were weighed to the nearest 0.01 kg wearing a bathing suit and without shoes on an electronic scale connected to the plethysmograph computer (BOD POD, Life Measurement Instruments, Concord, CA, USA). Height was measured to the nearest 0.1 cm with a stadiometer (Seca, Hamburg, Germany).

For results of *Chapter 3, 4 and 5* of this thesis, a trained researcher measured circumferences (waist, abdomen) according to the procedures of Lohman (3).

For data analysis, the averages of the three measurements were considered. Based on 10 repetitions, the technical error of measurement (TEM) and intraclass coefficient of correlation (ICC) were respectively, 0.37 cm and 1.00 for the abdominal circumference (AC) measured at the umbilical level and for the waist circumference (WC) measured midway between the last rib and the upper edge of the iliac crest, 0.62 cm and 1.00.

Physical Activity and Dietary Intake Assessment

Physical activity variables were measured at baseline and 4 months using one validated questionnaire for exercise and weight management behaviors (IPAQ- International physical activity questionnaire) (4). The questionnaire was design to be used by adults aged 18-65 yr and provided information on the time spent walking, in vigorous and moderate intensity activity and in sedentary activity. The IPAQ version used estimated total weekly physical activity by weighting the reported minutes per week within each activity category by a MET energy expenditure estimate assigned to each category of activity. MET levels were obtained from the 2000 compendium of physical activities to include moderate-intensity activities between 3 and 6 METs and vigorous-intensity activities as > 6 METs. The weight MET-minutes per week ($\text{MET} \cdot \text{Min} \cdot \text{wk}^{-1}$) were calculated as duration X frequency per week X MET intensity, which were summed across activity domains to produce a weighted estimate of total physical activity from all reposted activities per week ($\text{MET} \cdot \text{Min} \cdot \text{wk}^{-1}$) (4)

Vigorous physical activities are described as: the activities which take hard physical effort that have been done in the last 7 days. Vigorous physical activities make breath much harder than normal and may include heavy lifting, digging, aerobics, or fast bicycling. The register is only about those physical activities that have been done at

least 10 minutes at a time. Moderate physical activities are described as: the activities which take moderate physical effort that have been done in the last 7 days. Moderate physical activities make breath somewhat harder than normal and may include carrying light loads, bicycling at a regular pace, or doubles tennis. Do not include walking. The register is only about those physical activities that have been done at least 10 minutes at a time. Walking is described as: the time that has been spent walking in the last 7 days. This includes at work and at home, walking to travel from place to place, and any other walking that might be done solely for recreation, sport, exercise, or leisure. Sitting is described as: the time that has been spent sitting in the last 7 days. This includes time spent at work and at home, while doing course work, and during leisure time. This may include time spent sitting at a desk, visiting friends, reading or sitting or lying down to watch television (4). Dietary intake was estimated with 3-day 24h food records. Subjects were instructed regarding portion sizes, supplements, food preparation aspects, and others aspects pertaining to an accurate recording of their diet, previously to the collection of any diet data. Records were turned in and reviewed at the time of laboratory testing. Data was analyzed for energy (kilocalories). The diet records were entered and analyzed for energy nutrient intake using Food Processor SQL (ESHA, Salem, OR).

Statistical Analysis

The statistical analyses were completed using the Statistical Package for the Social Sciences version 14.0 (SPSS, Chicago, IL). Statistical significance was set at $p < 0.05$.

Descriptive statistics including means \pm SD was calculated for all outcome measurements in the three studies (*Chapter 3, 4 and 5*).

Multiple regression analysis was performed to assess the relationship between the independent variables and each of the dependent variables in separate models, adjusting for the effect of changes in exercise, energy intake change, and age in chapter 3 and 5. In this regression model, the selected predictors were forced into the model and the squared semi-partial correlation coefficient was calculated to quantify the unique contribution of each predictor to the variance in the dependent measure. In chapter 5 the correlations coefficients were compared by Med Calc program in order to assess the best predictors of total and abdominal fat mass and its alterations.

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CHAPTER 3

RESULTS

What baseline anthropometric measurements predict changes in total body, trunk, and abdominal fat mass with DXA and morphologic markers?

Abstract

Background: Abdominal fat can be estimated using a region of interest (ROI) selected by conventional whole body DXA. Using simple anthropometric measurements as pre-treatment predictors of body composition changes may be of great interest at clinical settings for weight-loss counseling. **Objective:** The purpose of this study was to identify the ability of pre-treatment anthropometric measures in predicting changes in total body fat mass (TBFMC), trunk fat region of interest (TF-ROIC), abdominal fat region of interest (AF-ROIC), assessed by DXA, waist circumference (WCC), body weight (BWC), abdominal circumference (ACC), sagittal diameter (SDC) and hip circumference (HCC) in a weight loss program. **Methods:** Subjects were 126 women (age:38.3±5.8yrs; BMI:30.3±3.8kg/m²). The International Physical Activity Questionnaire was used to evaluate physical activity (PA) and 3-day Food Records were used to estimate energy intake (EI). Multiple regression analysis was performed to assess the relationship between the independent variables and each of the dependent variables in separate models, adjusting for the effect of changes in exercise, energy intake change, and age. **Results:** TBFM and BW changes were -2.78±3.5 kg and -3.04±3.1 kg, respectively. WCC was -3.08±8.8 cm and ACC was -10.44±6.0 cm. TBFMC appear to be inversely related ($p<0.05$) with the initial BW ($\beta=-0.069$), BMI ($\beta=-0.194$), HC ($\beta=-0.100$), AC ($\beta=-0.064$) and SD ($\beta=-0.243$). ACC was inversely related ($p<0.05$) with initial BMI ($\beta=-0.327$), HC ($\beta=-0.294$) and AC ($\beta=-1.139$). **Conclusion:** Our findings showed that women with larger initial SD, BW, BMI, HC, and AC will lose higher amounts of total adiposity estimated by DXA. Baseline anthropometric measures could not predict changes in more specific areas of body fat than those estimated by DXA. However, higher initial BMI, HC and AC may predict changes in abdominal circumference.

Introduction

DXA has the potential to provide overall and regional assessment of body composition in terms of fat, lean mass and bone. DXA quantifies fat, rather than adipose tissue.

Several studies suggest that abdominal fat can be estimated using a region of interest selected by conventional whole body DXA (1-3). In addition, a few reports describe the capability of DXA to estimate changes in abdominal region (1, 4, 5). However, since this equipment is not always available in clinical settings, it is important to determine if DXA estimate changes can be predicted by simple pre-treatment anthropometric measurements, showing their usefulness in early detection of women with total and central fatness.

Simple anthropometric measurements, such as waist (WC) and hip (HC) circumferences, have been widely recommended to identify subjects at high risk of cardiovascular disease due to a strong relationship with atherosclerotic and thrombotic markers (6-10). Using these simple anthropometric measurements as pre-treatment predictors of body composition changes may be of great interest at clinical settings for weight-loss counseling. The National Heart, Lung, and Blood Institute (NHLBI) has recommended WC to be measured as part of the initial assessment of overweight and obese patients (11, 12). Despite its influence in health (8, 11, 13), WC has not been adopted in most clinical approaches. Klein and colleagues (8) has described the efficacy of WC measurements in different sites within the 10th rib and the iliac crest region. However, few studies have used initial anthropometric measurements such as abdominal circumference (AC), sagittal diameter (SD), HC, as baseline predictors of total and central adiposity loss, specifically regional changes estimated by dual-energy X-ray absorptiometry (DXA) (14, 15).

Therefore, the aim of the present study was to identify if simple pre-treatment anthropometric measurements predict changes in total body, trunk and abdominal fat mass among pre-

menopausal women who were involved in a weight control program based in caloric restriction and increased physical activity.

Methods

Subjects

Subjects were recruited from the community for a weight management program through newspaper ads, a website, email messages on listservs, and announcement flyers. In order to be included in the study, subjects had to be older than 24 years, be premenopausal and not currently pregnant, have a BMI higher than 24.9 kg/m^2 , and be free from major disease. After several orientation sessions, 152 women signed up for the program. During the run-in phase, four women decided not to participate (reporting new time and scheduling conflicts), four others were excluded as they did not comply with testing requirements, three women found out they were pregnant or decided to attempt pregnancy, and one subject was found to be ineligible due to medical reasons (untreated hyperthyroidism). Thus, a total of 140 women were considered for the study. Attrition was 17.1%. All participants agreed to refrain from participating in any other weight loss program and gave written informed consent prior to participation in the study. The Faculty of Human Movement's Ethics Committee approved the present study.

Assessments

Body composition was measured in the 126 females who concluded the study. After a 12-hour fast, all subjects came to the laboratory where all measurements were carried out on the same morning.

Anthropometric measurements

After voiding, body weight and height were measured on an electronic scale with a stadiometer (SECA, Hamburg, Germany). Body weight (BW) was measured to the nearest 0.01 kg. Briefly, WC was measured with the subject standing, midway between the last rib and the upper edge of the iliac crest; HC was measured at the greater gluteal curvature, and AC was measured at the umbilical level. These measurements were taken with a stiff fiberglass tape to the closest 0.1 cm. All anthropometric measurements were taken by previously trained technicians and repeated 3 times, with the mean value being used. BMI was calculated as weight divided by height squared (kilograms per square meter). SD was measured in a horizontal position with an anthropometer.

Dual energy X-Ray absorptiometry

A total body scanner (QDR-1500, Hologic, Waltham, USA, pencil beam mode, software version 5.67 enhanced whole-body analyses) was used to estimate total, absolute and relative, fat mass (TBFM, %TBFM), trunk fat mass region of interest (TF-ROI) and abdominal fat mass region of interest (AF-ROI - between L₂-L₄, excluding lateral subcutaneous fat) (16). In 2000, Kamel et al. (16) suggested that these DXA measurements may be used in predicting intra-abdominal fat. This scan measured the attenuation of x-rays pulsed between 70 and 140 kV synchronously with the line frequency for each pixel of the scanned image. Following the protocol for DXA described by the manufacturer, a step phantom with six fields of acrylic and aluminium of varying thickness and known absorptive properties was scanned alongside each subject as an external standard for the analysis of different tissue composition. The laboratory technician who collaborated in this study has positioned each subjects and performed the scans and posterior analysis according to the operator's manual using the standard analysis protocol. The coefficient of variation in our laboratory for fat mass is 2.9%, this being based on data from 10 subjects.

Physical activity and dietary intake assessment

Physical activity variables were measured at baseline and after 4 months using a validated questionnaire (IPAQ- International physical activity questionnaire). The questionnaire was designed to be applied to adults aged 18-65 yr and provides information on the time spent walking, in vigorous and moderate intensity activity, and in sedentary activity. The IPAQ version used estimated the total weekly physical activity by weighting the reported minutes per week in each activity category by a MET energy expenditure estimate assigned to each category of activity. MET levels were obtained from the 2000 compendium of physical activities classifying as moderate-intensity activities those with MET between 3 and 6 and vigorous-intensity activities for more than 6 METs. The weight MET-minutes per week ($\text{MET} \cdot \text{min} \cdot \text{wk}^{-1}$) were calculated as $\{\text{duration} \times \text{frequency per week} \times \text{MET intensity}\}$, which were summed across activity domains to produce a weighted estimate of total physical activity from all reported activities per week ($\text{MET} \cdot \text{min} \cdot \text{wk}^{-1}$) (17). Dietary intake was estimated with 3-day 24h food records. Subjects were instructed regarding portion sizes, supplements, food preparation aspects, and others aspects pertaining to an accurate recording of their diet, previously to the collection of any diet data. Records were turned in and reviewed at the time of laboratory testing. Data was analyzed for energy (kilocalories). The diet records were entered and analyzed for energy nutrient intake using Food Processor SQL (ESHA, Salem, OR).

