IMPACT OF A DIET INTERVENTION PROGRAM ON THE SERUM ALBUMIN CONCENTRATIONS, ANTROPOMETRICAL STATUS AND QUALITY OF LIFE OF BREAST CANCER PATIENTS RECEIVING CHEMOTHERAPY

by

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AI	Adequate Intakes
AJCC	American Joint Committee on Cancer
AMP	Adrenosine Monophosphate
AW	Actual weight
BEE	Basal Energy Expenditure
BEI	Bio-electrical Impedance
BF	Body Fat
BMI	Body Mass Index
BRM	Biological Response Modifiers
C	Control
CAF	Cyclophosphamide, Adriomison and 5FU
CHO	Carbohydrate
CI	Confidence Interval
CMF	Cyclophosphamide, Methotrexate and 5FU
DCs	Dendritic cells
DHA	Docosahexaenoic Acid
DNA	Deoxyribonucleic Acid
DRI	Dietary Reference Intakes
E	Experimental
ECOC	Eastern Cape Oncology Centre
EPA	Eicosapentaenoic Acid
FFA	Free Fatty Acids
GLA	Gamma Linoleic Acid
GMP	Guanosine Monophosphate
HIV	Human Immunodeficiency Virus
IBW	Ideal Body Weight
IL-1	Interleukin 1
IL-6	Interleukin 6
LA	Linoleic Acid
LIF	Leukemia-Inhibitory Factor
LM	Lean Muscle
LMF	Lipid-Mobilizing Factors
MAFA	Mid-Arm Fat Area
MAMA	Mid-Arm Muscle Area
MUAC	Mid-Upper Arm Circumference
MUFA	Mono-Unsaturated Fatty Acid
NHANES	National Health and Nutrition Examination Survey
Pan. Acid	Panthothenic Acid
PMF	Protein-Mobilizing Factor
PUFA	Poly-Unsaturated Fatty Acid

RDA	Recommended Dietary Allowances
SANAS	South African National Accreditation System
SFA	Saturated Fatty Acid
TE	Total Energy
TNF	Tumor Necrosis Factor
TSF	Triseps Skin Fold
Vit	Vitamin

CHAPTER 1

INTRODUCTION

1.1 INTRODUCTION

Each living cell, whether from plant or human origin, normal or abnormal, needs sufficient nutrients for survival. Adequate nutrition sustains normal cellular activity, whereas nutrition abnormalities lead to disturbed cellular functioning and clinical disease (McCallum & Polisena, 2000, p.160). A small percentage of cancers can be explained by genetics. Dietary choices or level of physical activity is almost as significant a risk factor as cigarette smoking (McCallum & Polisena, 2000, p.1). Research suggests that about 90% of cancer incidence is due to life-style and environmental factors, supporting the notion that most cancers are preventable (Curry, Byers & Hewitt, 2003). The relationship between nutrition and each of the stages in the development of cancer is becoming increasingly apparent (McCallum & Polisena, 2000, p.160; Mathers & Burn, 1999, p.402).

Cancer survivors include persons just diagnosed, patients receiving treatment, those recovering from cancer treatment, individuals who are post-recovery and disease free, and those in the advanced stages of the disease (McCallum, 2003, p.63). Cancer and its treatment take a toll on nutritional status. Many patients lose weight and/or lean body mass, while others may gain weight and/or adipose tissue. The primary goal of recovery is to achieve/maintain a healthy body and functional ability, optimize visceral protein stores, correct problems such as anaemia or impaired organ functioning and, most importantly, manage chronic treatment side effects. Patients who are unable to consume adequate macro- or

micronutrients to achieve these goals may require supplementation to achieve optimum nutrition (McCallum, 2003, p.63). Experts agree that eliminating modifiable risk factors, such as smoking and poor nutritional intake, is the most effective way to reduce the burden of cancer (Curry et al., 2003). About 25% of cancer deaths may be attributed to dietary factors (McCallum, 2000, p.11; Doll & Peto, 1996).

