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A RELAÇÃO ENTRE A COMPOSIÇÃO CORPORAL E A QUALIDADE DE VIDA EM PACIENTES E SOBREVIVENTES DE CANCRO

Dissertação de candidatura ao grau de Mestre em Nutrição Clínica submetida à Faculdade de Ciências da Nutrição e Alimentação da Universidade do Porto

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THE RELATIONSHIP BETWEEN BODY COMPOSITION AND QUALITY OF LIFE IN CANCER PATIENTS AND CANCER SURVIVORS.

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List of acronyms and abbreviations

Adj. R-sq - Adjusted R squared

AIC - Akaike Information Criterion

AKT - Protein Kinase B

BMI - Body mass index

Bootstrap 95% CI - Bootstrapped 95% Confidence Intervals

COX-2 - Cyclooxygenase-2

DEXA - Dual-energy X-ray absorptiometry

ERK - Extracellular Signal-Regulated Kinases

JAK2 - Janus Kinase 2

MAPK - Mitogen-activated Protein Kinases

MCAR - Missing Completely at Random

MCS - Mental Component Summary

MSE - Mean Squared Error

PI3K - Phosphoinositide 3-Kinase

PCS - Physical Component Summary

SF-36 - Short Form-36 Health Survey Questionnaire

SHBG - Sex Hormone-Binding Globulin

STAT3 - Signal Transducer and Activator of Transcription 3

TNF-α - Tumor Necrosis Factor alfa

ABSTRACT

Introduction: Body composition seems to be associated with cancer incidence and poor prognosis. Obesity can impact quality of life (QOL) after cancer, due to its relationships with other comorbid conditions and its effects on cancer symptoms. In this study, associations between measures of body composition and QOL are evaluated among cancer patients and survivors.

Methods: Secondary analyses were performed based on three study populations: BALANCE (31 breast cancer patients receiving neoadjuvant chemotherapy), Steps to Health (STH, 97 endometrial cancer survivors), and Healthy Moves (HM, 36 breast, colon and endometrial cancer survivors). Associations between measures of body composition and two quality of life scores based on SF-36 [physical component scores (PCS) and mental component scores (MCS)] were examined for each population, using Pearson correlation coefficients and linear regression analyses adjusting for age, education, and skin color (additionally adjusting for disease characteristics and treatment for STH and HM). Interpretations of results for the adjusted models were based on bootstrapped confidence intervals and adjusted p-values for multiple hypothesis testing.

Results: Across three study populations, BMI, body fat percentage predicted by skinfolds or DEXA, and waist circumference were negatively correlated with PCS. For BALANCE and STH, higher values of BMI, waist circumference and DEXA (the former only available for BALANCE) were significantly associated with PCS, adjusting for confounders. Between adjusted models, waist circumference and DEXA showed superior linear model fit compared to other body composition measures, in BALANCE and STH. Associations between measures of body composition and MCS were not significant in any of the models.

Conclusion: Our results indicate that higher values of body fatness are associated with lower scores for physical aspects of QOL. Among the measures of body composition, waist circumference and DEXA were preferred compared to BMI or body fat percentage measured by skinfold in predicting PCS scores using linear models.

Keywords: Body composition, cancer, survivors, patients, quality of life

RESUMO

Introdução: A composição corporal parece estar associada à incidência de cancro e a um prognóstico desfavorável. A obesidade pode afectar a qualidade de vida (QDV) após o cancro, por estar relacionada com outras co morbidades e os respectivos efeitos nos sintomas do cancro. Neste estudo, a associação entre as medidas de composição corporal e a qualidade de vida são avaliadas entre pacientes e sobreviventes de cancro.

Metodologia: Análises secundárias foram realizadas com base em três populações: BALANCE (31 pacientes com cancro de mama que receberam quimioterapia neoadjuvante), Steps to Health (STH, 97 sobreviventes de cancro do endométrio) e Healthy Moves (HM, 36 sobreviventes de vários tipos de cancro: mama, colon e endométrio). As associações entre as medidas da composição corporal e duas classificações de qualidade de vida com base no SF-36 [classificações da componente física (CF) e da componente mental (CM)] foram avaliadas em cada população, utilizando o coeficiente de correlação de Pearson e análises de regressão linear ajustando para a idade, escolaridade e cor da pele (adicionalmente foram acrescentadas as características da doença e o tratamento para STH e HM). As interpretações dos resultados dos modelos ajustados foram baseadas em intervalos de confiança e valores-p ajustados para um teste de hipóteses múltiplas.

Resultados: Em três populações de estudo, o IMC, a percentagem de gordura corporal obtida através das dobras cutâneas ou DEXA, e o perímetro da cintura foram correlacionados negativamente com a CF. No BALANCE e no STH, valores altos de IMC, perímetro da cintura e DEXA (apenas disponível no BALANCE) foram significativamente associados com CF, considerando possíveis confundidores. Entre os modelos ajustados, o perímetro da cintura e o DEXA aparentaram ser os melhores modelos quando comparados com outras medidas de composição corporal, no BALANCE e no STH. As associações entre medidas de composição corporal e CM não foram significativas em nenhum dos modelos.

Conclusão: Valores elevados de gordura corporal estão associados com classificações mais baixas da componente física da QDV. Entre as medidas de

composição corporal, o perímetro da cintura e o DEXA foram eleitos como melhores quando comparados com IMC ou percentagem de gordura corporal medida pela prega cutânea na previsão da classificação da CF usando modelos lineares.

Palavras-Chave: Composição corporal, Cancro, Pacientes, Sobreviventes, Qualidade de vida.

Chapter 1 – Introduction

Relationship of obesity and cancer

The prevalence of overweight and obesity (a condition characterized by an abnormal accumulation of body fat caused by an energy intake which overlaps energy expenditure) has been rising sharply worldwide. According to the World Health Organization, in 2008 1.5 billion adults worldwide were overweight and at least 400 million were obese. It is estimated that in 2015, 2.3 billion adults will be overweight and at least 700 million will be obese (Birks, Peeters, Backholer, O'Brien, & Brown, 2012). This increase is especially alarming considering the various adverse health consequences associated with excess of fat mass, such as type 2 diabetes, cardiovascular diseases, infertility and certain cancers, which contribute to morbidity, mortality and a reduced quality of life (King et al., 2013; Rothberg et al., 2013).

From the physiological point of view, fat mass and muscle mass are predominant factors with great impact on the oncological disease (Coronha & Camilo, 2011).

Adipose tissue, divided into visceral and subcutaneous adipose tissue, is considered an endocrine organ by its ability to secrete various cytokines and hormone-like-molecules (Irigaray, Newby, Lacomme, & Belpomme, 2007). Visceral fat is considered more metabolically active than subcutaneous fat, being more associated with metabolic complications and cancer (Doyle, Donohoe, Lysaght, & Reynolds, 2012; Pischon, Nothlings, & Boeing, 2008).

Obesity, considered a consequence of hypertrophy and hyperplasia of adipose tissue (Irigaray et al., 2007), is linked to cancer through biological mechanisms such as:

- Insulin resistance, caused by increased levels of non-esterifies fatty acids released by adipose tissue(Bianchini, Kaaks, & Vainio, 2002). High plasma concentrations of insulin and IGF1 stimulate cell proliferation, enhance angiogenesis and inhibit apoptosis (Bianchini et al., 2002; Irigaray et al., 2007; King et al., 2013).