Intervention

Subjects attended 15 treatment sessions in groups of 32 to 35 women, for approximately 4 months. Average attendance to the treatment sessions was 83%. Sessions lasted 120 minutes

and included educational and experiential content in the areas of physical activity and exercise, diet and eating behaviour, and behaviour modification. The intervention has been previously described (18). Physical activity topics included learning the energy expenditure associated with typical activities, increasing daily walking and adopting a physically activity lifestyle, planning and implementing a structured exercise plan, setting appropriate goals, using logs and a pedometer for self-monitoring, choosing the right type of exercise, among many others. Examples of covered nutrition topics are the energy, fat, and fiber contents, and the energy density of common foods, the role of breakfast and meal frequency on weight control, reducing portion size, strategies to reduce diet's fat content, preventing binge and emotional eating, planning for special occasions, and reducing hunger by increasing meal satiety (e.g., increasing fibre content). Cognitive and behaviour skills, such as self-monitoring, self-efficacy enhancement, dealing with lapses and relapses, enhancing body image, using contingency management strategies, and social support, were also part of the curriculum. Subjects were instructed to make small but enduring reductions in the energy intake and also to increase energy expenditure in order to induce a daily energy deficit of approximately 300 kcal. Although weight was monitored weekly, subjects were advised that long-term weight reduction (i.e., after 1-2 years), was the primary target, in opposition to a rapid weight change. Reaching a 3 to 5% weight loss at 4 months was set as an appropriate goal for all participants.

Statistical analysis

Descriptive statistics including mean values and standard deviations were calculated for all outcome measurements. The dependent measures obtained by DXA and simple anthropometric measures were expressed as the difference between 4-months and baseline observed values. The independent variables were the initial values of WC, HC, BW, BMI and SD.

Multiple regression analysis was performed to assess the relationship between the independent variables and each of the dependent variables in separate models, adjusting for the effect of changes in exercise, energy intake change, and age. The statistical analyses were completed using the Statistical Package for the Social Sciences version 14.0 (SPSS, Chicago, IL).

Results

Table 1 shows individual body composition changes for all 126 participants who concluded the program. Average weight change was -3.04 ± 3.1 kg ($p < 0.05$). The range for weight change was about 19 kg. About 56% of participants lost more than 3% of their initial BW, reaching the goal for 4-months weight loss. Forty four percent of all women did not reach the 4-months weight loss goal. Significant differences between the baseline and post-weight loss intervention were observed for BW, all body composition variables and exercise expenditure ($p < 0.05$).

Table 1- Mean, standard deviation of initial, final and change values

N =126	X \pm SD initial	X \pm SD final	X \pm SD change	Significance
Age (yrs)	38.13 \pm 5.9	-	-	
BW (kg)	78.02 \pm 10.9	74.97 \pm 10.7	-3.04 \pm 3.1	<0.001

BMI (kg/cm ²)	30.18±3.8	29.01±3.7	-1.17±3.2	<0.001
WC (cm)	91.42±8.9	88.34±9.4	-3.08±8.8	<0.001
AC (cm)	107.47±9.7	97.12±10.5	-10.44±6.0	<0.001
HC (cm)	111.48±7.2	108.73±7.2	-2.75±3.1	<0.001
TBFM (kg)	36.09±8.2	33.30±8.2	-2.78±3.5	<0.001
TF-ROI (kg)	17.99±4.9	16.21±5.1	-1.67±1.9	<0.001
TAF-ROI (kg)	3.85±1.46	3.33±1.25	-0.52±9.000	<0.001
AF-ROI (kg)	3.05±1.07	2.65±9.12	-0, 405±677.1	<0.001
TKD (kcal)	124.06±191.77	316.14±248.68	+192.07±256.8	<0.001

Body weight (BW), Body mass index (BMI), Waist circumference (WC), Abdominal circumference (AC), Hip circumference (HC), Total body fat mass (TBFM), Trunk fat region of interest (TF-ROI), Total abdominal fat region of interest (TAF-ROI), Abdominal fat region of interest (AF-ROI) and Total calories expended per day (TKD).

As seen in Figure 1 WC changed 3.36% (of an initial mean value of 91.42 cm) and AC changed 9,71% (of an initial mean value of 107.47 cm). Changes in these two abdominal variables were statistically significant ($p < 0.001$).

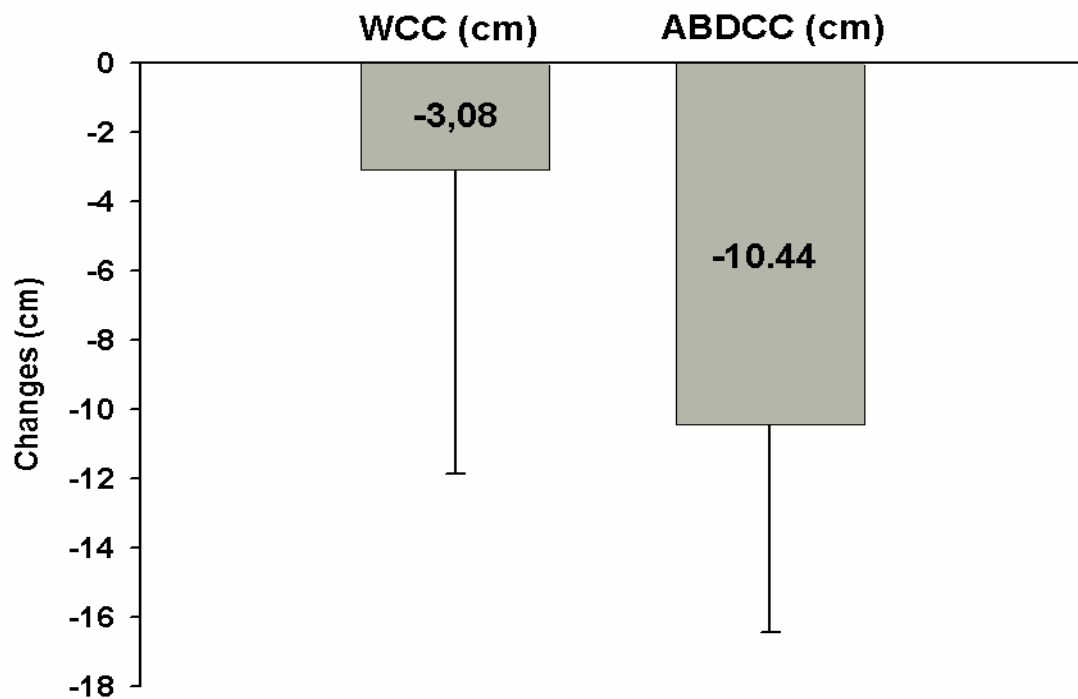


Figure 1: Changes in WC and AC

The results presented in table 2 show a consistent association of initial values of BW, BMI, HC, AC and SD with total body fat mass change, controlling for energy intake, caloric expenditure and age. WC did not explain any changes in total body fat mass. Given that change values were calculated as the difference between initial and post-intervention values, negative associations mean that women who lost more total body fat mass had higher initial values of BW, BMI, HC, AC and SD.

Table 2: Linear regression analysis for the selected independent variables and changes in total body fat mass

Independent Variables	Total Body Fat Mass Change		
	β	SE	p
<i>Body Weight</i>	-0.069	0.028	0.016*
<i>Body Mass Index</i>	-0.194	0.084	0.024*
<i>Waist Circumference</i>	-0.061	0.037	0.099
<i>Hip Circumference</i>	-0.100	0.043	0.021*
<i>Abdominal Circumference</i>	-0.064	0.032	0.048*
<i>Sagittal Diameter</i>	-0.243	0.121	0.047*

β , Beta; SE, Standard error; p, significance; Controlling for caloric expenditure, energy intake and age.

As indicated in table 3, the initial values of BW, BMI, WC, AC, HC and SD did not predict trunk fat region of interest change and abdominal fat region of interest change.

Table 3: Linear regression analysis for the selected independent variables and changes in trunk fat region of interest and abdominal fat region of interest

Independent Variables	Trunk Fat ROI Change			Abdominal Fat ROI Change		
	β	SE	p	β	SE	p

Body Weight	-0.020	0.016	0.211	-4.347	5.610	0.440
Body Mass Index	-0.081	0.047	0.090	-19.031	17.245	0.272
Waist Circumference	-0.017	0.020	0.399	-4.283	7.266	0.395
Hip Circumference	-0.028	0.024	0.404	4.988	8.682	0.567
Abdominal Circumference	-0.015	0.018	0.399	-0.030	6.510	0.993
Sagittal Diameter	-0.097	0.068	0.152	-11.794	24.117	0.626

β , Beta; SE, Standard error; p, significance; Controlling for caloric expenditure, energy intake and age.

The results presented in table 4 showed a consistent association between initial values of BMI, AC and HC with abdominal circumference change, controlling for energy intake, caloric expenditure and age. WC changes were not explained by any independent variables. Initial values of HC were negatively associated with changes in HC. Again, these results suggest that women who had higher initial values of BMI, AC and HC lost more centimetres at the abdominal area. The same happens with initial values of HC and changes in the hip area.

Table 4: Linear regression analysis for the selected independent variables and changes in waist circumference, abdominal circumference and hip circumference

Independent Variables	Waist Circumference Change			Abdominal Circumference Change			Hip Circumference Change		
	β	SE	p	β	SE	p	β	SE	p
Body Weight	-0.023	0.027	0.405	-0.091	0.050	0.073	-0.021	0.026	0.43

Body Mass Index	-0.067	0.081	0.410	-.327	0.151	0.032*	-.042	0.079	0.596
Waist Circumference	-.010	0.035	0.775	-.021	0.066	0.748	.009	0.034	0.789
Hip Circumference	-.035	0.041	0.400	-.294	0.073	0.000*	-.101	0.039	0.011*
Abdominal Circumference	0.018	0.031	0.517	-1.139	0.057	0.016*	-.030	0.030	0.315
Sagittal Diameter	-.054	0.116	0.642	-.156	0.219	0.477	-.067	0.113	0.556

β, Beta; SE, Standard error; p, significance; Controlling for caloric expenditure, energy intake and age.

Discussion

The purpose of this study was to identify the best pre-treatment anthropometric body composition predictors of short-term total body, trunk and abdominal fat mass loss, estimated by DXA, among pre-menopausal women who were involved in a weight control program based in caloric restriction and increased physical activity.

To this end, we initially built a large database of anthropometrics variables as potential predictors. In the present report, five variables, which were shown to be related with weight loss in previous studies (19-22), were examined to understand how body composition anthropometrics parameters predict fat mass loss.

By the end of this short-term weight loss program participants lost 3.04 kg (3.9% of their initial weight). These results were more modest than those reported for other interventions with the same characteristics and duration (23-26). Some short-term investigations showed a superior weight loss in women with the same age, however, these studies, usually, have a higher caloric

restriction (27-30). In fact, the present study did not suggest a very-low calorie diet (VLCD). The aim of the intervention was to reduced energy intake below the body's energy needs in a small negative balance, introducing the concept of a healthy lifestyle adaptable to the rest of their life.

It is common for weight loss programs to reduce energy intake to 1200-1500 kcal per day to induce weight loss in overweight adults, which has been shown to be safe and effective for weight reduction in individuals averaging 78.0 kg (range of 59.1 kg to 113.7 kg) before weight loss. In addition, this intervention showed that these women expended about 192 kcal d⁻¹ in physical activity. Despite these mean values, each woman had her energy intake adjusted to her body weight, to elicit an energy deficit of 500-1000 kcal.d⁻¹, according to initial levels of energy expenditure.