Increased body weight, including body fat are associated with high health risk, and therefore body fat distribution and Body Mass Index (BMI) are major predictors of obesity associated risks (Abu-Abid et al., 2002). The number of women that survive breast cancer is increasing, but weight gain and psychosocial distress is commonly encountered as adverse responses to breast cancer and treatment. Being overweight has been associated with increased cancer risk, especially the risk for breast cancer (Saxton et al., 2006; Calle & Thun, 2004). Eng et al. (2005) states that women who had gained more than 15 kg since age 20 years were at a 1.6-fold increased risk of breast cancer, relative to women with a stable body weight. Women who gain more than 11 kg during the peri- and postmenopausal years, had 1.62 times the risk of breast cancer of those whose weight remained unchanged during this time period. Weight loss over the life time was associated with decreased risk of postmenopausal breast cancer (Eng et al., 2005). Up to 60% of women diagnosed with breast cancer experience an increase in weight with chemotherapy and treatment-related menopause, and evidence show that women who gain weight after diagnosis have an increased risk of disease recurrence compared to normal weight women (Saxton et al., 2006). On the basis of observational studies, women with breast cancer who are overweight, particularly higher levels of obesity, or women who gain weight after diagnosis are found to be at greater risk for breast cancer recurrence and death compared with lighter women. Obesity is also associated with hormonal profiles likely to stimulate breast cancer growth (Flegal et al.,

2005; Chlebowski et al., 2002). Obesity is a growing problem in contemporary societies, due to the rapid adoption of a modernized lifestyle that results in increased carbohydrate and fat-rich dietary intake and reduced physical activity (Abu-Abid et al., 2002). Dietary energy restriction can reduce body weight and induce a positive effect on psychological well being in obese women and breast cancer survivors. Weight loss interventions that reduce dietary intake of fat to 18% to 25% of the total energy can also evoke a significant reduction in serum estrogen levels in pre- and postmenopausal women (Wu et al., 1999).

Specific associations between dietary fat intake and cancer have also been established by epidemiological and laboratory research. A good example is the fact that breast cancer is less common in Japan, and that Japanese breast cancer patients have a better prognosis than their peers in America (Frankmann, 2000, p.868). Studies have shown that populations with a high total fat intake, such as the Danes, suffer five times more cancer fatalities due to breast cancer than populations with a lower total fat intake, such as the Japanese (Alberts, 1993, p.17). Laboratory research over the last 50 years and research derived from data provided by 39 countries show that total dietary fat and energy intake has a significant effect on the growth and development of tumors, including breast cancer (McCallum & Polisena, 2000, p.160; Alberts, 1993, p.17). On the other hand, studies by Ross et al. (2006) indicate that post menopausal women on a low-fat diet did not result in a statistically significant reduction in invasive breast cancer risk over an eight year follow-up period. Non significant trends observed by the researchers did however suggest a reduced risk associated with a low-fat diet, with longer nonintervention periods. Breitkreutz et al. (2005) states that a high-fat diet may possibly support the maintenance of body weight and body cell mass in patients with cancer. The available prospective data from epidemiological studies and intervention trials do not support the overall

hypothesis that higher fat intakes are a relevant risk factor for breast cancer development. More important seems the relative distribution of various fatty acids (Hanf & Gonder, 2005). There has been much speculation regarding the type of fat and the risk of cancer. Specific types of fat, particularly monounsaturated fat and the ratio of n-3 to n-6 fatty acids, demonstrate more potential to influence breast cancer risk (Duncan, 2004). Experiments have shown that diets which are rich in linoleic acid, such as sunflower oil, can act as a stimulant for tumors (Alberts, 1993, p.17). An increased intake of n-3 fatty acids or an improved intake of n-3 to n-6 ratio is associated with a reduced breast cancer risk (Goodstine, Zheng, Holford, Ward, Carter, Owens & Mayne, 2003). Implanted human breast cancer cells in mice were suppressed by a diet high in n-3 fatty acids (McCullem & Polisena, 2000, p. 160). This could explain the low incidence of breast cancer amongst Eskimos, who traditionally consume large quantities of fish and fish oils (Alberts, 1993, p.17). More recent studies have considered other possible dietary determinants of risk, such as consumption of meat, fiber, fruit and vegetables, and phyto-oestrogens (Key, Verkasalo & Banks, 2001, p.136).

Willett (2001, p.401) states that epidemiological studies have shown that populations consuming a plant-based diet presented with a reduced incidence of certain types of cancers. Follow-up studies on isolated nutrients, like beta-carotene, have not produced the same results. It is likely that it is the synergistic effect of the nutrients and the phytochemicals in a low-fat plant-based diet that provide protection. Table 1.1 shows the American Institute for Cancer Research's six simple steps to prevent cancer.