- Secretion of adipokines, such as leptin and adiponectin, by the adipose tissue. Leptin is positively correlated with body mass index (BMI) and promotes carcinogenesis through its mitogenic, proinflamatory, antiapoptotic and proangiogenic characteristics. (King et al., 2013; Pichard, Plu-Bureau, Neves, & Gompel, 2008; Vucenik & Stains, 2012). Adiponectin is inversely correlated with adiposity and also with cancer occurrence and cancer stage (King et al., 2013; Vucenik & Stains, 2012).

- Inflammatory responses in obesity that are involved in the initiation and promotion of cancer cells through tumor necrosis factor alfa (TNF-α), that is involved in carcinogenesis, tumor growth that leads to an increased growth and survival of tumor cells, cancer cell invasion and metastasis (Prieto-Hontoria et al., 2011; Vucenik & Stains, 2012). High levels of C-reactive protein, a biomarker of inflammation, have been shown to be associated with colorectal cancer (Slattery et al., 2011).

According to some studies, excess fat mass is not only associated with the etiology and bad prognosis of various cancers but is also considered a factor with great influence on the increased morbidity and mortality in cancer patients (Coronha & Camilo, 2011). Between others, the most common obesity-related cancers are: breast, endometrial and colorectal cancer (Birks et al., 2012; Doyle et al., 2012; Parker & Folsom, 2003; Polednak, 2008). Prostate cancer is also mentioned as being influenced by obesity in a sense that this condition appears to cause a more aggressive form of prostate cancer and is also associated with prostate cancer mortality (Spitz et al., 2000). It is estimated that between 15% and 45% of these obesity-related cancers may be attributed to excess body fat, and that obesity is associated with an increased cancer-related mortality (accounting for 14% of all deaths from cancer in men and 20% in women); (Doyle et al., 2012; King et al., 2013).

- **Breast Cancer**

Breast cancer is the second most common type of cancer, being the first among women (Ferlay et al., 2010). Given its high incidence and mortality worldwide, breast cancer is now considered a major public health problem (Felden & Figueiredo, 2009). Obesity is associated with an increased risk of developing post-menopausal breast cancer and it is also common to observe weight gain in most patients with early-stage breast cancer during treatment (Rock et al., 2013) putting them at risk given the inherent consequences of being overweight.

Recent evidence argues that weight gain after diagnosis of breast cancer is associated with a poor prognosis, a shorter survival time and increased recurrence; however this information is still not consistent (Caan et al., 2012; McTiernan, Irwin, & Vongruenigen, 2010). Several studies have reported the existence of a significant association between overweight or obesity and increased risk of recurrent disease or increased risk of death among women with breast cancer (McTiernan et al., 2010). Additionally, observational studies showed that, in women with a history of breast cancer, adiposity increased risk of mortality by 30% (Rock et al., 2013).

As biological and hormonal factors, such as estrogens, sex hormone binding globulin (SHBG), insulin and leptin are implicated as mediators that link obesity to breast cancer progression and recurrence (Rock et al., 2013). Excess adiposity results in increased production of estrogens (which promotes breast cancer pathogenesis and tumorgenesis), decreased production of sex hormone binding protein (which binds to circulating estrogen), and insulin and leptin (which exhibit proliferative, mitogenic and antiapoptotic activities in mammary cells, thus promoting tumor growth) (Ligibel, 2011; Sinicrope & Dannenberg, 2010).
One study showed a positive relationship between high levels of serum estrogens and higher risk of breast cancer among post-menopausal women. Several studies have also demonstrated a positive association between increased insulin and

leptin levels and increased risk of breast cancer and progression (Lann & LeRoith, 2008).

Overweight, obese or sedentary individuals show increased levels of insulin and C-peptide, which are associated with increased disease recurrence and risk of death (Frank et al., 2005). In a cohort study of 535 women with early-stage breast cancer, it has been shown that an increase of 1-ng/mL C-peptide is associated with an increased risk of death in patients with breast cancer (58%) and the decreased levels of adiponectin and improved insulin resistance is associated with fewer deaths among patients with breast cancer (Duggan et al., 2011).

Obesity, overweight and sedentary behavior are also associated with an increase of inflammatory markers, of which we highlight: C-reactive protein, serum amyloid A protein, interleukin - 6, interleukin-1 and tumor necrosis factor α (Pierce, Neuhouser, et al., 2009). Increased levels of the first two inflammatory markers are associated with decreased survival of the patient(Pierce, Ballard-Barbash, et al., 2009).

It is also noted that women with breast cancer who are underweight (BMI <18.5 kg / m²), compared with women with breast cancer with normal weight (BMI between 18.5 and 24.9), have a lower survival rate (Barnett et al., 2008; Moon, Han, & Noh, 2009). It is assumed therefore that diet, physical activity and weight may influence the prognosis of patients with breast cancer, which justifies the need of directing all attention and efforts on this issue.

- **Endometrial Cancer**

Endometrial cancer is considered the most common gynecologic malignancy in the world and obesity has been demonstrated to be a risk factor for endometrial cancer in various epidemiological studies, most likely because adipose tissue is an important source of endogenous estrogens (Nakamura, Hongo, Kodama, & Hiramatsu, 2011; Yang et al., 2012).

There is evidence that confirms the role of adiposity in endometrial cancer, in fact most of case-control studies and some cohort studies have shown to be an increased risk of developing cancer in overweight and obese individuals (Bianchini et al., 2002). As previously mentioned, obesity is associated with increased levels of leptin and insulin. High leptin levels have been associated to endometrial cancer due to its ability to promote endometrial cancer cell proliferation by the functional activation of cyclooxygenase-2 (COX-2) through Janus kinase 2 and Signal Transducer and Activator of Transcription 3 (JAK2/ STAT3), Mitogen-activated Protein Kinases and Extracellular signal-regulated Kinases (MAPK/ERK), and Phosphoinositide 3-kinase and Protein Kinase B (PI3K/AKT)-dependent pathways, suggesting that cyclooxygenase-2 (COX-2) may be a critical factor of endometrial carcinogenesis in obesity (Gao et al., 2009). Regarding hyperinsulinemia, studies have shown a positive association between high insulin levels and endometrial adenocarcinoma, mostly in overweight and obese individuals (Prieto-Hontoria et al., 2011).

- **Colorectal cancer**

The colorectal cancer is the third most common type of cancer and the fourth leading cause of cancer death in the world (Steins Bisschop et al., 2014). According to the International Agency for Research on Cancer, this form of cancer is the third most common among men and the second most common form among women, worldwide.

Several studies support the existence of an association between obesity (as determined by BMI) and an increased risk of developing colon cancer as well as rectal cancer, although to a lesser extent in the former (Laake et al., 2010; Leitzmann et al., 2009; Sinicrope, Foster, Sargent, O'Connell, & Rankin, 2010). However, it remains unclear whether the effect of weight changes and body composition affect the patient's prognosis and survival time of the same. Studies have suggested that obese women (BMI > 30 kg/m²), compared with women with BMI between 21.0 and 24.9 kg/m², have shorter disease-free survival. Regarding to cancer recurrence or patient’s death, patients with BMI over 35.0 kg/m² appear to be at greater risk than those who were normal weight. Another study also notes an association between increased visceral fat area, and a shorter disease-free survival (Meyerhardt, Ma, & Courneya, 2010).

Colorectal cancer is considered one of the cancer sites which show a strong link to excess body fatness; however rectal cancer is less affected by body fatness than colon cancer. It was also found that the relationship between body fatness and colon cancer was higher in men than in women (Boeing, 2013).