An important finding was that WC only decreased 3.08 cm, comparing with a greater reduction in abdominal circumference (10.44 cm). This shows that these women lost more volume in the abdominal area than in waist area. Usually, WC is used as an indirect measurement of weight change (19, 22, 31) and is often used as a surrogate marker of abdominal fat mass, because WC correlates with abdominal fat mass (32) and it is also associated with cardiometabolic disease risk (33). However, our study shows a higher reduction of abdominal circumference, which suggests that this particular body region is more affected by weight loss. These results are in agreement with the question raised by the Shaping America's Health: Association for Weight Management and Obesity Prevention (8). This consensus statement's main goal was to address the issue of the best morphological measurement in the abdominal region to estimate abdominal fat mass. Another study has compared 4 sites to measure WC and concluded that the WC measured just above the iliac crest presented higher values in women (34). The authors observed that the waist shape superior to the iliac crest decreases more than the waist shape in other regions of the trunk above the iliac crest. This WC measurement is usually applied in

studies measuring VAT with a single computed tomography (35) or magnet resonance imaging (36) slice at the L4-L5 level, because the iliac crest is closer to L4-L5 than are the others WC sites. Our study used the WC site recommended by the NIH Guidelines (37) and as it was applied in the third National Health and Nutrition Examination Survey. However, the abdominal circumference found in our study was even higher than this WC change. Therefore, this abdomen area could be seen as another site to take into consideration in weight management interventions, particularly in women. The same study (34) considered 14 different sites to measure WC and grouped them into 4 sites for analysis. These 14 sites were all located within the region from the 10th rib to the iliac crest and none of them were located at the higher abdominal area as ours.

Another interesting result was the proportion of trunk fat mass change considering total body fat mass change, more precisely, 60.0% (1.67 kg) of total body fat mass loss was in the trunk area, suggesting that fat located in the trunk has a higher predisposition to be eliminated in obese and overweight women. From total trunk fat mass loss, 31.8% was in total abdominal region and 24.2% was in abdominal region of interest. These findings are in agreement with the studies that describe a higher predisposition to eliminate trunk fat mass relatively too hip fat mass as a consequence of a higher incidence of lipolytic action in the trunk area, namely, in abdominal region (38, 39). All the studies with the same results regarding trunk fat mass loss, including abdominal fat mass, have described the influence of exercise on fat distribution losses (38, 40). However, our research showed the same results, even when weight loss was only due to a daily physical activity approach and not to a great emphasis on structured exercise.

The results of the analysis examining the explanation for total body, trunk, and abdominal fat mass changes demonstrated some differences in the interpretation of the results. In the regression model, the relation between initial body weight and the dependent variable, total body fat mass change, has shown a significant negative association revealing a higher

predisposition of heavier women to lose fat mass, controlling for energy expenditure, energy intake and age.

In this model, initial BMI presented a negative significant association with total body fat mass change, which accentuates the fact that women with higher BMI has a higher predisposition to lose total body fat mass. Total body fat mass change was negatively influenced by initial values of hip circumference, meaning that women with higher levels of hip circumference lost more fat mass in the whole body even when exercise, energy intake and age were controlled, showing that this happened independently of energy expenditure, energy consumed or pre-menopause state. Similar results were seen analysing the predictability of sagittal diameter in total body fat mass change. These results suggest that baseline values of body weight, BMI, sagittal diameter, and hip circumference are good predictors of total body fat mass changes. Abdominal circumference showed a higher reduction, caused by weight loss, than WC and showed a higher capability to predict total body fat mass change, because no association was present between initial WC values and this dependent variable. The negative significant association observed between initial abdominal circumference and reduction in body fat mass shows that abdominal circumference may predict total body fat mass loss in opposition to WC, which cannot predict changes in total body fat mass. For that reason we suggest the use of abdominal circumference in clinical approaches for an early detection of total fat mass loss, instead of WC.

Additionally, baseline anthropometric measures could not predict changes in more specific areas of body fat estimated by DXA. These findings indicate that simple morphological parameters are able to predict changes in total body fat mass but unable to predict regional fat mass changes in the trunk and the abdomen areas during a weight loss program in overweight and obese women. However, there are several studies (22, 32) describing the capability of WC

and sagittal diameter to predict visceral fat mass measured with sophisticated equipment. Nevertheless, WC and sagittal diameter have not the same capability to monitor changes in DXA regions of interest.

Conclusion

The present study highlighted the differences between fat losses in waist and abdominal area, showed a higher capability of abdominal circumference to predict body fat mass loss than waist circumference and identified important technical measurement issues that require further discussion and exploration. Baseline values of body weight, BMI, sagittal diameter and hip circumference appear to be good predictors of total body fat mass changes. Our findings suggest that BMI, abdominal circumference and hip circumference may predict abdominal circumference changes. Baseline anthropometric measures could not predict changes in DXA regions of interest.

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CHAPTER 4

RESULTS

The association between type and intensity of physical activity and changes in total and abdominal fat mass during weight reduction in overweight and obese women

Abstract

Background: Physical activity (PA) may interact with energy intake and affect body balance.

Objective: Examine the influence of different types of PA in body weight (BW), total body fat mass (TBFM), abdominal fat region of interest (AF-ROI) and trunk fat region of interest (TF-ROI)

selected by conventional whole body DXA in two different levels of excess BW. **Methods:** Data

was collected in 121 overweight and obese women (age, 38.2 ± 5.9 y; BMI, 30.2 ± 3.8 kg/m²) that

attended a 4-months weight loss program. PA changing values such as total PA (TPAC), total

minutes sit (SITC), vigorous PA (VPAC), moderate PA (MPAC), total minutes walking (WKC) and

total calories spent per day (TKDC) were measured using a validated questionnaire (IPAQ-

International Physical Activity Questionnaire). Changes in TBFM (TBFMC), TF-ROI (TF-ROIC) and

AF-ROI (AF-ROIC) were estimated by DXA. Changes in BW (BWC), WC (WCC) and HC (HCC)

were assessed using the standard anthropometric procedures. Variables were measured at

baseline and at the end of the intervention. Changes in all variables were computed as the

difference between final and baseline values. Multiple regression analysis was performed to

assess the multivariate relationships between PA variables and body composition variables. Of

all participants, 20.3% (31 subjects) did not finish the program. **Results:** After the intervention,

the mean TBFMC and BWC were -2.84 ± 3.5 kg and -3.11 ± 13 kg, respectively. Controlling for

age, all PA change variables were not associated with TBFMC, BWC and TF-ROIC ($p > 0.05$).

TPAC was inversely associated with AF-ROIC ($\beta = -0.367$, $p = 0.037$). An inverse association

between WKC and AF-ROIC ($\beta = -0.805$, $p = 0.003$) was found. These results were observed in

obese women but not in overweight women. **Conclusion:** An increase in total physical activity

and in total minutes walking plays an important role on reducing central obesity in obese

women.

Introduction

Physical activity may interact with energy intake and affect the balance of both (1). Several short-term weight loss programs (6 months or less), document the effect of exercise and energy intake in human body composition (2) and some other studies report a high contribution of exercise on weight loss (3-5). Ross et al. (5) have reported a weight loss of about 7.6 kg for two groups who participated in a 3 months weight loss program, which was based on energy restriction (700 kcal/d). This restriction was induced by a reduction in energy intake in the diet group, compared with an increase in energy expenditure promoted by physical activity in the exercise group. Hagan et al. (6) reported a greater reduction on body weight in interventions including physical activity. Similar results are documented in a review of literature developed by the National Heart Lung and Blood Institute, confirming the effect of exercise in clinic intervention programs (7).

In clinical interventions terms, it is important to understand the role of physical activity in weight loss and in health. As energy expenditure may not be sufficient to promote weight loss, although it may promote health benefits related with fat loss in specific metabolic regions (eg. abdominal area) (5).

It is important to understand which dimension of exercise promotes weight loss, in particular abdominal fat mass, as upper body fat mass is related with an increasing risk of developing metabolic disorders, such as insulin resistance (8), hypertension and hyperlipidemia, when compared with lower body fat mass in obese and non-obese women (9, 10). Besides total energy expenditure, moderate or intense physical activity may have selected effects on total or local depots.

Some studies claim that subjects who participate in exercise programs have only a small decrease on body weight and measures of body fatness, and this appears to occur in a dose-

response manner (11). An increase in total energy expenditure and high intensity exercise appear to be the most important aspects of successful exercise-induced weight loss (4). Nevertheless, it is important to understand if this occurs with specific body regions. There is insufficient evidence to determine whether an increase on physical activity and its different dimensions is associated with a reduction of abdominal obesity in a dose-response manner (12). On the other hand, all the literature reports the effect of structured exercise on the reduction of abdominal fat mass, which is measured using sophisticated equipment (13, 14), but for lifestyle interventions only the waist circumference has been considered (15-19).

Therefore, the aim of the present study was to examine the influence of different types and intensities of physical activity in body weight, waist and hip circumferences, total body fat mass, abdominal fat mass and trunk fat mass regions of interest in overweight and obese women, promoted by a lifestyle intervention program.

Methods

Subjects

Women for this study were recruited from the community for a 2-year weight management program through newspaper ads, a website, email messages on listservs, and flyers. In order to be eligible for the study, these subjects had to be older than 24 years, be pre-menopausal and not currently pregnant, have a BMI higher than 24.9 kg/m², and be free from major disease. After several orientation sessions, 152 women signed up for the program. During the run-in phase, four women decided not to participate (reporting unexpected time and scheduling conflicts), four did not comply with testing requirements, three women found out they were pregnant or decided to attempt pregnancy, and one woman was found ineligible due to medical reasons (untreated hyperthyroidism), leaving a total of 140 women who started the intervention.

Attrition was 20.3%. All participants agreed to refrain from participating in any other weight loss program and gave written informed consent prior to their participation in the study. The Faculty of Human Movement's Ethics Committee approved the present study.

Assessments

Body composition was measured in the 121 females who concluded the study. After a 12-hour fast, all subjects came to the laboratory where all measurements were carried out on the same morning.

Anthropometric measurements:

After voiding, body weight and height were measured on an electronic scale with a stadiometer (SECA, Hamburg, Germany). Body weight (BW) was measured to the nearest 0.01 kg. Briefly, WC was measured with the subject standing, midway between the last rib and the upper edge of the iliac crest; and HC was measured at the greater gluteal curvature. Both measurements were taken with a stiff fiberglass tape to the closest 0.1 cm. All anthropometric measurements were taken by previously trained technicians and repeated 3 times, with the mean value being used. Body mass index was calculated as weight divided by height squared (kilograms per square meter).

Dual energy X-Ray absorptiometry.

A total body scanner (QDR-1500, Hologic, Waltham, USA, pencil beam mode, software version 5.67 enhanced whole-body analyses) was used to estimate total, absolute and relative, fat mass (TFM, %TFM), trunk fat mass region of interest (TF-ROI) and abdominal fat mass region of interest (AF-ROI between L₂-L₄, excluding

lateral subcutaneous fat) (20). This scan measured the attenuation of x-rays pulsed between 70 and 140 kV synchronously with the line frequency for each pixel of the scanned image. Following the protocol for DXA described by the manufacturer, a step phantom with six fields of acrylic and aluminium of varying thickness and known absorptive properties was scanned alongside each subject as an external standard for the analysis of different tissue composition. The laboratory technician who collaborated in this study has positioned each subjects and performed the scans and posterior analysis according to the operator's manual using the standard analysis protocol. The coefficient of variation in our laboratory for FM is 2.9%, this being based on data from 10 subjects.

Physical activity and dietary intake assessment

Physical activity variables were measured at baseline and after 4 months using a validated questionnaire for exercise and weight management behaviours (IPAQ-International physical activity questionnaire). The questionnaire was designed to be applied to adults aged 18-65 yr and provides information on the time spent in walking, in vigorous and moderate intensity activity and in sedentary activity. The IPAQ version used estimates total weekly physical activity by weighting the reported minutes per week within each activity category by a MET energy expenditure estimate assigned to each category of activity. MET levels were obtained from the 2000 compendium of physical activities including moderate-intensity activities (between 3 and 6 METs) and vigorous-intensity activities (> 6 METs). The weight MET-minutes per week ($\text{MET} \cdot \text{Min} \cdot \text{wk}^{-1}$) was calculated as (duration \times frequency per week \times MET intensity) which were added across activity domains to produce a weighted estimate of total physical activity from all reported activities per week ($\text{MET} \cdot \text{Min} \cdot \text{wk}^{-1}$). Overall, the IPAQ questionnaires produced repeatable data (Spearman's rho clustered around 0.8), with

comparable data from short and long forms. Criterion validity had a median rho of about 0.30, which was comparable to most other self-report validation studies (21).