TABLE 1.1 American Institute for Cancer Research's steps to prevent cancer

Simple steps to prevent cancer
1. Choose a diet rich in a variety of plant-based foods.
2. Eat plenty of vegetables and fruit.
3. Maintain a healthy weight and be physically active.
4. Drink alcohol only in moderation, if at all.
5. Select foods low in fat and salt.
6. Prepare and store food safely.

The existence of genes that act as tumour suppressors is a very important and recent discovery (Cassidy, Bisset & Spence, 2002, p.656). Several genes have been identified, such as the abnormal gene found on the thirteenth chromosome, which causes retinoblastoma. Other suppressor genes identified, are the Wilms tumour suppressor gene (which causes kidney cancer in children), the P53 gene, the Nm23 gene, the P16 gene, as well as the FAP gene (the absence of this gene causes colon cancer, with a definite familial history). Precisely how these suppressor genes control cell division is not yet quite clear (Alberts, 1993, p.9). The replacement of these genes with normal copies using viral vectors has resulted in the suppression or even reversal of the malignant phenotype in *in vivo* tumour models. Combining successful restoration of genes such as the wild type P53 and sequential administration chemotherapy appears to be synergistic in reducing the malignant expression in these cell lines (Cassidy et al., 2002, p.657). Except for a rare type of eye cancer, cancers are not hereditary. However, specific types of cancer, such as breast cancer, colon cancer and melanoma, often manifest in a particular family, and persons are usually affected at an early stage (Alberts, 1993, p.9).

Attempts to enhance the naturally weak immunogenicity to tumours followed from a clearer understanding of antigen recognition, processing and presentation

at molecular level and, in particular, the nature of effector (T-cell) responses to antigenic stimulation (Cassidy et al., 2002, p.660). A number of approaches are currently being evaluated. One is systemic immunotherapy for cancer with recombinant cytokine therapy, which is associated with low response rates at the expense of high systemic toxicity. Another is transducing tumour cells *ex vivo* with the same cytokine, allogenic human leucocyte antigen (HLA), or genes encoding co-stimulatory molecules prior to re-infusion (after irradiation of eliminate malignant activity) so that T-cell recognition of tumour antigens is changed. Dendritic cells (DCs) are potent antigen-processing and antigen-presenting cells that are critical to the development of primary MHC-restricted T-cell immunity to infectious agents, in auto-immune diseases and anti-tumour immunity (Cassidy et al., 2002, p.661).

Genetic tagging is being used to determine the effectiveness of chemotherapy. The insertion of a foreign marker gene into cells during a tumour biopsy, and the replacement of the marked cells prior to treatment, can provide a sensitive new indicator of minimal residual disease after chemotherapy. Neomycin phosphotransferase (NeoR), an enzyme that metabolizes the aminoglycoside, G418, has been retrovirally transduced *ex vivo* into purged marrow from AML and neuroblastoma patients prior to re-infusion. In those individuals with relapsed disease, as few as one in 10^6 cells expressing the NeoR gene has been detected by PCR, indicating failure of the purging process (Cassidy et al., 2002, p.663).

1.2 PROBLEM

The cancer cell is exposed to many nutritional and environmental factors that could be both positive and negative (McCallum & Polisena, 2000, p.160).

Carlson (2000, p.380) states that 25 to 50% of women responds to second-line chemotherapy with a taxane such as Docetaxel. Tamoxifen improves disease-free overall survival, while combination chemotherapy reduces recurrence and mortality with an absolute ten year survival benefit for seven to 11% of women less than 50 years of age, and two to three per cent for women over 50 years of age. Other chemotherapy regimens that are effectively used, include Cyclophosphamide, Methotrexate or 5-Fluorouracil (5FU) (Cassidy et al., 2002, p.316). Cytotoxic chemotherapy destroys the cancer cells. The lack of selectivity to affect only cancer cells has limited the ability to kill cancer cells, while leaving normal dividing cells unaffected (Cassidy et al., 2002, p.136). The mucous membrane of the mouth may, for instance, become tender, and mouth ulcers may develop, which could affect nutritional intake (Alberts, 1993, p.64). Combination therapy aims to increase 'fractional cell kill', leading to improved overall response of the tumour. Higher doses of cytotoxic drugs tend to produce increased cell kill (Cassidy et al., 2002, p.136). Oncology patients may experience altered food intake from chemotherapy-induced side effects, which could have a lowering effect on serum albumin concentrations (McCallum & Polisena, 2000, p.61). Other chemotherapy agents, such as L-asparaginase, causes decreased protein synthesis, while Glucocorticoids cause a negative nitrogen balance, affecting serum albumin concentrations (McCallum & Polisena, 2000, p.65).