Relationship of obesity and body fatness with quality of life

Obesity is linked to long-term both physical and mental health complications. Besides being associated with an increased mortality, obesity contributes to various complications, including cardiovascular, endocrine-metabolic and orthopedic disorders, and to psychosocial issues such as low self-esteem, due to changes in physical appearance caused by weight gain and consequently anxiety, depression and social maladjustment. This set of problems leads to an impairment on quality of life, which is a more complete and multidimensional construct that includes physical, emotional and social functioning (Schwimmer, Burwinkle, & Varni, 2003).

The quality of life in obese individuals has then been an object of study and it has been shown that there is an inverse association between BMI scoresand quality of life, which varies among greater degrees of obesity, defending that obese persons experience significant impairment in quality of life even if there is no comorbidity associated with it. (Kolotkin, Crosby, & Williams, 2002; Pratt, Lazorick, Lamson, Ivanescu, & Collier, 2013). Additionally, there is evidence that suggests the existence of a negative association between adiposity and quality of life by showing that obesity and overweight can affect physical and psychosocial well-being (Gopinath, Baur, Burlutsky, & Mitchell, 2013). It has also been shown that weight loss improves physical function and quality of life in obese individuals undergoing treatment (Villareal, 2005), being recommended weight-loss therapies that maintain muscle and bone mass.

Relationship of sarcopenia and sarcopenic obesity with quality of life

It is frequent to observe weight loss in cancer patients in more advanced stages of cancer. Although weight loss is mainly associated with the loss of fat mass, it is the loss of lean mass, also known as sarcopenia, that appears to a have a greater negative impact on the prognosis of cancer disease, being associated with adverse clinical outcomes, and greater morbidity and mortality (Parsons, Baracos, Dhillon, Hong, & Kurzrock, 2012; Prado et al., 2013).

Sarcopenia, considered an independent prognostic factor in patients with solid tumors, is characterized by loss of muscle mass, muscle strength and muscle function that arises from an imbalance between protein synthesis and protein breakdown which derives either from physiological or pathological causes such as aging, chronic diseases, malnutrition and disuse (Boirie, 2009; Morishita et al., 2012). Muscle mass corresponds to 60% of the total body’s protein reserves. Considering that proteins have an essential role in cell function and that, in a metabolic stress situation, they are mobilized to provide amino acids to the immune system, liver and gut, excessive protein catabolism will result into an immune function impairment compromising the capacity to respond to an insult (Morishita et al., 2012).

Muscle mass depletion, observed in sarcopenic patients, requires greater attention because it is associated with loss of autonomy, increased risk of falls, impaired respiratory function and decreased functional capacity which influence these individual’s quality of life (Muscaritoli et al., 2010; Neto, Karnikowiski, Tavares, & Lima, 2012; Thibault, Cano, & Pichard, 2011). Studies have shown that sarcopenic cancer patients have a greater risk of developing a secondary malignancy, increased toxicity of anti-cancer treatments, longer hospital stay and shorter time to death than the patients without sarcopenia (Prado et al., 2013).

It is also possible to observe progressive loss of muscle mass associated with excess fat mass known as sarcopenic obesity, a condition that combines the health risks arising from being overweight and from the loss of muscle mass. This condition can affect the patient’s recovery process and their quality of life. There is evidence that shows that excess fat mass coupled with loss of lean body mass worsens the risk of developing multiple health problems resulting in a shorter survival time (Fearon, 2011; Villasenor et al., 2012)

Evidence has shown that both the excess fat mass and lean mass loss have a major role in health and well-being by affecting the individual's medical condition and also by negatively influencing the individual's functional capacity and quality of life (de Hollander et al., 2013; de Zwaan et al., 2009; Grandy, Fox, & Bazata, 2012). Additionally, changes in body composition (referring to the proportion of fat and fat-free mass) have been associated with the incidence of cancer and the outcome of cancer's therapy (Coronha & Camilo, 2011; Parsons et al., 2012). Both cancer patients and survivors have reported a reduced quality of life with respect to physical, emotional, and social functioning (Fader, Frasure, Gil, Berger, & von Gruenigen, 2011; Milne, Gordon, Guilfoyle, Wallman, & Courneva, 2007; Sanda et al., 2008). Body composition changes observed in cancer patients are normally related to tumor location, tumor type and the presence and duration of gastrointestinal symptoms, which affect the functional ability of the patient, their response to treatment, their quality of life and also their survival. As such, over the years, body composition changes seen in cancer patients have been considered an object of study.

Thus, although the role of obesity and sarcopenia in the quality of life of cancer patients and survivors still is not well understood, it is predicted that there is an adverse impact of excess body fat and lean mass loss in the quality of life of these individuals. Therefore, it becomes important to focus on the relationship between body composition and the outcomes in cancer in order to create strategies that cause a positive impact on the patient's prognosis, treatment response and quality of life.

Body Composition Measurements

In order to identify the health risks associated with high body fat and low lean mass it is important to measure body composition which is done through various techniques that are required to be precise, consistent, practical and accommodating to a wide range of potential individuals and study situations (e.g., clinical-based studies, population research) (Hillier, Beck, Petropoulou, & Clegg, 2014). Here we list some examples and discuss their strengths and weaknesses.

BMI, a simple measurement of body weight, calculated from weight and height [weight (kg)/height (m) ^{2}], was introduced in 19th century by Quetelet and is used to classify overweight and obesity (Bergman et al., 2011; Flegal et al., 2009). The use of this technique is simple, fast, convenient and does not require special equipment. However, in obesity, which is characterized by excess of body fat, this technique may not always be an accurate measure of adiposity, particularly in individuals with elevated lean body mass, mainly because it does not differentiate fat mass and fat-free mass which has been shown to be very important in the clinical context but has been devalued in oncology (Bergman et al., 2011; Flegal et al., 2009; Foo, Teo, Abdullah, Aziz, & Hills, 2013).

Waist circumference, a simple measure to evaluate adiposity, reflects fat centralization and is considered a better indicator of visceral adipose tissue and obesity outcomes (such as metabolic and cardiovascular diseases) than BMI, however, it has some accuracy issues for not being able to differentiate lean and fat tissue, and also subcutaneous and visceral fat (Cameron, Jones, Griffiths, Norris, & Pettifor, 2009). Waist circumference is considered a quick and inexpensive technique yet it may be subject to observational errors. (Browning et al., 2011; Cameron et al., 2009; Flegal et al., 2009).

Skinfold thickness measurements are used to measure subcutaneous fat located beneath the skin and to estimate percent body fat through three-site skinfold measures that have been shown to be highly correlated with percent body fatness (Balady, Berra, & Golding, 2000). This measurement is read with a caliper at the upper arm, below the scapula, above the hip bone, the abdomen and the thigh. It is a practical technique used in clinical context but it is liable to measurement errors which can jeopardize the validity of the results. This technique only measures the subcutaneous fat, and cannot assess visceral fat which makes it imprecise and less accurate when measuring body fatness (Goncalves et al., 2012).

Hydrostatic underwater weighing is a method of body composition assessment that gives information about a person's total body density based on the Archimedes principle. This principle states that the volume of a submerged object equals to the weight of the fluid that the object displaces. That is, a person who has more body fat than lean mass, whereas lean mass is heavier than fat mass, weighs less under water than a person who has more lean mass than fat mass. This technique is impractical, requires training and involves cooperation from the individual to be measured since the individual has to be motionless long enough to be measured(Lee RD & DC, 2003).

Bioelectrical impedance analysis is a technique that allows us to calculate fat mass percentage by passing a low and safe electrical current through the body via electrodes. Lean mass has higher electrical conductivity and lower impedance than fat mass due to its electrolyte tenor, thus the current encounters resistance when it passes through fat tissue. This then allows us to compute body fat percentage when set against a person's height, gender and weight. This method is safe, easy, noninvasive, portable and fast but requires that the patient is well hydrated, has not exercised in the previous 4 to 6 hours, and have not consumed alcohol, caffeine or diuretics in the previous 24hours(Indorato D, 2001).