Vigorous physical activities are described as the activities done in the last 7 days which take a big physical effort. Vigorous physical activities make breath much harder than normal and may include heavy lifting, digging, aerobics, or fast bicycling. Were only considered physical activities performed for at least 10 minutes at a time.

Moderate physical activities are described as the activities which take a moderate physical effort that have been done in the last 7 days. Moderate physical activities make breath somewhat harder than normal and may include carrying light loads, bicycling at a regular pace, or doubles tennis, not including walking. Were only considered physical activities performed for at least 10 minutes at a time.

Walking is described as the time that has been spent walking in the last 7 days. This includes at work and at home, walking when travelling from place to place, and any other walking that might be done solely for recreation, sport, exercise, or leisure.

Sitting is described as the time that has been spent sitting in the last 7 days. This includes time spent at work and at home, while doing course work, and during leisure time. This may include time spent sitting at a desk, visiting friends, reading or sitting or lying down to watch television.

Dietary intake was estimated with 3-day 24h food records. Subjects were instructed regarding portion sizes, supplements, food preparation aspects, and others aspects pertaining to an accurate recording of their diet, previously to the collection of any diet data. Records were turned in and reviewed at the time of laboratory testing. Data was analyzed for energy (kilocalories). The diet records were entered and analyzed for energy nutrient intake using Food Processor SQL (ESHA, Salem, OR).

Intervention

Subjects attended 15 treatment sessions in groups of 32 to 35 women, for approximately 4 months. Average attendance to the treatment sessions was 83%. Sessions lasted 120 minutes and included educational and experiential contents in the areas of physical activity and exercise, diet and eating behaviour, and behaviour modification. Some of these behaviour modification have already been studied by Teixeira et al. (22). Physical activity topics included: learning the energy cost associated with typical activities, increasing daily walking and lifestyle physical activity, planning and implementing a structured exercise plan, setting appropriate goals, using logs and the pedometer for self-monitoring, and choosing the right type of exercise, among many others. Examples of covered nutrition topics are the caloric, fat, and fiber content, and the energy density of common foods, the role of breakfast and meal frequency for weight control, reducing portion size, strategies to reduce the diet's fat content, preventing binge and emotional eating, planning for special occasions, and reducing hunger by increasing meal satiety (e.g., increasing fiber content). Cognitive and behaviour skills like self-monitoring, self-efficacy enhancement, dealing with lapses and relapses, enhancing body image, using contingency management strategies, and social support, were also part of the curriculum. Subjects were instructed and motivated to make small but enduring reductions in caloric intake and to increase energy expenditure to induce a daily energy deficit of approximately 300 kcal. Although weight was monitored weekly, subjects were advised that a long-term weight reduction (i.e., after 1-2 years), was the primary target, in opposition to a rapid weight loss. Reaching a 3 to 5% weight loss at 4 months was set as an appropriate goal for all participants.

Statistical analysis

Measures of central tendency and dispersion, distribution, and normality were examined for all variables at baseline and after 4 months. The dependent measures were expressed as the difference between 4-month and baseline body composition variables. The dependent variables were body weight change (BWC), total body fat mass change (TBFMC), trunk fat region of interest change (TF-ROIC) and abdominal fat region of interest change (AF-ROI).

Physical activity changing values as, total physical activity (TPAC), total minutes sit (SITC), vigorous physical activity (VPAC), moderate physical activity (MPAC), total minutes walking (WKC) and total calories expended a day (TCDC) were the independent variables.

Multiple regression analysis was performed to assess the multivariate relationship between the independent variables and BW, abdominal, trunk fat regions of interest and TBFM changes, controlling for age in all sample, in overweight and in obese women.

Statistical analyses were completed using the Statistical Package for the Social Sciences version 14.0 (SPSS, Chicago, IL).

Results

Table 1 presents mean, standard deviation and range of initial values.

Table 1- Mean, standard deviation and limits of initial values

N =121	X ± SD initial	Range
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Age (yrs)	38.2±5.9	25.0-49.0
BW (kg)	78.3±11.0	59.1-113.1
BMI (kg/m ²)	30.2±3.8	25.1-45.2
WC (cm)	91.6±9.0	73.9-125.
HC (cm)	111.7±7.2	94.7-134.6
TBFM (kg)	36.3±8.3	23.5-60.3
TF-ROI (kg)	17.9±4.9	8.9-32.3
AF-ROI (kg)	3.02±1.03	1.36-7.59
TCD (Kcal)	125.8±193.5	0.00-1172.2
WK (min/week)	82.8±137.3	0.00-840.0
MPA (min/week)	41.2±79.9	0.00-420.0
VPA (min/week)	28.4±75.0	0.00-375.0
TPA (min/week)	152.4±204.1	0.00-885.00
SIT (min/week)	2442.8±1119.9	240.0-6420.0

Body weight (BW), Body mass index (BMI), Waist circumference (WC), Hip circumference (HC) Total body fat mass (TBFM), Trunk fat mass (TF-ROI), abdominal fat mass (AF-ROI), Total calories expended per day (TCD), Total Minutes Walking (WK), Moderated Physical Activity (MPA), Vigorous Physical Activity (VPA), Total Physical Activity (TPA), Total minutes sit (SIT).

Table 2 shows individual body composition changes for all 121 participants who completed the program. Average weight change was -3.11 ± 1.3 kg. The range for weight change was about 19 kg. The participants lost 3.9% of their initial weight.

Significant differences ($p < 0.05$) between baseline and post-weight loss intervention were observed for BW, WC and HC, and all other body composition and exercise variables, except for MPA. The group of overweight women ($N=65$) ($BMI < 30 \text{ kg/cm}^2$), with a mean age of 37.4 yrs and 71.26 ± 5.3 kg of weight, showed individual body composition changes in 65

participants. The average weight change was -2.65 ± 2.8 kg, about 3.7 % of their initial weight. Significant differences ($p < 0.05$) between the baseline and the pos-weight loss intervention were observed for BW and all body composition and exercise variables. The group of obese women ($N = 56$) ($BMI \geq 30$ kg/cm²), with a mean age of 39.1 yrs and 86.4 ± 10.4 kg of weight, showed individual body composition changes in 56 participants. The average weight change was -3.64 ± 3.4 kg, about 4.2 % of their initial weight. Significant differences ($p < 0.05$) between baseline and pos-weight loss intervention were observed for BW, anthropometric variables, and all other body composition and exercise variables.

Table 2- Change values for all the three groups

Age (yrs)	X ± SD change	X ± SD change	X ± SD change
38.24±5.9	N= 121/ BMI ≥ 25	N=65/ BMI < 30	N=56/ BMI ≥ 30
	kg/cm²	kg/cm²	kg/cm²
BW (kg)	-3.11±1.3*	-2.65±2.8*	-3.64±3.4*
BMI (kg/cm ²)	-1.19±1.2*	-1.01±1.1*	-1.41±1.3*
WC (cm)	-3.15±3.2*	-2.87±2.5*	-3.47±3.9*
HC (cm)	-2.81±3.2*	-2.90±3.0*	-2.71±3.4*
TBFM (kg)	-2.84±3.5*	-2.37±2.9*	-3.39±3.0*
TF-ROI (kg)	-1.67±1.9*	-1.52±1.6*	-1.84±2.3*
AF-ROI (kg)	-0, 374±0.63*	-0, 290±0.36*	-0, 464±0.82
TCD	+189.1±260.1*	+184.6±253.9*	196.5±269.5*
WK (min/week)	108.7±199.4*	125.0±203.1*	89.9±195.3*
MPA (min/week)	85.5±194.9	93.2±214.3*	76.4±171.2*
VPA (min/week)	51.8±92.3*	53.9±102.5*	49.9±79.7*

TPA (min/week)	245.9±338.7*	272.2±365.3*	185.0±252.1*
SIT (min/week)	-505.8±924.4*	-613.3±1085.6*	-384.6±690.6*

Body weight (BW), Body mass index (BMI), Waist circumference (WC), Hip circumference (HC) Total body fat mass (TBFM), Trunk fat mass (TF-ROI), abdominal fat mass (AF-ROI), Total calories expended per day (TCD), Total Minutes Walking (WK), Moderated Physical Activity (MPA), Vigorous Physical Activity (VPA), Total Physical Activity (TPA), Total minutes sit (SIT). P<0.05

The results from the regression models presented in Table 3, for the whole sample did not show any association between energy expenditure variables and total body fat mass loss ($p > 0.05$) in all the three groups. The same results were seen between physical activity variables and BW ($p > 0.05$).

Table 3: Linear regression analysis for the selected independent variables and changes in total body fat mass and in body weight

Independent Variables	Body Weight Change			Total Body Fat Mass Change		
	β	SE	p	β	SE	p
N= 121						
<i>Vigorous Physical Activity</i>	-0.004	0.003	0.169	-0.006	0.004	0.126
<i>Moderate Physical Activity</i>	0.000	0.001	0.985	0.000	0.002	0.948
<i>Total Physical Activity</i>	0.000	0.001	0.638	0.001	0.001	0.593
<i>Walking</i>	0.000	0.001	0.860	0.000	0.002	0.864
<i>Sitting</i>	0.000	0.000	0.526	0.000	0.000	0.586
<i>TCD</i>	-0.001	0.001	0.559	-0.001	0.001	0.363
N= 65						
<i>Vigorous Physical Activity</i>	-0.005	0.004	0.196	-0.003	0.004	0.370
<i>Moderate Physical Activity</i>	-0.003	0.002	0.113	-0.001	0.002	0.507
<i>Total Physical Activity</i>	-0.001	0.001	0.355	0.000	0.001	0.730

Walking	0.001	0.002	0.578	0.001	0.002	0.627
Sitting	0.000	0.000	0.924	0.000	0.000	0.893
TCD	-0.001	0.000	0.269	-0.001	0.001	0.655
N= 56						
Vigorous Physical Activity	-0.003	0.006	0.563	-0.009	0.007	0.206
Moderate Physical Activity	0.004	0.003	0.147	0.001	0.003	0.705
Total Physical Activity	0.000	0.002	0.953	-0.001	0.002	0.507
Walking	-0.002	0.002	0.347	-0.002	0.003	0.389
Sitting	-0.001	0.001	0.269	0.001	0.001	0.493
TCD	0.001	0.002	0.790	-0.002	0.002	0.445

β, Beta; SE, Standard error; p, significance. Controlling for age and energy intake.

As shown in Table 4, when considering the whole sample and controlling for age and energy intake, TPAC ($\beta = -0.367$, $p < 0.05$) and WKC ($\beta = -0.805$, $p < 0.01$) were inversely related with abdominal fat region of interest and the same results were seen in the obese group alone related to WKC ($\beta = -1.670$, $p < 0.01$).

Table 4: Linear regression analysis for the selected independent variables and changes in internal abdominal fat mass and in trunk fat mass

Independent	Abdominal Fat Mass Change	Trunk Fat Mass Change
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	β	SE	p	β	SE	p
<i>Vigorous Physical Activity</i>	-0.562	0.681	0.411	-0.003	0.002	0.091
<i>Moderate Physical Activity</i>	-0.144	0.306	0.639	-0.001	0.001	0.517
<i>Total Physical Activity</i>	-0.367	0.174	0.037*	0.001	0.001	0.357
<i>Walking</i>	-0.805	0.291	0.007*	0.000	0.001	0.853
<i>Sitting</i>	-0.019	0.072	0.789	0.000	0.000	0.685
<i>TCD</i>	-0.457	0.231	0.051	-0.001	0.001	0.201
N= 65						
<i>Vigorous Physical Activity</i>	-0.305	0.513	0.554	-0.004	0.002	0.059
<i>Moderate Physical Activity</i>	-0.317	0.230	0.175	-0.001	0.001	0.238
<i>Total Physical Activity</i>	-0.182	0.132	0.174	0.000	0.001	0.537
<i>Walking</i>	-0.184	0.240	0.446	0.001	0.001	0.325
<i>Sitting</i>	-0.003	0.051	0.864	0.000	0.000	0.905
<i>TC</i>	-0.257	0.186	0.172	-0.001	0.001	0.290
N= 56						
<i>Vigorous Physical Activity</i>	-0.933	1.431	0.517	-0.002	0.004	0.545
<i>Moderate Physical Activity</i>	0.218	0.660	0.743	0.000	0.002	0.984
<i>Total Physical Activity</i>	-0.680	0.360	0.065	-0.001	0.001	0.388
<i>Walking</i>	-1.670	0.531	0.003*	-0.002	0.002	0.262
<i>Sitting</i>	-0.049	0.183	0.792	0.000	0.001	0.581
<i>TCD</i>	-0.629	0.445	0.164	-0.001	0.001	0.453

β , Beta; SE, Standard error; p, significance. Controlling for age and energy intake.