Lowered serum albumin concentrations offer unique challenges, seeing that the half-life of albumin is approximately 21 days, which implies that the patient's nutritional intake must be closely regulated for a minimum of 21 days (Carlson, 2000, p.380). Lowered serum albumin concentrations result in symptoms such as tiredness and weakness, as well as prolonged treatment time for medical conditions, with both financial and emotional implications (Robinson, Lawler, Chenoweth & Garwick, 1990, p.391; McCallum, 2003, p.13; McCallum & Polisena, 2000, p.45). Research has proven that besides dietary factors, malignant

diseases such as breast cancer could significantly lower serum albumin concentrations (Frankmann, 2000, p.874; Robinson et al., 1990, p.391). Non-dietary factors that could affect serum albumin concentrations are age, sex, seasons and race. Significant loss of blood or protein malnutrition could also cause reduced serum albumin concentrations (Meyer & Grey, 1988, p.22.4). Serum albumin concentrations are similarly affected in both underweight and overweight patients due to illness and medical stress (McCallum, 2003, p.121; Franch-Arcas, 2001). As indicated by current literature, serum albumin concentrations and anthropometrical measures can be manipulated by increased protein and adequate energy intake in non-cancer individuals (Carlson, 2004, p.440; Simpson, 1995, p.579).

Serum albumin concentrations are often used as a tool of measure for effective dietary treatment, but are not considered an effective marker for periods shorter than ten days, due to albumin's relative long plasma half-life (McCallum & Polisena, 2000, p.47). McCallum and Polisena (2000, p.47) state that a positive nitrogen balance and adequate energy intake is necessary to optimize the chance of maintaining lean body mass and immune competence. Adequate levels of serum albumin are important in the human body, as albumin is partially responsible for controlling the distribution of fluid between the intra- and extra cellular compartments. Plasma protein and albumin are responsible for the transport of substances such as nutrients, vitamins, minerals and hormones, as well as medication. Plasma protein promotes the viscosity of the plasma, which helps to regulate effective blood pressure, prevents the sedimentation of blood cells in arteries, and slows the flow of blood through the arteries to improve fluid exchange. Plasma protein acts as a buffer and by doing so, helps to stabilize the pH of the plasma. It protects the body against infection, is involved with blood clotting, and is a source of protein during times of malnutrition (Meyer & Meij, 1992, p.12.5).

The nutritional problem is exacerbated by a small appetite, which also contributes to weight loss, the lowering of anthropometrical measures and lowered protein intake which, in turn, affect serum albumin concentrations (McCallum, 2003, p.121; Frankmann, 2000, p.874). Other acute side effects often experienced by patients receiving chemotherapy are nausea and vomiting. In addition, the nervous system is affected, resulting in symptoms such as a pins and needles sensation in the hands and feet; and hearing problems and a general feeling of weakness are experienced, having a negative effect on the patient's quality of life (Alberts, 1993, p.64). Research shows a relationship between nutritional status and the outcome of malignant diseases (Frankmann, 2000, p.874).

According to Rock and Denmark-Wahnefried (2002, p.3302), epidemiological studies have identified obesity as an important negative prognostic factor of survival after the diagnosis of breast cancer. Obesity and weight gain during adulthood are associated with increased breast cancer risk among postmenopausal women, while obesity has the opposite effect on breast cancer risk among younger premenopausal women. Those young women with a high BMI is at a lower risk than those with a low BMI (Carpenter & Bernstein, 2006, p.187). A higher energy intake and a lower level of physical activity are independently associated with an increased risk for weight gain after the diagnosis of breast cancer. Strategies to modify these behaviours are likely to influence the long-term pattern of weight change (Rock et al., 1999). Medical nutritional therapy guidelines for lowering the risk for primary and secondary breast cancers firstly include the adjustment of the patient's energy intake to attain and maintain a healthy body weight, with a BMI of 20-25 kg/m^2. Secondly, to achieve a protein intake of 15% to 20% of the total daily energy intake. Thirdly, the addition of a daily, low dose, multi-vitamin/mineral supplement during the acute treatment of the disease, when requirements are increased (Wood et al., 1996). Harvie et al. (2005) states that it is important to