Dual-energy X-ray absorptiometry (DEXA) assesses body composition in a more accurate and precise way (Flegal et al., 2009; Goncalves et al., 2012). This method is able to accurately measure whole body and regional distribution of lean and fat tissue (Browning et al., 2011; Kaul et al., 2012). DEXA is a relatively inexpensive technique, easy to undertake, the X-ray radiation associated with it is very low and requires little cooperation from the patient (Foo et al., 2013). However it requires participants to go to a clinic or other setting with the appropriate equipment to use it. It also cannot be used in a field study and it is difficult to use in a very large epidemiological studies that might involve participants spread over a large geographic region.

Aims

In a secondary analysis of cross sectional data from four different studies, we propose to evaluate whether body composition is a factor that interferes with the quality of life in breast cancer patients, and breast, endometrial and colon cancer survivors. We also intend to analyze which measure of body composition assessment is most highly associated to quality of life.

Chapter 2 – Methodology

Sample

A secondary analysis was conducted of base line data from four previous studies conducted at the MD Anderson Cancer Center in Huston, Texas, United States of America.

These studies included a total of 31 female breast cancer patients (receiving chemotherapy) and a total of 133 post-treatment female cancer survivors (103 endometrial cancer survivors, 29 breast cancer survivors and 1 colon cancer survivor. The studies addressed weight gain prevention for breast cancer patients (Project BALANCE); predictors of exercise adoption in endometrial cancer survivors (Steps to Health); weight management delivered by telephone counseling or internet (Healthy Moves 2); and diet and physical activity intervention delivered with and without a spouse (Healthy Moves 4).

Project Balance included 31 breast cancer patients, and measures used to assess body composition included BMI, waist circumference, body fat percentage estimated from the combination of three site skinfold measures (triceps, suprailium, quadriceps), and body fat percentage measured using DEXA. Steps to Health (Basen-Engquist K. et al., 2014) included 97 post-treatment endometrial cancer survivors and to assess body composition the following techniques were used: BMI, waist circumference, and body fat percentage estimated from three-site skinfold measures (triceps, suprailium and quadriceps). Healthy Moves 2 and 4, combined together, included 36 cancer survivors, with different types of cancer, and the techniques used to assess body composition were: BMI, waist circumference and body fat percentage as measured in a whole body DEXA. Quality of life was assessed in the same way in the four studies, using the Medical Outcomes Study Short Form-36 Health Survey Questionnaire (SF-36) (Appendix 1). For this study, we only selected individuals who had complete information of the body composition and quality of life assessment. Since Healthy Moves 2 and Healthy Moves 4 used the same body composition measures it was decided to combine and analyze the two studies together. As to the other studies, because each study used different methods to assess body composition, it was decided to analyze them separately. It was also decided to include only women since the number of male participants was very low and existed only in the Healthy Moves study.

It should be noted that the study entitled "Steps to Health" has been accepted for publication, while the other two studies have not been published into research article yet. However, results for Healthy moves study have been presented in a conference poster, at a meeting called ASPO (American Society of Preventive Oncology).

Table 1 Characterization of the studies used in the realization of the present work.

Study name	Study purpose	Sample size	Sample's characteristic	Cancer types	Age (mean)	Age range	Body composition measures	QoL measures
Project BALANCE	Weight gain prevention	31	Newly diagnosed with cancer	Breast cancer (stage II and III)	50	27-77	BMI Waist circ. Skinfolds DEXA	SF-36
Steps to Health	Predictors of exercise adoption	97	Post-treatment survivors	Endometrial cancer (stage I, II, III)	56	25-76	BMI Waist circ. Skinfolds	SF-36
Healthy Moves	HM2 - weight management delivered by telephone counseling or internet. HM4 - diet and physical activity intervention delivered with and without a spouse	36	Surgery only (16) Chemotherapy only (1) Surgery and chemotherapy (17) Other treatment (2)	Breast cancer (n=29) Endometrial cancer (n=6) Colon cancer (n=1)	58	39-73	BMI Waist circ. DEXA	SF-36

Measures

To conduct this analysis, study records of the females subjects involved in each study were consulted to collect data related to anthropometric, body composition and quality of life measures. Several anthropometric and body composition measures were used, including BMI, percent body fat estimated from skinfold measures, waist circumference and DEXA. Skinfold measurement is a means of assessing body fat mass, based on subcutaneous adipose tissue, and the combination of three site skinfold measures (triceps, suprilium, quadriceps) appears to reflect best body adiposity (Balady et al., 2000). On each study, skinfold assessments were performed on all participants by the same person to avoid inter-operator variance, and calculated by using the formula recommended in the American College of Sports Medicine (Balady et al., 2000). Waist and hip circumference were measured using a cloth tape to measure to the nearest 0.1 cm at the narrowest part of the torso and the maximum extension of the hip/buttocks area with proper tension applied to the tape. DEXA is a means of assessing bone mineral density and is now used in research to measure fat and lean body mass in whole body and in specific regions (Glickman, Marn, Supiano, & Dengel, 2004). From each scan it was collected: percent of body fat, fat and lean mass for total body region as well as defined body zones (trunk, leg and arms) expressed in grams. The values of fat mass percentage were evaluated based on the ranges of percentage of fat mass stipulated by the American College of Sports Medicine.

In order to assess the patient's quality of life, participants completed The Medical Outcomes Study Short Form-36 Health Survey Questionnaire (SF-36). SF-36 has proved to be a valid, reliable and consistent measure for rating health-related quality of life in several research fields and comprises eight dimensions of health: physical function, social function, bodily pain, mental health, energy and fatigue, general health perceptions, role limitations caused by physical problems, and role limitations caused by emotional problems (Ware, 2000). These eight scales form two distinct groups: physical component summary (PCS) and mental component summary (MCS) which capture more than 80% of the reliable variance in the eight subscales (Ware, 2000).

Methods

Linear regression analyses were performed to examine associations between measures of adiposity and two quality of life scores based on SF-36 (physical component score and mental component score), adjusting for confounders of age, skin color and education, for each study population (Project BALANCE, Healthy Moves, Steps to Health). Additional confounders of cancer type and treatment type were considered in Healthy Moves and Steps to Health data analyses. In order to find the best fitting linear regression model, interaction effects between confounders and body fat measures were examined. Best subset of the full model including all interaction effects was identified using Akaike Information Criterion (AIC). Final model selection considered the significance of the interaction term and F test to compare model fit between the best subset and the main effects models.

Chapter 3 – Results

Sample characteristics

1 – Project Balance

Data from 31 participants who had DEXA data at baseline were examined. All 31 participants were female with newly diagnosed stage II or III breast cancer, who had not undergone treatment until the time when the data was collected. The average age was 50 years old (sd = 12), and ranged from 27 to 77 years old. Majority of the participants in the data were white (58,1%), while 41.9% were Black and Hispanic. and 48% of the participants had at least a four year college degree.

The table below describes the anthropometric characteristics of the sample. It can be observed that the mean of BMI is 29.1, corresponding to overweight. The mean for the waist circumference was 88.60 centimeters. Regarding body fat measured by skinfolds and DEXA, both the means show a high fat mass which is shown to increase the risk of developing health problems such as cardiovascular disease, respiratory problems, metabolic disorders and cancer.