Discussion

This study aimed to identify the influence of physical activity on body composition changes in women undergoing a weight control intervention program based in a multidisciplinary strategy

towards a healthy lifestyle. In the present study, four body composition variables, which were previously shown to be related with weight loss (23-26), were examined in order to assess how different levels of excess weight could be influenced by different dimensions of physical activity.

From the obtained results, we can conclude that the intervention program allowed body composition changes in the overweight and obese women in this study. In fact, these women lost 3.9% of their initial weight in the end of the short-term weight loss program (after 4 months). These results are more modest than those obtained in other interventions with the same characteristics and duration (3, 6, 7, 27) and superiors to others (28). However, it is important to mention that there was a high variability in this sample (range for weight change =19 kg) showing different adaptations to the weight loss intervention model.

Analyzing the results by levels of excess body weight, it was observed a loss of 3.7% of the initial weight for women with BMI below 30 kg/m². The obese women lost about 4.2% of their initial weight. These results are in accordance with the literature, which documented small losses for less heavy participants due to less daily energy expenditure (29). Possibly, these losses are related with a basal daily increased metabolism effort related with a higher BMI(30).

On average, waist circumference changed -3.15 ± 3.2 cm. Less changes were seen in hip circumference (-2.81 ± 3.2), which is in agreement with the literature available. In fact, it appears that women lost preferentially fat mass in the abdominal area when comparing with the gluteo-femoral region (8, 31, 32).

Our results also showed that 9.5% of weight loss was through fat free mass in the whole sample. The obese women alone lost 6.9% of fat free mass; for the overweight women the loss of fat free mass was 10.5%. These results are in favor of a greater fat free mass loss in overweight women than in obese women. This may be explained by the higher metabolism of obese women, which allowed less caloric intake restriction, resulting in a higher loss of fat mass

and saving fat free mass. On the other hand, the same exercise applied to heavier women promotes greater muscle stimulation.

Another interesting result was the proportion of trunk fat mass change considering total body fat mass change. From our data, 59% of TBFM was lost in trunk region, suggesting that fat located in trunk has a higher predisposition to be eliminated. Simultaneously, 17.4% all fat mass change was lost in total abdominal region, specifically between L2-L4, and 13.2% of change in total adiposity was lost in abdominal fat region of interest between L2-L4. This particular region is more associated with visceral fat mass (20). Overweight women lost 64% of trunk fat region of interest. However, in the abdominal fat region these women only lost 13.8%, including 12.2% in abdominal fat region of interest (20). Obese women lost 50% of fat mass in trunk and 19.1% in total abdominal region, including 13.5% in abdominal fat region of interest. These results indicate that, in relative terms, obese women have a higher predisposition to lose fat mass in abdominal region, which is beneficial because substantial reductions in health risk, often associated with modest weight loss (<10%), may be mediated in part by preferential reductions in visceral fat (33).

The whole sample increased their daily energy expenditure in 1325 kcal/wk. However, overweight women spent more energy than obese women. These figures were smaller than those recommended by Lakka et al. (34), whom suggests an increase in total energy expenditure of 2500 kcal/wk to promote a successful exercise-induced weight loss. This may justify the moderated weight loss after 4 months in our intervention. However, it is important to consider that these women were inactive for at least 6 months and it was, therefore, less likely for any of them to spend the recommended 2500 kcal/wk. One should also take into consideration the fact that this 4 months intervention program is a part of a longer trial (24 months) and for this reason the strategy was to initiate gradually physical activity, according with some guidelines, which recommended 1000 kcal/week to beginners (3). Moreover, it is

commonly accepted that in order to improve health related outcomes, it is necessary to exercise the equivalent of at least 150 min/wk of moderate-intensity physical activity (35-37) and in this study women have exercised for 245.9 min/wk (38).

The β coefficients obtained in the linear regression models, in which we examined possible predictors for BW and TBFM, did not show any association with physical activity variables with or without controlling for age and energy intake in any BMI groups. The analysis of a specific region, as TF-ROI, did not suggest any association with the different dimensions of physical activity in all the three groups, showing no influence of the different dimensions of physical activity in trunk fat mass loss. However, abdominal fat region of interest was influenced by an increase of TPA and WK. These results are in agreement with studies which documented important visceral fat mass losses caused by physical activity in both overweight and obese women (24). However, our study indicated that this influence is due only to obese women, clarifying the fact that walking is perhaps the first step to initiate physical activity in obese women, who need to reduce their abdominal fat in order to improve their metabolic health. Curiously, the fact that this influence was only seen in obese women was also reported by Williams et al. (39).

Some studies report that women who participated in exercise programs with modest decreases in weight loss and body fatness, this appeared to occur in a dose-response manner (5). However, relatively to abdominal fat mass, there are no studies describing the dose-response effect as our study documents. Our results are in agreement with those found by Williams et al. (40), who studied the relations between walking (km/week) and changes in WC, indicating that these cross-sectional associations are consistent with the hypothesis that exercise may mitigate age-related increases in adiposity. The literature only document changes in abdominal fat mass measured by WC (15-19) and there are insufficient data describing the effect of lifestyle interventions programs measured by other body composition techniques as DXA.

Our study reports significant associations between losses in this abdominal region, measured by DXA, and WK and TPA in a dose-response manner. As observed in this study, Miyata et al. (41) described improvements in parameters of body composition in a moderate exercise intervention as the steps taken per day were significantly increased. As seen by the same author, exercise capacity and energy intake were not significantly related to changes in visceral adipose tissue area, while a change in steps per day was significantly correlated with the diminution of visceral adipose tissue area.

Based on these results, it appears that as long as there is a sufficient increase in energy expenditure through walking, there are beneficial body composition changes. Given this, it is possible to list a number of lifestyle behaviours that promote weight and fatness loss, which include physical activity, walking rather than using motorized machines (i.e., automobiles, elevators, and escalators), amongst others. It has been reported that lifestyle approaches to physical activity may result in cardio-respiratory fitness and body weight changes, that are similar to what is observed with more traditional forms of exercise (42, 43). According to Grediagin (44), fat loss is a function of energy expenditure rather than exercise intensity. However, as questionnaires are less accurate in assessing physical activity intensity compared to an objective method such as an accelerometer; our findings may have been affected by this methodological limitation (45).

Conclusion

Physical activity variables did not induce changes in total body fat mass and body weight. Independently of age and energy intake, an increase in the total amounts of physical activity and total minutes walking play an important role in reducing abdominal fat region of interest, measured by DXA, which is more correlated with visceral fat mass. Therefore, the inclusion of

physical activity in a weight-loss lifestyle program may provide health-related benefits by reducing abdominal fat mass in obese women.

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CHAPTER 5

RESULTS

Usefulness of anthropometric measurements in predicting DXA-based measures of adiposity in a weight loss intervention

Abstract

Background: Abdominal fat can be estimated using a region of interest (ROI) selected by conventional whole body DXA. Using simple anthropometric measurements as pre-treatment predictors of body composition changes may be of great interest at clinical settings for weight-loss counseling. **Objective:** To analyze the usefulness of waist circumference (WC), abdominal circumference (AC), hip circumference (HC), and BMI to predict total body fat mass (TBFM) and abdominal fat ROI (AF-ROI), assessed by DXA, at baseline and their changes in overweight and obese women who participated in a short-term weight loss program. **Methods:** Subjects were 121 healthy overweight and obese women (age, 38.2 ± 5.9 y; BMI, 30.2 ± 3.8 kg/m²) who participated in a 4-month lifestyle weight loss program, which consisted of a group-based behaviour therapy to improve diet and increase physical activity. At baseline and by the end of the study, WC, AC, HC, and BMI were measured while TBFM and AF-ROI were estimated by DXA. Changes in these variables (WCC, ACC, HCC, TBFMC, and AF-ROIC) were computed as the difference between final and baseline values. The International physical activity questionnaire (IPAQ) was used to evaluate physical activity (PA) and 3-day Food Records were used to estimate energy intake (EI). Multiple regression analysis was performed to assess the relationships between WC, AC, HC and BMI, and TBFM and AF-ROI at baseline and change after the intervention, controlling for PA, EI, and age. The analysis was performed in the whole sample and in the group of overweight (BMI < 30 kg/m²) and obese (BMI \geq 30 kg/m²) women, separately. **Results:** Baseline values of TBFM, AF-ROI, and BW were, 36.30 ± 8.3 kg, 3.02 ± 1.03 kg and 78.29 ± 11.0 kg, respectively. After the intervention, TBFM, AF-ROI, and BW changes were -2.78 ± 3.5 kg, -0.374 ± 0.635 kg and -3.04 ± 3.1 kg, respectively ($p < 0.05$ for all). When controlling for PA, EI, and age, WCC, ACC, HCC and BMIC were

positively associated with AF-ROIC ($\beta=66.9$, $r=0.34$ $p<0.001$; $\beta=31.96$, $r=0.32$ $p=0.001$; $\beta=57.82$, $r=0.33$, $p=0.001$; $\beta=255.82$, $r=0.51$ $p<0.001$; respectively), for the whole sample. The same set of variables (WCC, ACC, HCC and BMIC) were positively associated with TBFMC ($\beta=0.636$, $r=0.58$, $p=0.000$; $\beta=0.266$, $r=0.47$, $p=0.000$; $\beta=0.638$, $r=0.61$, $p=0.000$; $\beta=2.139$, $r=0.74$, $p=0.000$; respectively), when controlling for PA and EI.

Conclusion: In overweight and obese women, BMI, waist, abdominal, and hip circumferences, are significantly associated with total body and abdominal fat. However, these selected anthropometric markers were less accurate to track total body and abdominal adiposity changes.

Introduction

DXA has the potential to provide overall and regional assessment of body composition in terms of fat, lean mass and bone. DXA quantifies fat, rather than adipose tissue.

Some studies support the possibility of estimating abdominal fat using a region of interest (ROI) selected by conventional whole body dual-energy X-ray absorptiometry (DXA) (1-3). In addition, there are some reports describing the ability of DXA to assess changes in fat in the abdominal region (3-5). Thus, there is increasing interest in testing and comparing methods used for assessing body fat distribution. Simple anthropometric measurements cannot estimate abdominal fat mass, but there are several studies documenting their ability to predict these fat depots (6-8), which supports previous findings from epidemiologic studies in which increased BMI and WC were shown to be strongly associated with the metabolic syndrome (9).

Despite its usefulness, DXA is not always available in clinical settings. It is important to test if changes in simple anthropometric measurements may track changes in DXA total body fat mass (TBFM) and abdominal fat region of interest (AF-ROI) (2), to assess the usefulness of the bedside measures in the context of weight loss interventions. In fact, the predictability of anthropometric measures is important since this method is less expensive and it is available in many clinical settings. Unfortunately, the prediction of changes in the abdominal region through anthropometric measurements is not well documented in the literature. Another relevant issue that needs further inquiry is the selective usefulness of anthropometric variables to track changes in fatness markers among overweight and obese women who lost weight.

The aim of this study was to evaluate the usefulness of BMI, waist, abdominal, and hip circumferences, to predict total body and abdominal fat predicted by DXA at baseline and their changes in overweight and obese women after a weight loss intervention program.