meet breast cancer patient's energy requirements but also prevent the loss of fat free mass during their chemotherapy and dietary treatment. Dewys et al. (1980) found from a cohort of nine studies that the median survival of cancer patients was significantly shorter for the patients with weight loss during chemotherapy treatment, compared with no weight loss. Chemotherapy response rates were lower in the patients with weight loss and this difference was statistically significant in breast cancer patients. Decreasing weight was correlated with decreasing performance status. These observations emphasize the negative prognostic effect of weight loss during chemotherapy treatment, especially in patients with a favourable performance status.

By closely monitoring patients, staff at the Eastern Cape Oncology Centre (ECOC) in Nelson Mandela Bay (previously Port Elizabeth), South Africa it was noted that breast cancer patients receiving chemotherapy often present with lowered serum albumin concentrations, so much so that the lowered serum albumin concentration first has to be treated before the next cycle of chemotherapy can be administered. The treatment of the lowered serum albumin concentrations has often meant a delay of seven days in chemotherapy treatment. Some patients have to travel long distances for chemotherapy treatment, and such postponement has had financial, medical and emotional effects on the patients.

A lowered serum albumin concentration and lack of nutritional intake are often identified as major problems in patients receiving chemotherapy. No studies could be found that investigated the effect of a nutrition intervention programme on the serum albumin concentrations of breast-cancer patients receiving chemotherapy. Current literature confirms the beneficial effect of an optimal energy, high-protein diet on serum albumin concentrations in non-cancer patients (Fuhrman et al., 2004). Because overweight and weight gain is associated with an increased risk of breast cancer and breast cancer recurrence, it was decided that an optimal energy intake, for the purpose of this study,

would constitute an individually calculated energy intake. The energy calculation would be based on the energy required to maintain each patient's ideal body weight. This would then imply that overweight or obese patients should show a slow and gradual weight loss, seing that they would not receive an energy intake to sustain their increased, actual body weight. The energy calculation based on each patient's ideal body weight should therefor prevent any further weight gain in overweight and obese patients. By suggesting such a controlled energy intake it would not further increase breast cancer risk of overweight or obese breast cancer patients.

This study was undertaken in an attempt to determine whether an optimal energy intake based on the patients ideal body weight and not the patients current body weight and an increased protein intake would affect the serum albumin concentrations, anthropometrical measures and quality of life of breast-cancer patients receiving chemotherapy.

1.3 AIM

The aim of the study was to determine the effect of an optimal energy, increased protein (OEIP) diet intervention programme on the serum albumin concentrations, anthropometrical status, nutritional intake and quality of life of breast-cancer patients receiving chemotherapy.

If the OEIP dietary intervention programme shows an improvement in the serum albumin concentrations, anthropometrical status and quality of life of breast-cancer patients receiving chemotherapy, it will be implemented as routine dietary treatment for all breast-cancer patients receiving chemotherapy at the ECOC in Nelson Mandela Bay, South Africa.

1.3.1 Objectives

The objective of this study is to monitor the effect that a diet intervention programme has on breast-cancer patients receiving chemotherapy in respect of:

- Serum albumin concentrations;
- Anthropometrical status;
- Quality of life; and
- Dietary intake.

1.4 STRUCTURE OF DISSERTATION

In the following chapters, the nutritional and anthropometrical status, serum albumin concentrations and quality of life of breast-cancer patients receiving chemotherapy will be discussed. The methodology and techniques used in conducting this study will be described, results will be given and the interpretation of the results will be discussed. The conclusions and recommendations will be followed by a summary of the study.