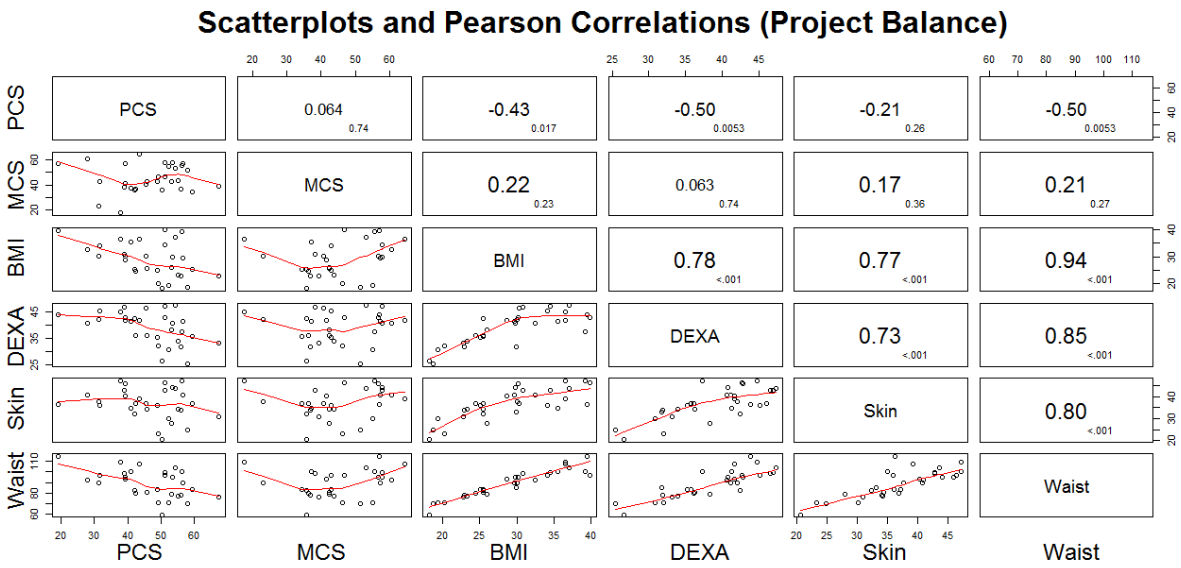
Table 2 Demographic characteristics of the sample from Project Balance study.

Skin color		
Non-White	n (%)	13 (41.9)
White	n (%)	18 (58.1)
Education		
Less than four year college degree	n (%)	16 (51.6)
At least four year college degree	n (%)	15 (48.4)
Age, years	mean (sd)	50 (12)

	range	27-77
Body mass index, kg/m²	mean (sd)	29.1 (6.3)
	range	18.3 - 40.0
Waist Circumference, cm	mean (sd)	88.60 (13.28)
	range	59.00 - 115.00
Body fat by skin folds, %	mean (sd)	36.7 (6.89)
	range	20.6 – 47.3
DEXA, %	mean (sd)	38.78 (5.98)
	range	25.40 - 47.30
Weight, kg	mean (sd)	75.13 (15.87)
	range	46.10 – 101.20
PCS	Mean (sd)	46.65 (10.53)
	range	19.22 - 67.54
MCS	Mean (sd)	44.99 (11.06)
	range	17.54 – 64.31

Pearson correlations between physical component summary (PCS) and measures of adiposity indicated significant inverse associations between physical component summary (PCS) and BMI (r = -0.43, p-value = 0.017), body fat percentage from DEXA (-0.50, p-value = 0.005), as illustrated in Figure 1. Waist circumference was also inversely associated with PCS score (r = -0.50, p-value =0.005), and highly correlated with BMI (r = 0.94, p-value < 0.001), body fat percentage from DEXA (r = 0.85, p-value < 0.001), and body fat percentage from skin fold measures (r = 0.80, p-value < 0.001). Scatterplots of physical component summary (PCS) and measures of adiposity and waist circumference indicate that the associations are linear. Scatterplots of mental component summary (MCS) and measures of adiposity and waist circumference indicate no linear associations; smoothed line (red) in the scatterplots of Figure 1 looks quadratic, but the indicated shape is mostly due to few observations with very low mental component summary (MCS) scores.

Figure 1 Scatter plot matrix and Pearson correlation estimates for Project Balance study.



The graphs reflect whether there is a statistically significant relationship between physical and mental component of quality of life and the various techniques for assessing body composition (BMI, DEXA, Skinfold, Waist circumference), and whether the relationship is positive or negative. The cells above the main diagonal show the values of r (larger font) and p (lower case).

2 – Steps to Health

The sample for this test includes 97 endometrial cancer survivors who responded to all questionnaires for the baseline SF-36, all females, diagnosed with stage I, II or IIIa endometrial cancer in the past five years that have completed surgical or radiation treatment at least six months ago. The average age was 56 years old (sd = 11), and ranged from 25 to 76 years old.

The majority of the sample was white, corresponding to 74.2%, while 25.8% were Black and Hispanic. Majority of the participants had less than four year college degree (58.8%).

The following table describes the anthropometric characteristics of the sample. It can be observed that the mean of BMI is 34.4, corresponding to obesity. The mean for the waist circumference was 99.88 centimeters. Regarding the body fat measured by skin folds, the mean (38.27%) shows a high fat mass which is known to increase the risk of developing health problems such as cardiovascular disease, respiratory problems, gastrointestinal diseases and cancer.

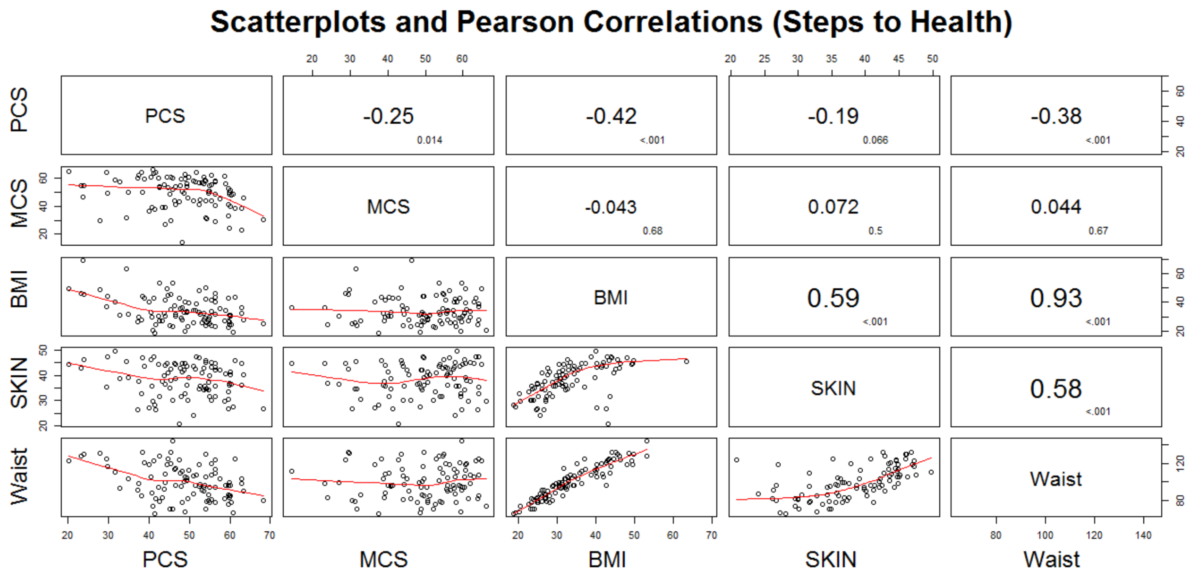
Table 3 Demographic characteristics of the sample from Steps to Health study.