Methods

Subjects

Subjects, all females, were recruited from the community for a weight management program through newspaper ads, a website, email messages on listservs, and announcement flyers. In order to be eligible for the study, these women were required to be older than 24 years, be pre-menopausal and not currently pregnant, have a BMI higher than 24.9 kg/m^2 , and be free from any major disease. After several orientation sessions, 152 women signed up for the program. During the run-in phase, four women decided not to participate (reporting new time and scheduling conflicts), four did not comply with testing requirements and were excluded, three women found out they were pregnant or decided to attempt pregnancy and were also excluded, and one subject was

found ineligible due to medical reasons (untreated hyperthyroidism), leaving a total of 140 women who started the intervention. Attrition was 20.3%. All participants agreed to refrain from participating in any other weight loss program and gave written informed consent prior to participation in the study. The Faculty of Human Movement's Ethics Committee approved the present study.

Assessments

Body composition was measured in the 121 females who concluded the study. After a 12-hour fast, all subjects came to the laboratory where all measurements were carried out on the same morning.

Anthropometric measurements

After voiding, body weight (BW) and height were measured on an electronic scale with a stadiometer (SECA, Hamburg, Germany). Body weight (BW) was measured to the nearest 0.01 kg. Briefly, WC was measured with the subject standing, midway between the last rib and the upper edge of the iliac crest; and hip circumference (HC) was measured at the greater gluteal curvature. Abdominal circumference (AC) was measured at the umbilical level. All measurements were taken with a stiff fiberglass tape to the closest 0.1 cm. All anthropometric measurements were taken by previously trained technicians and repeated 3 times, with the mean value being used. Body mass index (BMI) was calculated as weight divided by height squared (kilograms per square meter).

Dual energy X-Ray absorptiometry

A total body scanner (QDR-1500, Hologic, Waltham, USA, pencil beam mode, software version 5.67 enhanced whole-body analyses) was used to estimate total, absolute and relative, fat mass (TFM, %TFM), and abdominal fat region of interest (AF-ROI between L₂-L₄, excluding lateral subcutaneous fat) (2). This scan measured the attenuation of x-rays pulsed between 70 and 140 kV synchronously with the line frequency for each pixel of the scanned image. Following the protocol for DXA described by the manufacturer, a step phantom with six fields of acrylic and aluminium of varying thickness and known absorptive properties was scanned alongside each subject as an external standard for the analysis of different tissue composition. The laboratory technician who collaborated in this study has positioned each subjects and performed the scans and posterior analysis according to the operator's manual using the standard analysis protocol. The coefficient of variation in our laboratory for fat mass is 2.9%, this being based on data from 10 subjects.

Physical activity and dietary intake assessment

Physical activity variables were measured at baseline and after 4 months using a validated questionnaire (IPAQ- International physical activity questionnaire). The questionnaire was designed to be applied to adults aged 18-65 yr and provides information on the time spent walking, in vigorous and moderate intensity activity, and in sedentary activity. The IPAQ version used estimated the total weekly physical activity by weighting the reported minutes per week in each activity category by a MET energy expenditure estimate assigned to each category of activity. MET levels were obtained from the 2000 compendium of physical activities classifying as moderate-intensity activities those with MET between 3 and 6 and vigorous-intensity activities for more than 6 METs. The weight MET-minutes per week (MET·min·wk⁻¹) were

calculated as {duration × frequency per week × MET intensity}, which were summed across activity domains to produce a weighted estimate of total physical activity from all reported activities per week ($\text{MET} \cdot \text{min} \cdot \text{wk}^{-1}$) (10). Dietary intake was estimated with 3-day 24h food records. Subjects were instructed regarding portion sizes, supplements, food preparation aspects, and others aspects pertaining to an accurate recording of their diet, previously to the collection of any diet data. Records were turned in and reviewed at the time of laboratory testing. Data was analyzed for energy (kilocalories), The diet records were entered and analyzed for energy nutrient intake using Food Processor SQL (ESHA, Salem, OR).

Intervention

Subjects attended 15 treatment sessions in groups of 32 to 35 women, for approximately 4 months. Average attendance to the treatment sessions was 83%. Sessions lasted 120 minutes and included educational and experiential content in the areas of physical activity and exercise, diet and eating behaviour, and behaviour modification. The intervention has been previously described (11). Physical activity topics included learning the energy expenditure associated with typical activities, increasing daily walking and adopting a physically activity lifestyle, planning and implementing a structured exercise plan, setting appropriate goals, using logs and a pedometer for self-monitoring, choosing the right type of exercise, among many others. Examples of covered nutrition topics are the energy, fat, and fiber contents, and the energy density of common foods, the role of breakfast and meal frequency on weight control, reducing portion size, strategies to reduce diet's fat content, preventing binge and emotional eating, planning for special occasions, and reducing hunger by increasing meal satiety (e.g., increasing fibre content). Cognitive and behaviour skills, such as self-monitoring, self-efficacy enhancement, dealing with lapses and relapses, enhancing body image, using

contingency management strategies, and social support, were also part of the curriculum. Subjects were instructed to make small but enduring reductions in the energy intake and also to increase energy expenditure in order to induce a daily energy deficit of approximately 300 kcal. Although weight was monitored weekly, subjects were advised that long-term weight reduction (i.e., after 1-2 years), was the primary target, in opposition to a rapid weight change. Reaching a 3 to 5% weight loss at 4 months was set as an appropriate goal for all participants.

Statistical analysis

Measures of central tendency and dispersion, distribution, and normality were examined for all variables at baseline and after 4 months. All change measures obtained by DXA and simple anthropometric measures were expressed as the difference between 4-months and baseline observed values. Multiple regression analysis was performed to assess the relationship between the selected anthropometric variables and TBFM and AF-ROI at baseline and their respective changes after the weight loss intervention. All relationships were controlled for PA, CI and age. The coefficients of correlation were compared with a Z-score using the MedCalc® statistical software. The remaining statistical analyses were completed using the Statistical Package for the Social Sciences version 14.0 (SPSS, Chicago, IL).

Results

Table 1 presents the mean and standard deviation of baseline values, change values, and limits of change values for all 121 participants who completed the program. Average weight change

was -3.11 ± 1.3 kg. The range for weight change was about 19 kg. On average, participants lost 3.9% of their initial BW.

Significant differences ($p < 0.05$) between baseline and post-weight loss intervention measurements were observed for BW and all body composition variables.

Table 1- Mean, standard deviation of initial values, change values and limits of change values

N =121	initial	change	(change)
	Mean \pm SD	Mean \pm SD	Range
Age (yrs)	38.24 \pm 5.9	-	-
BW (kg)	78.29 \pm 11.0	-3.11 \pm 1.3*	-13.85-5.38
BMI (kg/cm ²)	30.20 \pm 3.8	-1.19 \pm 1.2*	-5.34-2.03
WC (cm)	91.45 \pm 9.0	-3.15 \pm 3.2*	-22.80-4.35
AC (cm)	107.70 \pm 10.1	-10.53 \pm 6.1*	-27.70-7.50
HC (cm)	111.74 \pm 7.2	-2.81 \pm 3.2*	-13.00-7.30
TBFM(kg)	36.30 \pm 8.3	-2.84 \pm 3.5*	-14.60-6.86
AF-ROI (kg)	3.02 \pm 1.03	-0.374 \pm 0.635*	-0.525-0.914
TKD (kcal)	125.82 \pm 193.50	+189.13 \pm 260.1*	-611.87-1014.80

Body weight (BW), Body mass index (BMI), Waist circumference (WC), Hip circumference (HC) Total body fat mass (TBFM), Abdominal fat region of interest (AF-ROI), Total calories expended per day (TKD). * All de values were significantly different ($p < 0.05$)

Table 2 presents regression models based for initial abdominal fat region of interest and total body fat mass using WC, AC, HC and BMI as the independent variables.

Considering the initial abdominal fat region of interest values, the coefficients of correlation between WC, AC, and BMI and the dependent variables were significantly higher ($p < 0.05$) when compared with coefficient of correlation for HC. Among the other coefficients of correlation, there were no significant differences ($p > 0.05$). HC explained 17.9% and 59.1% of the variability observed in AF-ROI and TBFM, respectively. AC explained 53.9% of the AF-ROI variability and 82.6% of the TBFM variability. WC explained 66.6% of the AF-ROI variability and 71.1% of the TBFM variability. BMI explained 55.2% of the AF-ROI variability and 78.9% of the TBFM variability.

For TBFM, the coefficient of correlation obtained with BMI and AC were significantly different ($p < 0.005$) when compared with those obtained from HC. Between all the other coefficient of correlation there were no significant differences ($p > 0.05$).

Table 2- Abdominal fat region of interest and total body fat mass estimations equations

N =121	Interception		Slope		R	
	AF-ROI	TBFM	AF-ROI	TBFM	AF-ROI	TBFM
BMI	-2.995	21.390	0.199	1.910	0.743	0.888
WC	-5.492	34.373	0.093	0.773	0.816	0.843
AC	-5.152	44.494	0.076	0.750	0.734	0.909
HC	-3.805	62.929	0.061	0.888	0.423*	0.769*

Body mass index (BMI), Waist circumference (WC), Abdominal circumference (AC) Hip circumference (HC), Abdominal fat region of interest (AF-ROI), Total body fat mass (TBFM). The entire correlations coefficients were < 0.05 . *Correlation coefficient (r) significantly different the other r values.

As described in Table 3, controlling for energy intake, energy expenditure, and age, BMI change (BMIC) showed a significant association with abdominal fat region of interest change (AF-ROIC) ($\beta = 255.820$, $p < 0.001$). All circumferences changes were related to AF-ROIC. There were no significant differences between coefficients of correlation.

Table 3: Linear regression analysis for the selected independent variables and changes in abdominal fat region of interest

Independent Variables	AF-ROIC		AF-ROIC		AF-ROIC	
	N=121		N=65		N=56	
	N=121		IMC \leq 30		IMC $>$ 30	
	β	r	β	r	β	r
BMIC	255.820	0.510	181.181	0.550	320.741	0.507
WCC	66.901	0.345	47.865	0.372	80.300	0.334
ACC	31.962	0.321	25.552	0.409	40.842	0.309
HCC	57.817	0.333	43.670	0.382	71.884	0.352

β , Beta; r, correlation coefficient represents the coefficient of correlation (bivariate correlation) which indicates the degree of association between the independent variables and AF-ROIC. The entire coefficients of correlation were < 0.05 . There were not significant differences between coefficients of correlation ($p > 0.05$).

As indicated in Table 4, changes in the anthropometric variables were related to total body fat mass change. BMIC coefficient of correlation was significantly different from WC change (WCC) and AC change (ACC) coefficients of correlation for all the groups ($p < 0.05$). BMIC coefficient of correlation was significantly different from WCC, ACC, and HCC coefficients of correlation in overweight women ($p < 0.05$).

Table 4: Linear regression analysis for the selected independent variables and changes in total body fat mass

Independent Variables	TBFMC N=121		TBFMC N=65 IMC ≤ 30		TBFMC N=56 IMC > 30	
	β	r	β	r	β	r
	BMIC	2.139	0.740	2.213	0.817	2.022
WCC	0.636	0.583*	0.757	0.664*	0.585	0.671*
ACC	0.266	0.473*	0.172	0.384*	0.356	0.551*
HCC	0.638	0.611	0.618	0.670*	0.643	0.664

β, Beta; r, correlation coefficient represents the coefficient of correlation (bivariate correlation) which indicates the degree of association between the independent variables and TBFMC. The entire coefficients of correlation were < 0.05 . *BMI coefficient of correlation was significantly different ($p < 0.05$) from WC, AC and HCC correlation coefficients.

Discussion

The aim of this study was to evaluate the usefulness of simple anthropometric measurements in predicted changes in total and abdominal obesity assessing by DXA, among obese and overweight women who lost weight.

By the end of this short-term weight loss program participants lost 3.11 kg (3.9% of their initial BW). These results were more modest than those reported for other interventions with the same characteristics and duration (12-15) but superior to some others (16). However, it is important to mention that there was a high variability in this sample (range for weight change =19 kg) showing different adaptations to the weight loss intervention model.