Skin color		
Non-White	n (%)	25 (25.8)
White	n (%)	72 (74.2)
Education		
Less than four year college degree	n (%)	57 (58.8)
At least four year college degree	n (%)	40 (41.2)
Age, years	mean (sd)	56 (11)
	range	25-76
Body mass index, kg/m²	mean (sd)	34.4 (9.6)
	range	18.7 – 69.3
Waist Circumference, cm	mean (sd)	99.88 (18.33)
	range	65.1 - 144.1
Body fat by skin folds, %	mean (sd)	38.27 (6.49)

	range	20.9 – 49.8
PCS	mean (sd)	48.33 (10.03)
	range	20.2 - 68.34
MCS	mean (sd)	49.47 (11.13)
	range	14.32 – 66.17

Pearson correlations between physical component summary (PCS) and measures of adiposity indicated significant inverse associations between physical component summary (PCS) and BMI ($r = -0.42$, p-value < 0.001), as illustrated in Figure 2. Waist circumference was also inversely associated with physical component summary (PCS) score ($r = -0.38$, p-value < 0.001), and highly correlated with BMI ($r = 0.93$, p-value < 0.001) and body fat percentage from skin fold measures ($r = 0.58$, p-value < 0.001). Scatterplots of physical component summary (PCS) and measures of adiposity and waist circumference indicate that the associations are linear. Scatterplots of mental component summary (MCS) and measures of adiposity and waist circumference indicate no linear associations.

Figure 2 Scatter plot matrix and Pearson correlation estimates for Steps to Health study.



The graphs reflect whether there is a statistically significant relationship between physical and mental component of quality of life and the various techniques for assessing body composition (BMI, Skinfold, Waist circumference), and whether the relationship is positive or negative. The cells above the main diagonal show the values of r (larger font) and p (lower case).

3 – Healthy Moves

This study includes a sample of 36 female cancer survivors; more precisely 29 breast cancer survivors, 1 colon cancer survivor, and 6 endometrial cancer survivors. 16 of the individuals had undergone surgery only, 1 had undergone chemotherapy only, 17 had undergone surgery and chemotherapy and 2 had undergone other cancer treatment. The average age was 58 years old (sd = 8) and ranged from 39 to 73 years old. The majority of the sample is white (75%), corresponding to 27 individuals, while 25% were Black and Hispanics. The majority of the participants had less than four-year college degree (52.8%).

Regarding the anthropometric characteristics, as can be seen in the following table, the mean of BMI is 31.3, corresponding to obesity. The mean for the waist circumference was 92.26 centimeters. As to DEXA, the mean of body fat percentage obtained is 44.3%, corresponding to obesity and ranged from 35.2% to 55.4%.

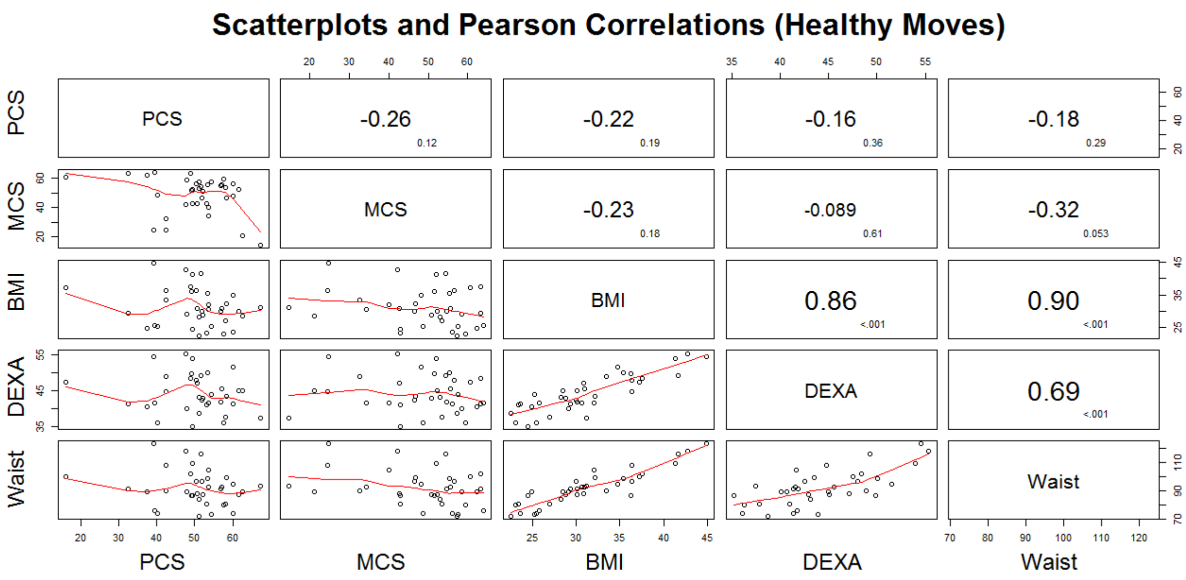
Table 4 Demographic characteristics of the sample from Healthy Moves study.

Skin color		
Non-White	n (%)	9 (25)
White	n (%)	27 (75)
Education		
Less than four year college degree	n (%)	19 (52.8)
At least four year college degree	n (%)	17 (47.2)
Age, years	mean (sd)	58 (8)
	range	39-73
Body mass index, kg/m²	mean (sd)	31.3 (5.9)
	range	22.6 – 44.9
DEXA, %	mean (sd)	44.29 (5.24)
	range	33.24 – 55.39
Waist Circumference, cm	mean (sd)	92.26 (12.58)
	range	71.75 - 123.19
PCS	Mean (sd)	50.22 (9.60)
	range	16.10 - 67.34
MCS	Mean (sd)	48.47 (12.48)

	range	14.66 – 63.96

Pearson correlations between physical component summary (PCS) and measures of adiposity indicated no significant linear associations between physical component summary (PCS) and measures of adiposity. Waist circumference was highly correlated with BMI (p-value < 0.001) and body fat measured by DEXA (p-value < 0.001). Scatterplots of PCS and measures of adiposity and waist circumference indicate weak linear associations. Scatterplots of mental component summary (MCS) and measures of adiposity and waist circumference indicate no linear associations.

Figure 3 Scatter plot matrix and Pearson correlation estimates for Healthy Moves study.



The graphs reflect whether there is a statistically significant relationship between physical and mental component of quality of life and the various techniques for assessing body composition (BMI, DEXA, Waist circunference), and whether the relationship is positive or negative. The cells above the main diagonal show the values of r (larger font) and p (lower case).

Associations between adiposity and quality of life scores

1 – Project Balance

Results from four linear regression analysis to predict physical component summary (PCS) from BMI, waist circumference, skinfold body fat and DEXA, each adjusting for confounder effects of age, education level, and skin color suggests that BMI, body fat percentage from DEXA, and waist circumference are significantly associated with lower physical component summary (PCS) score, adjusting for confounders (age, education and skin color), as indicated by the bootstrapped 95% confidence intervals (Table 1). Although some individuals had missing values for BMI, body fat measured by skinfold, and waist circumference, measures of model fit indicates that a larger proportion of variance is explained by body fat measured by DEXA (adjusted R-square = 0.36). In addition, model with body fat measured by DEXA had better fit (AIC = 219.40, MSE = 58.88) compared to other three models. Measures of adiposity and waist circumference were not significantly associated with mental component summary (MCS), adjusting for confounders (age, education and skin color); (Table 2).

Table 5 Estimates from four linear regression analysis to predict PCS from BMI, DEXA, skinfold body fat and waist circumference

	N	Estimate	Raw P-value	Bootstrap 95% CI[a]	Adj. R-sq[b]	MSE	AIC
BMI	30	-0.605	0.031	(-1.21, -0.16)	0.33	62.26	221.08
DEXA	31	-0.745	0.014	(-1.54, -0.32)	0.36	58.88	219.40
Skinfold	30	-0.275	0.282	(-0.77, 0.13)	0.22	71.81	225.36
Waist	29	-0.311	0.023	(-0.58, -0.09)	0.35	61.54	213.77

[a] Bootstrapped confidence intervals are based on 2000 resamples.

[b] Adjusted R squared is a function of R squared value such that $R^2_{adj} = 1 - (1 - R^2)\left(\frac{n-1}{n-p-1}\right)$.

Table 6 Estimates from four linear regression analysis to predict MCS from BMI, DEXA, skinfold body fat, and waist circumference.

	N	Estimate	Raw P-value	Bootstrap 95% CI[a]	Adj. R-sq[b]	MSE	AIC
BMI	30	0.501	0.146	(-0.09, 1.22)	0.03	99.33	235.09
DEXA	31	0.307	0.424	(-0.18, 1.00)	-0.03	105.46	236.89
Skinfold	30	0.299	0.329	(-0.23, 0.86)	-0.02	71.81	225.36
Waist	29	0.254	0.133	(-0.06, 0.57)	0.03	61.54	213.77

[a] Bootstrapped confidence intervals are based on 2000 resamples.

[b] Adjusted R squared is a function of R squared value such that $R^2_{adj} = 1 - (1 - R^2)\left(\frac{n-1}{n-p-1}\right)$.

2 – Steps to Health

Results from three linear regression analysis to predict physical component summary (PCS) from BMI, body fat percentage from skinfold, and waist circumference, each adjusting for confounder effects of age, education level, skin color, disease stage and treatment suggests that BMI and waist circumference was significantly associated with lower physical component summary (PCS) score, adjusting for confounders of age, education, skin color, disease stage and treatment, as indicated by the bootstrapped 95% confidence intervals. Measures of adiposity and waist circumference were not significantly associated with mental component summary (MCS), adjusting for confounders of age, education, skin color, disease stage and treatment.

Table 7 Estimates from three linear regression analysis to predict PCS from BMI, skinfold body fat, and waist circumference.

	N	Estimate	Raw P-value	Bootstrap 95% CI[a]	Adj. R-sq[b]	MSE	AIC
BMI	97	-0.438	< 0.001	(-0.63, -0.23)	0.27	67.00	701.13
Skinfold	93	-0.298	0.042	(-0.60, 0.01)	0.15	72.34	680.09
Waist	95	-0.197	<0 .001	(-0.30, -0.09)	0.24	65.62	685.07

[a] Bootstrapped confidence intervals are based on 2000 resamples.

[b] Adjusted R squared is a function of R squared value such that $R^2_{adj} = 1 - (1 - R^2)\left(\frac{n-1}{n-p-1}\right)$.

Table 8 Estimates from three linear regression analysis to predict MCS from BMI, skinfold body fat, and waist circumference.

	N	Estimate	Raw P-value	Bootstrap 95% CI[a]	Adj. R-sq[b]	MSE	AIC
BMI	97	0.073	0.547	(-0.16, 0.33)	0.14	97.43	737.45
Skinfold	93	0.138	0.406	(-0.20, 0.47)	0.16	94.41	704.86
Waist	95	0.092	0.143	(-0.04, 0.22)	0.15	96.24	721.44

[a] Bootstrapped confidence intervals are based on 2000 resamples.

[b] Adjusted R squared is a function of R squared value such that $R^2_{adj} = 1 - (1 - R^2)\left(\frac{n-1}{n-p-1}\right)$.

3 – Healthy Moves

Results from three linear regression analysis to predict physical component summary (PCS) from BMI, body percentage from DEXA, and waist circumference, each adjusting for confounder effects of age, education level, skin color, treatment type, and cancer type suggests that we do not have sufficient statistical evidence to conclude that the measures of adiposity are significantly associated with the PCS score, adjusting for confounders of age, education and skin color, as indicated by the bootstrapped 95% confidence intervals. Measures of adiposity and waist circumference were not significantly associated with mental component summary (MCS), adjusting for confounders of age, education, skin color, treatment type, and cancer type.

Table 9 Estimates from three linear regression analysis to predict PCS from BMI, DEXA and waist circumference.

	N	Estimate	Raw P-val.	Bootstrap 95% CI[a]	Adj. R-sq[b]	MSE	AIC
BMI	36	-0.528	0.101	(-1.09, 0.01)	0.06	62.46	273.01
DEXA	36	-0.435	0.246	(-1.19, 0.32)	0.01	65.86	274.92
Waist	36	-0.190	0.207	(-0.50, 0.08)	0.02	65.22	274.57

[a] Bootstrapped confidence intervals are based on 2000 resamples.

[b] Adjusted R squared is a function of R squared value such that $R^2_{adj} = 1 - (1 - R^2)\left(\frac{n-1}{n-p-1}\right)$.

Table 10 Estimates from three linear regression analysis to predict MCS from BMI, DEXA and waist circumference.

	N	Estimate	Raw P-val.	Bootstrap 95% CI[a]	Adj. R-sq[b]	MSE	AIC
BMI	36	-0.326	0.446	(-1.35, 0.78)	-0.02	115.33	295.08
DEXA	36	-0.195	0.693	(-1.31, 1.21)	-0.04	117.27	295.68
Waist	36	-0.239	0.223	(-0.66, 0.25)	0.01	111.32	293.81

[a] Bootstrapped confidence intervals are based on 2000 resamples.

[b] Adjusted R squared is a function of R squared value such that $R^2_{adj} = 1 - (1 - R^2)\left(\frac{n-1}{n-p-1}\right)$.

Chapter 4 – Discussion and Conclusion

Discussion

Obesity, by itself, is a risk factor for the development of certain chronic diseases and is associated with an increased risk of mortality and reduced quality of life. Among the many diseases for which obesity is connected, we can highlight cancer wherein the excess of adiposity is considered a risk factor for being associated with a high mortality rate and with an increased risk of recurrence of cancer. Whereas millions of people worldwide are living with a diagnosis of cancer, and considering that this disease figures among the leading causes of death worldwide, constant research on this topic becomes essential. Previous studies argue that nutritional deterioration in cancer patients is detrimental to their quality of life (Ravasco, Monteiro-Grilo, & Camilo, 2007; Ravasco, Monteiro-Grilo, Vidal, & Camilo, 2004, 2006).

In this study we aimed to evaluate the impact of adiposity on quality of life of cancer patients and cancer survivors and, as predicted, we can consider that excess body fat has a negative impact in the well-being of the individual hindering and decreasing their quality of life both in cancer patients and in cancer survivors. However, throughout this study there were a few limitations that should be noted which may possibly have influenced the results.

Initially, we intended to pooldata from the three studies differed in terms of study population and measures. Thus, we were not able to combine the samples across different studies. Consequently, some of the studies had relatively small sample size compared to others, especially for BALANCE and Healthy Moves. Albeit the limitations in sample size, we observe evidence of statistically significant associations between quality of life measures and adiposity in project BALANCE. A future study with larger sample size may be needed to generalize the associations between quality of life and adiposity in breast cancer patients.