Analyzing the results by levels of excess BW, it is possible to confirm a loss of 3.7% of their initial BW for overweight women, whereas obese women lost about 4.2% of their initial BW. These results are similar to those found in the literature, which report small losses for less heavy participants due to less daily energy expenditure without physical activity (17). Possibly, these losses are related to metabolic aspects, since basal and effort metabolism increases with BMI increment (18). On average, WC decreased by 3.15 ± 3.2 cm and smaller changes were seen in HC (-2.81 ± 3.2 cm), in agreement with results in the available literature (19). In fact, it appears that premenopausal women lost fat mass preferentially in the abdominal area when compared with the gluteo-femoral region (20). About 17.4% of total body fat mass change was lost in the total abdominal region of interest, specifically between L2-L4, and 13.2% of all body fat mass change was lost in abdominal region of interest between L2-L4. These results indicate, in relative terms, a higher predisposition to lose fat mass in the abdominal area, which is beneficial since substantial reductions in health risk, which are often associated with modest weight loss (<10%), may be mediated in part by reductions in visceral fat (21).

Initial AF-ROI estimations was strongly predicted by initial WC ($R^2=0.70$), although other anthropometric variables (BMI, AC) also showed a high association.

The AC was the best predictor of initial total adiposity, explaining almost 83% of the variability in the observed values. The other anthropometric variables also showed a significant association, ranging from 61.2% (HC) to 78.9% (BMI). It is important to note that, despite the association between HC and AF-ROI and TBFM, HC showed to be less sensitive to predict the values obtained by DXA. The comparison of correlations coefficients also showed significant differences between BMI, AC and HC with the initial values of AF-ROI and TBFM, showing that only WC presented a similar predictive power to assess these two dependent variables. Contrary to our study, Neovius et al. (22) observed a low capability to predict abdominal and total body fat, measured by DXA.

Demura et al. (23) considered that BMI and WC may predict abdominal fat and fat at the trunk, estimated by DXA. The coefficients of correlation obtained by this research were similar to those observed in our study. There are a few studies using anthropometric variables to predict abdominal fat mass assess by DXA. On the other hand, there are several studies, with obese and overweight women, using other imaging techniques, confirming a relation between BMI and abdominal fat (24-32). Some of these studies have shown an association between WC and the AF-ROI (24, 25, 27-31) and TBFM (24, 29, 30). None of the studies analysed documented a relation between HC and AC with AF-ROI.

Changing values of WC, AC, HC, and BMI were positively associated with abdominal fat region of interest and total body fat mass changes, in the non-obese and obese groups, as well as in the whole sample, controlling for energy expenditure, energy intake and age, which suggests that alterations in DXA abdominal fat region of interest and total body fat mass were tracked by all the anthropometric variables. For DXA to be used in longitudinal or interventions studies, it must be sensitive to changes in the abdominal region. Some studies confirm the capability of DXA to determine changes in abdominal fat mass (1, 2). However, there are no studies documenting the associations between anthropometric variables and DXA-specific regions

assessments in weight loss interventions programs. The existing studies used others imaging techniques, as MRI and TC, to analyse changes in weight loss. In a systematic review of the literature by Kay et al. (33), the authors mention that in a total of 10 RCTs using imaging techniques to measure change in abdominal fat in overweight or obese subjects, seven studies (including 3 trials with type 2 diabetic participants) reported significant reductions compared with controls. Reductions in visceral and total abdominal fat may occur in the absence of changes in body mass and WC. These results demonstrated that in those studies WC was not a reliable measure to detect changes in regional adiposity in exercise studies. According to Srdić et al. (34) WC is a good predictor of abdominal fat. However, extreme individual variations in visceral to subcutaneous ratio demonstrate the limitations of external anthropometry. Similar results were found in our study. For example, changes in abdominal fat region of interest were significantly associated with changes in BMI. However, BMI only explained 23% of the variability of the AF-ROI loss estimated by DXA, after adjusting for the effect of energy expenditure, energy intake, and age.

The highest correlation was found between BMI and DXA variables. These results indicate that, although changes observed in WC, BMI, HC, and AC were associated with total and abdominal fat mass losses, these variables were not able to accurately detect the magnitude of change. The results showed that initial correlations were more significant than associations between variables representing change.

Conclusion

Anthropometric variables, specially waist and abdominal circumferences were useful to predict baseline total body fat and abdominal fat region of interest. However, these selected anthropometric markers were less accurate to track total body and abdominal fat region of interest changes.

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CHAPTER 6

GENERAL DISCUSSION

Discussion

The prevalence of obesity in the world and in Portugal has increased at an alarming rate in the past few decades (1). However the link between obesity and its related co-morbidities and death is the concomitant increase in fat mass observed as body weight increases (2). These health concerns related to excess body fat and altered body composition have been a major focus of research education and clinical efforts. Thus, measurement of body fat in humans has become increasingly important in clinical settings, these data are equally important as a way of assessing the efficacy of interventions designed to alter body fat. Accordingly, weight loss programs should not solely focus on decreasing body weight but, in addition, to focus on decreasing fat mass, particularly abdominal fat mass which is associated with several metabolic diseases (3). Consequently, it has arisen the need for accurate assessment tools in the management of obesity and in the evaluation and efficacy of weight loss programs.

Some work in the area of body composition methodology it is still necessary to improve the accuracy of the available methods to assess different markers of body composition, especially, within the scope of longitudinal studies. How much accurate are field methods when compared with specific laboratory methods? Which simple method would be more convenient to use in the evaluation of a weight loss management program, particularly total body, abdominal and trunk fat mass loss, in overweight or obese women? These are some problems that need to be solved with the advent of new methodological solutions to monitoring total body and abdominal fat mass loss.

The study developed in chapter 3 was aimed at identify if simple pre-treatment anthropometric measurements predict changes in total body, trunk and abdominal fat mass

among pre-menopausal women who were involved in a weight control program based in energy restriction and increased physical activity.

In this study it was observed a higher capability of abdominal circumference to predict body fat mass loss than waist circumference, identified important technical measurement issues that require further discussion and exploration. These results are in concordance with the question raised by the Shaping America's Health: Association for Weight Management and Obesity Prevention (4). This consensus statement main goal was to respond to several questions related to waist circumference, and one of them was to identify the better location to estimate the abdominal fat mass. Another study compared 4 sites to measured waist circumference, and the waist circumference measured immediately above the iliac crest was the one who presented the higher values in women (5). The authors observed that the waist shape superior to the iliac crest decreases more than the waist shape in other regions of the trunk above the iliac crest. This waist circumference measurement is usually used for studies measuring VAT with a single computed tomography (6) or magnet resonance imaging (7) slice at the L4-L5 level, because the iliac crest is closer to L4-L5 than are the others waist circumference locations. Our study used the same waist circumference, recommended by the NIH Guidelines (8) and as applied in the third National Health and Nutrition Examination Survey. However, the abdominal circumference used in our study was even higher than this waist circumference, and possibly this abdomen area could be another site to observe in weight management interventions, particularly in women. The same study (5) grouped 14 different sites to measured waist circumference and grouped them into 4 sites to analyse them. These 14 sites were all located within the region from the tenth rib to the iliac crest and none of them were located at the higher abdominal area as ours.

These results suggest, also, that a negative energetic balance, caused by changes in lifestyle, may provide a stimulus to lose trunk fat mass essentially abdominal fat mass during weight

loss. These findings are in concordance with the studies who describe a higher predisposition to eliminate trunk fat mass relatively too hip fat mass because of the higher incidence of lipolytic action in the trunk area, namely, in abdominal region (9, 10). The analysis from several studies, which presents the same predisposition to eliminate trunk fat mass, including abdominal fat mass, described the influence of exercise on fat distribution losses (9, 11). However, our research documented the same results, even when weight loss was only based in moderate physical activity approach and structured exercise was not the main goal. Concordant results were found by Waller (12) in a 30-year longitudinal twin study. The authors concluded that, persistent long-term participation in leisure-time physical activity is associated with decrease rate of weight-gain and smaller waist circumference in adults.

Baseline values of body weight, BMI, sagittal diameter, abdominal circumference and hip circumference are good predictors of total body fat mass changes. Abdominal circumference, as seen, showed a higher reduction, caused by weight loss, than waist circumference and showed a higher capability to predict total body fat mass change, because no association was present between initial waist circumference values and this dependent variable. For that reason abdominal circumference may be used in clinical approaches to earlier detection of total body fat mass loss instead of waist circumference. Baseline anthropometric measures could not predict changes in more specific areas of body fat estimated by DXA. These findings indicate that simple morphological parameters are able to predict changes in total body fat mass but unable to predict regional fat mass changes in the trunk and the abdomen during a weight loss program in overweight and obese women. The results of the analyses, examining the explanation for waist circumference, abdominal circumference and hip circumference changes revealed a negative association between BMI, abdominal circumference and hip circumference with abdominal circumference changes, showing that the women with higher BMI, abdominal circumference and hip circumference at the beginning of the intervention were the ones who lost more centimeters in abdominal circumference. The women who had

higher areas on hip circumference were the ones who showed more losses in the hip region. Any association was seen between waist circumference change and anthropometric predictors. In summary, the present study highlighted the differences between fat losses in waist and abdominal area, showed a higher capability of abdominal circumference to predict body fat mass loss than waist circumference and identified important technical measurement issues that require further discussion and exploration. Baseline values of body weight, BMI, sagittal diameter and hip circumference appear to be good predictors of total body fat mass changes. Our findings suggest that BMI, abdominal circumference and hip circumference may predict abdominal circumference changes. Baseline anthropometric measures could not predict changes in DXA regions of interest.

In clinical interventions terms is important to understand the role of physical activity in weight loss and in health, because energy expenditure, in some cases, may not be sufficient to contribute for weight loss, but may promote health benefits related with fat loss in specific metabolic regions, as abdominal area (13). It is important to analyse what dimension of exercise promote weight loss and specifically abdominal fat mass because as we know upper body fat mass is related with an increased risk of developing metabolic disorders such as insulin resistance (14), hypertension and hyperlipidemia compared with lower body obese women and nonobese women (15, 16). Therefore, the aim of chapter 4 was to examine the influence of different types and intensities of physical activity in body weight, total body fat mass, abdominal and trunk fat regions of interest changes in two different levels of excess body weight.

The results presented in chapter 4, analysing β Coefficients from linear regression models examining the explanation for body weight and total body fat mass changes did not showed any association with physical activity variables with or without controlling for age and energy intake in any BMI groups. The analysis of a specific region as trunk fat mass change did not revealed

any association with the different dimensions of physical activity in all the 3 groups, showing no influence of different dimensions of physical activity in trunk fat mass loss. However, abdominal fat region of interest was influenced by the increment of total physical activity and incremented minutes walking. These results are in agreement with studies who documented important visceral fat mass losses caused by physical activity, in overweight and obese women (13), however our study indicated that this influence is due only to obese women, clarifying the fact that probably walking is the first step to initiate physical activity in obese women who need to reduce their abdominal adiposity in order to improved their metabolic health. Curiously, the fact that this influence was only seen in obese women was also document by Williams et al (17).

Some studies report that women who participated in exercise programs with modest decreases in weight loss and body fatness, this appeared to occur in a dose-response manner (13). However, relatively to abdominal fat mass, there are not studies describing the dose-response effect as our study document. The literature only document changes in visceral fat mass measured by waist circumference (18-22) and there are insufficient data describing the effect of lifestyle interventions programs measured by other body composition techniques as DXA. Our study report significant associations between losses in DXA- abdominal fat region of interest and dimensions of physical activity as, total minutes walking and total physical activity in a dose-response manner. Based on this, it appears that, low-intensity endurance exercise, as walking, may to generate beneficial metabolic effects that would be similar to those produced by high-intensity exercise, as describe by Poirier et al. and Ohkawara et al. (23, 24). Based on that, it is possibly to create alternatives adopting a lifestyle physical activity, using walking rather than motorized machines (ie, automobiles, elevators, and escalators) for the purpose of transportation and mobility.