Observations with missing values were not included in any of the analyses. In this study, we assumed that observations were missing completely at random (MCAR). Potentially, the missing data mechanism may not be MCAR. In such conditions, estimates based on the assumption may be biased. In addition, for Healthy Moves study, only females were included in the analyses, due to large imbalance in the proportions of men and women in this study: the sample was mostly women (85.71%), with very small proportion of men (14.29%). Thus, results for Healthy Moves study is only representative of the women population.

It should also be noted that we did not account for possible measurement errors in the measures of body composition. In presence of substantial measurement errors in covariates, regression coefficient estimates may be biased (Carroll, Ruppert, Stefanski, & Crainiceanu, 2006; Fuller, 2006). Measurement errors in measuring body composition have been reported for BMI (Rothman, 2008), skinfold measures (Arroyo, Freire, Ansotequi, & Rocandio, 2010), and also for DEXA(Wosje, Knipstein, & Kalkwarf, 2006). Thus, a future study may be needed to investigate the impact of measurement errors across different measures of body compositions in associations to quality of life.

As to the method of assessing body composition that best predicts the relationship between adiposity and quality of life, based on our linear regression model fit, we found that DEXA and waist circumference seem to be the best body composition measurements to predict physical component summary (PCS) scores. However, the information that we have in the present study is not enough to draw these conclusions. Although the linearity assumption seemed to be adequate based on our samples, there may be possibly a more complex association between PCS and the measures of body composition.

Regarding the Healthy Moves study, the results differed from the studies BALANCE and Steps to Health, not showing statistically significant evidence. However, the direction of association between the body composition measurements (BMI, DEXA and waist circumference) and quality of life seemed to be consistent with what we found for the other studies.

After completing the study, we apprehended that obesity not only represents a risk factor in cancer development but it also influences the quality of life of people with cancer during and after treatment. These findings coincide with other obtained by other studies which argue that maintaining or increasing lean body mass along with a percentage of fat mass between the recommended levels, can contribute to an improved quality of life in these individuals (Brown et al., 2003; Caro, Laviano, Pichard, & Candela, 2007; Marín Caro, Laviano, & Pichard, 2007; Ravasco et al., 2004). Thus, in the fight against cancer, it becomes important to uphold the importance of maintaining a balanced body composition, to establish it as goal, so that both cancer patients and cancer survivors benefit from it. We then advocate the importance of nutritional therapy in optimizing the balance between energy expenditure and food intake, as well as physical activity, as part of the integral oncological support since it contributes positively to a better quality of life.

Conclusion

Body composition appears to have an important role in cancer patients with respect to the onset of cancer, in which obesity is associated with the development of malignancies; to treatment, wherein the treatment response may decrease if depletion of lean body mass; and to the follow-up, in which weight loss and lean mass loss is associated with cancer recurrence, poor prognosis and shorter survival.

Through this study and from the obtained results we find that higher values of body fatness are associated with lower scores for physical aspects of quality of life, suggesting that excess body fat contributes to a marked limitation in self-care, in physical, social and role activities, severe bodily pain, frequent tiredness and poor health both in cancer patients and survivors.

Among the measures of body composition, waist circumference and DEXA were preferred compared to BMI or body fat percentage measured by skinfold, in predicting physical component summary (PCS) scores using linear models.

Since the evidence is based on a small sample and yet shows indication of significant association, it would be interesting to test the same hypothesis in a larger sample of the same population.

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APPENDIX 1

Medical Outcome Study Short-Form 36

1. In general, would you say your health is:	
Excellent	1
Very good	2
Good	3
Fair	4
Poor	5

2. **Compared to one year ago**, how would your rate your health in general **now**?	
Much better now than one year ago	1
Somewhat better now than one year ago	2
About the same	3
Somewhat worse now than one year ago	4
Much worse now than one year ago	5

The following items are about activities you might do during a typical day. Does **your health now limit you** in these activities? If so, how much?

(Circle One Number on Each Line)

	Yes, Limited a Lot	Yes, Limited a Little	No, Not limited at All
3. **Vigorous activities**, such as running, lifting heavy objects, participating in strenuous sports	[1]	[2]	[3]
4. **Moderate activities**, such as moving a table, pushing a vacuum cleaner, bowling, or playing golf	[1]	[2]	[3]
5. Lifting or carrying groceries	[1]	[2]	[3]
6. Climbing **several** flights of stairs	[1]	[2]	[3]

7. Climbing **one** flight of stairs	[1]	[2]	[3]
8. Bending, kneeling, or stooping	[1]	[2]	[3]
9. Walking **more than a mile**	[1]	[2]	[3]
10. Walking **several blocks**	[1]	[2]	[3]
11. Walking **one block**	[1]	[2]	[3]
12. Bathing or dressing yourself	[1]	[2]	[3]

During the **past 4 weeks**, have you had any of the following problems with your work or other regular daily activities **as a result of your physical health**?

(Circle One Number on Each Line)

	Yes	No
13. Cut down the amount of time you spent on work or other activities	1	2
14. **Accomplished less** than you would like	1	2
15. Were limited in the **kind** of work or other activities	1	2
16. Had **difficulty** performing the work or other activities (for example, it took extra effort)	1	2

During the **past 4 weeks,** have you had any of the following problems with your work or other regular daily activities **as a result of any emotional problems** (such as feeling depressed or anxious)?

(Circle One Number on Each Line)

	Yes	No
17. Cut down the **amount of time** you spent on work or other activities	1	2
18. **Accomplished less** than you would like	1	2
19. Didn't do work or other activities as **carefully** as usual	1	2

20. During the **past 4 weeks,** to what extent has your physical health or emotional problems interfered with your normal social activities with family, friends, neighbors, or groups?

(Circle One Number)

Not at all 1

Slightly 2

Moderately 3

Quite a bit 4

Extremely 5

21. How much **bodily** pain have you had during the **past 4 weeks**?

(Circle One Number)

None 1

Very mild 2

Mild 3

Moderate 4

Severe 5

Very severe 6

22. During the **past 4 weeks,** how much did **pain** interfere with your normal work (including both work outside the home and housework)?

(Circle One Number)

Not at all 1

A little bit 2

Moderately 3

Quite a bit 4

Extremely 5

These questions are about how you feel and how things have been with you **during the past 4 weeks**. For each question, please give the one answer that comes closest to the way you have been feeling.

How much of the time during the **past 4 weeks** . . .

(Circle One Number on Each Line)

	All of the Time	Most of the Time	A Good Bit of the Time	Some of the Time	A Little of the Time	None of the Time
23. Did you feel full of pep?	1	2	3	4	5	6
24. Have you been a very nervous person?	1	2	3	4	5	6
25. Have you felt so down in the dumps that nothing could cheer you up?	1	2	3	4	5	6
26. Have you felt calm and peaceful?	1	2	3	4	5	6
27. Did you have a lot of energy?	1	2	3	4	5	6
28. Have you felt downhearted and blue?	1	2	3	4	5	6
29. Did you feel worn out?	1	2	3	4	5	6
30. Have you been a happy person?	1	2	3	4	5	6
31. Did you feel tired?	1	2	3	4	5	6

32. During the **past 4 weeks,** how much of the time has your **physical health or emotional problems** interfered with your social activities (like visiting with friends, relatives, etc.)?

(Circle One Number)

All of the time 1

Most of the time 2

Some of the time 3

A little of the time 4

None of the time 5

How TRUE or FALSE is each of the following statements for you.

(Circle One Number on Each Line)

	Definitely True	Mostly True	Don't Know	Mostly False	Definitely False
33. I seem to get sick a little easier than other people	1	2	3	4	5
34. I am as healthy as anybody I know	1	2	3	4	5
35. I expect my health to get worse	1	2	3	4	5
36. My health is excellent	1	2	3	4	5