In chapter 5 was evaluate the usefulness of simple anthropometric measurements in assessing changes in abdominal fat region of interest and total body fat mass, estimated by DXA, among obese and overweight women who lost weight.

Analyzing the results, by levels of excess body weight, it is possible to confirm a loss of 3.7 % of their initial weight, in overweight women. The obese women lost about 4.2 % of their initial weight. It appears that women lost preferentially fat mass in the abdominal area when compared with gluteo-femoral region (25, 26). About 17.4 % of total body fat mass change was lost in abdominal area, specifically between L2-L4, and 13.16 % of total body fat mass change was lost in abdominal fat region of interest area between L2-L4. These results indicate that, in relative terms, a higher predisposition to lose fat mass in abdominal area, which is beneficial because substantial reductions in health risk, often associated with modest weight loss (<10%), may be mediated in part by preferential reductions in visceral fat (27).

Initial DXA abdominal fat region of interest and total body fat mass estimations equations, based on initial data provided by the independent variables, waist circumference, abdominal circumference, hip circumference and BMI were presented and showed a high std error of estimation. However, when compared, correlation coefficients between initial abdominal fat region of interest and BMI, abdominal circumference and waist circumference were significantly different from hip circumference correlation coefficient showing that hip circumference is a less sensitive measure to estimate abdominal fat region of interest. Near the same results were seen comparing correlation coefficients of total body fat mass, revealing significant differences between BMI and abdominal circumference with hip circumference. The comparison of correlations coefficients also showed significant differences between BMI, abdominal circumference and hip circumference with the initial values of abdominal fat region of interest and total body fat mass, showing that only waist circumference presented a similar predictive power to assess these two dependent variables.

Contrary to our study, Neovius et al. observed a low capacity of waist circumference and BMI to estimate abdominal and total fat mass measured by DXA (28). Demura et al (29) considered that BMI and waist circumference may predict abdominal fat mass and fat mass at the trunk, estimated by DXA. The coefficient correlation obtained, by the author, were similar to those observed in our study. There are a few studies using anthropometric variables to predict abdominal fat mass estimated by DXA. In addition, there are several studies, with obese and overweight women, using other imaging technics confirming a relation between BMI and intra abdominal fat mass (30-37). Some of these studies revealed a relation of waist circumference with internal abdominal fat mass (30, 33-36) and total body fat mass (32, 33, 35), a few studies related significantly abdominal circumference with internal abdominal fat mass (38, 39), however, none of them used DXA abdominal fat regions of interest estimations. Any of the studies analysed documented a relation between hip circumference and abdominal fat region of interest.

Changing values of waist circumference, abdominal circumference, hip circumference and BMI were positively associated with abdominal fat region of interest change, in all the three groups, controlling for energy expenditure, energy intake and age, showing that alterations in DXA abdominal fat mass estimation were detected by all the anthropometric variables. There are no studies documenting the associations between anthropometric variables and DXA specific regions estimations in weight loss interventions programs. The existing literature used others imaging techniques as MRI and TC to analysed changes in weight loss. Kay et al. (40) in a systematic review of the literature, described that in RCTs using imaging techniques to measure changes in abdominal fat in overweight or obese subjects, seven out of 10 studies (including three trials with type 2 diabetics) reported significant reductions compared with controls. Reductions in visceral and total abdominal fat may occur in the absence of changes in body mass and waist circumference. These results demonstrated that in those studies waist circumference was not a sensitive measure of change in regional adiposity in exercise studies.

To Srdić et al. (41) waist circumference is a good predictor of abdominal fat, but, extreme individual variations in visceral to subcutaneous ratio demonstrate the limitations of external anthropometry. In our study the results were near the same. Anthropometric measurements, as waist circumference, abdominal circumference, hip circumference, and BMI, detected the alterations in DXA abdominal fat mass estimation and total body fat, demonstrating their usefulness in the evaluation of weight loss, but the individual variation inhibits the quantifications of internal abdominal fat mass loss during the intervention. For example, changes in abdominal fat region of interest were significantly associated with changes in BMI, however, BMI only explained 25% of the variability in abdominal fat region of interest loss estimated by DXA. These results indicate that waist circumference, BMI, hip circumference and abdominal circumference are good predictors of total and abdominal fat mass loss, but cannot measure or quantify accurately the magnitude of change.

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CHAPTER 7

GENERAL CONCLUSION

Conclusion

The major findings of the present thesis are as follows:

Chapter 3

1. Changes in lifestyle may provide a stimulus to trunk fat mass loss, predominantly abdominal fat mass, during weight loss.
2. Abdominal circumference is a better predictor of body fat mass loss than waist circumference.
3. Baseline values of BW, BMI, SD and HC are good predictors of TBFM changes.
4. BMI, ABDC and HC may predict abdominal circumference changes.
5. Baseline anthropometric measures were not able to predict fat changes, estimated by DXA, in more specific body regions.

Chapter 4

1. These results suggest that physical activity variables did not induce changes in total body fat mass and body weight.
2. Independently from age and caloric intake, an increase in the total amount of physical activity and the increment of total minutes walking, played an important role in the reduction of internal abdominal fat mass measured by DXA.
3. Therefore, the inclusion of physical activity in a weight-loss lifestyle program may provide health-related benefits by reducing abdominal fat mass in obese women.

Chapter 5

1. HC is a less sensitive measure to estimate fat in the abdominal region of interest assessed by DXA.
2. Alterations in DXA abdominal fat mass estimation were reasonably detected by all the anthropometric variables.
3. WC, AC, HC and BMI may be used in weight loss clinical approaches to evaluate changes in total and abdominal fat losses, but cannot be used to quantify how much was lost.

Added value of this thesis

This thesis was conceived to investigate the appropriation of methods used in weight management clinical practice, whose validity it is not well documented in body composition research in overweight and obese women. This theme is very relevant for an evidence-based clinical practice and for the precise monitoring of the different body composition phenotypes and its alterations, irrespective of the energetic process behind the mass change of the different tissues.

In this field area, scientific research has been characterized by waist circumference and total body fat mass validation through sophisticated equipment, of difficult applicability, and investigating its association with health risk factors. Besides, this was only performed with more homogeneous populations, limiting its use and even the results when women with different overweight conditions were enrolled.

Published studies analyzed, mainly, cross-sectional associations, not allowing to monitor alterations in weight loss interventions. Until the present, the literature has never taken into consideration the abdominal circumference, measured at the greatest abdominal volume. However, our results showed that this body circumference is a better indicator of total and abdominal fat mass loss than waist circumference. Therefore, current research results advise the use of this circumference in weight loss clinical practice. This thesis facilitates clinical practice by promoting the use of easy applicable and less expensive body composition methods.

This work also documented that the increase of physical activity contributes to the decrease of intra-abdominal fat mass in obese women, as shown in other studies, although with different characteristics. The literature did not analyze the effects of moderate intensity physical activity in pre-menopausal women with different levels of excessive weight. The results of the present work allow the distinction of exercise prescription based on overweight degree, making it possible to prescribe different exercise intensities accordingly to body weight. Thus, intra-abdominal fat mass reduction can be accomplished and, consequently, health improvement can be achieved.

Finally, this thesis allows to conclude that circumferences and BMI are able to detect body fat mass changes during weight loss interventions, therefore their use should be recommended when monitoring body composition alterations. The investigation developed in this work is a relevant contribution of science to the professional practice in which physical activity is an important adjuvant to combat the atherogenic phenotype, as it is the case of abdominal fat mass.

The effect of physical activity on abdominal fat mass has been discussed in scientific research. This thesis added evidence to the irreplaceable contribution of the complex behavior of physical activity for the reduction of abdominal fat mass in weight loss programs. Present

findings indicate that, in obese women, body fat mass changes promoted by the increase of physical activity differ depending on the body region.

In summary, the obesity combat must include physical activity but should be well monitored by means of simple morphologic markers such as abdominal circumference. So, for a complex health problem, the scientific evidence from this thesis revealed that solutions may be simple, not expensive and accessible.

After all, the added value of this work relies on the reinforcement of the selective contribution of physical activity for body composition of obese women, and on the evidence of the relevance of surface morphology for the efficacy of abdominal fat mass changes monitoring. This thesis represents an important additional value to an economic and efficient combat of abdominal obesity, with the virtue of recognizing that the resources needed are in each person's autonomy.

Valor acrescido desta tese

Esta tese foi elaborada para investigar a apropriação de métodos usados na prática clínica em gestão do peso, cuja validade não está devidamente documentada no âmbito da alteração da composição corporal em mulheres com excesso de peso e obesidade.

Este tema é muito relevante para uma prática clínica baseada na evidência e numa monitorização precisa dos diferentes fenótipos da composição corporal e respectivas

alterações independentemente do processo energético conducente à modificação da massa dos diferentes tecidos. A investigação científica neste âmbito tem sido caracterizada por um lado, pela validação do perímetro da cintura e da massa gorda total através de equipamentos muito sofisticados e de difícil aplicabilidade e a sua associação com os factores de risco, mas em populações com excesso de peso pouco heterogéneas, limitando a sua utilização e até os resultados em mulheres com diferentes graus de excesso de peso. Por outro lado, os trabalhos publicados referem-se essencialmente a associações transversais não permitindo a monitorização das alterações decorrentes das intervenções na perda de peso. Na literatura existente nesta área, o perímetro abdominal, ou seja, o perímetro avaliado na região de maior volume abdominal, nunca foi tido em consideração. No entanto, os nossos resultados demonstraram que este perímetro expressa melhor, do que o perímetro da cintura, a perda de massa gorda total e abdominal. Assim, é possível recomendar com base científica a utilização deste perímetro na prática clínica da perda do peso. Os resultados obtidos nesta tese facilitam a prática clínica nesta área promovendo a utilização de métodos de avaliação da composição corporal simples e pouco dispendiosos.

Este trabalho também documentou que o aumento da actividade física moderada contribui para a diminuição da massa gorda intra-abdominal em mulheres obesas, facto que já foi demonstrado noutros trabalhos, embora com características diferentes.

Os estudos realizados não analisaram os efeitos da actividade física moderada em mulheres pré-menopáusicas com níveis diferentes de excesso de peso. Os resultados apresentados neste trabalho permitem diferenciar a prescrição do exercício com base no grau de excesso de peso deste tipo de mulheres, sendo possível prescrever diferentes intensidades de exercício, de acordo com o seu peso corporal, com a perspectiva de diminuir a massa gorda intra-abdominal e conseqüentemente melhorando a saúde.

Finalmente, foi possível concluir que os perímetros e o BMI são unidades de medida que conseguem detectar as alterações da massa gorda corporal ao longo de um programa de perda de peso, sendo por isso recomendável a sua utilização na monitorização das alterações da composição corporal.

A investigação desenvolvida na presente tese é um contributo relevante da ciência para a prática profissional que considere a actividade física como um importante coadjuvante para combater o fenótipo mais aterogénico, como seja a concentração abdominal de massa gorda.

O efeito da actividade física nesta massa gorda tem sido muito discutida na investigação científica. Esta tese adiciona evidência à insubstituível função do complexo comportamento que é a actividade física em programas de redução de peso em que as alterações são mais selectivas na zona abdominal.

Não é assim reconhecido que a alteração da massa gorda corporal promovida pelo aumento da actividade física ocorra de natureza homogénea no organismo.

Em síntese, o combate ao perigo da obesidade abdominal deve contar com o contributo da actividade física, sendo que o resultado deste combate pode ser devidamente monitorizado com marcadores morfológicos tão simples como o perímetro abdominal.

Para um problema complexo de saúde, a evidência científica decorrente desta tese revela que as soluções podem ser simples, não dispendiosas e acessíveis.

Afinal um reenfatizar do contributo selectivo da actividade física na composição corporal no âmbito do excesso ponderal e a descoberta do valor da morfologia de superfície para a monitorização eficaz das alterações da massa gorda na zona abdominal.

Esta tese representa um importante valor adicional para o combate económico e eficaz à obesidade abdominal, com a virtude de se reconhecer que os recursos necessários para este processo estão no domínio da autonomia das pessoas.