CHAPTER 2

LITERATURE OVERVIEW

2.1 INTRODUCTION

It is estimated that 80 to 90% of cancers could in some way be related to the environment. This leads to the assumption that the majority of cancers must be potentially preventable. Recent evidence suggests that up to 50% of all cancers may be diet related. This potential diet-cancer link has obviously been the focus of much attention and debate. If this link can be confirmed, then, through educating the public with regard to certain dietary guidelines, we may be able to lower the incidence of cancer (Simpson, 1995, p.571).

Even though all people are vulnerable, different cancers tend to affect different segments of the population. Lung and bronchus cancer is most dominant in men aged 40 years and older; acute lymphocyte cancer is most common in children and, after lung cancer, breast cancer is the leading cause of cancer deaths in women worldwide (Jemal, Murray & Sameuls, 2003). Optimal nutritional status is recognized as an important goal during all stages of cancer treatment. Optimal nutritional status is associated with improved immune status; better tolerance of chemo- and radiotherapy, with fewer side effects; maintenance of a better quality of life; and less post-operative complications in cancer patients (Donnoghue, Nunnally & Yasko, 1982, p.19).

The characteristics of cancer, the nutritional implications of cancer and the effects of cancer chemotherapy on the body and on the patient's quality of life,

as well as the nutritional requirements of the patient receiving chemotherapy, will be reviewed in this chapter.

2.2 CHARACTERISTICS OF CANCER

2.2.1 Definition of cancer

Cancer is not a single disease, but a term used to describe at least 100 different diseases with a variety of causes, symptoms and outcomes (McCallum, 2003, p.42). Carcinogenesis is the process by which a normal cell undergoes malignant transformation. It is a complicated process that is not yet fully understood. Cancer cell functioning deviates from that of normal cells (Ward, 1995, p.17). Cancer is the abnormal, uncontrolled growth of cells in a lump or mass that also destroys normal tissue. Oncogenes in a tumour cell may be identifying markers (Escott-Stump, 2002, p.525).

2.2.2 Pathogeneses

Cancer cells differ in their biochemical composition, rates of reproduction and the degree of danger they pose toward humans. This is why there are many different types of cancers, and why some are more harmful than others. Despite their diversity, cancer cells have much in common, according to Smeltzer and Bare (1992, p.341):

- Cancer cells reproduce more rapidly than normal cells.
- Cancer cells have undefined cell membranes, most probably because the membranes contain less fibronectin. The reduced amount of fibronectin causes decreased cohesion and adhesion to adjacent cells.
- The membrane of cancer cells has markers by which the body can identify them as foreign, which may set them up for elimination by the body's immune system.

- The nucleus of the cancer cell is called a pleomorph, which means that it is often large, with an irregular shape, or even distorted. Abnormal and fragile chromosomes are also characteristic of cancer cells.
- Cancer cells do not have contact inhibition, which means that where other cells will only grow till a certain size and not invade another cell's "space", cancer cells ignore all built-in growth limitations.
- Cancer cells have altered biochemistry. Cancer cells use more glucose and produce more lactic acid than normal cells. Cyclic adenosine monophosphate (AMP) and cyclic guanosine monophosphate (GMP) are found in altered amounts in cancer cells. AMP and GMP are the building blocks of nucleic acids and significantly enhance cell growth and division.

2.2.3 Stages of cancer development

Cancer cells are identified by tissue biopsy, and a microscopic examination is used to describe its characteristics, where after cells are classified into five categories, from normal cells to the diagnosis of cancer cells, displayed in Table 2.1 (Cotugna & Vickery, 2003, p.6; Cassidy et al., 2002, p.76).

TABLE 2.1: Category classification of cancer cells

Cell classification	
Class I:	Normal cells
Class II:	Probably normal, but slightly atypical or abnormal cells
Class III:	Abnormal cells, possible dysplasia, suggestive of malignancy
Class IV:	Probably cancer
Class V:	Cancer

A cell may be abnormal without being cancerous. Infection or inflammation often causes temporary cell abnormalities. Once cancer has been diagnosed, i.e.

it is categorised into a specific stage (see Table 2.2), and a Class V category cell has been identified, the course of treatment and the prognosis are established (Cotugna & Vickery, 2003, p.7). Carcinogenesis takes place in three steps: initiation; promotion; and progression. However, in practice, these three steps are not clearly distinguished (Alberts, 1993, p.7).

During the initiation stages of cancer development, a single normal cell is converted to a cancer cell. Initiation involves genetic damage or the alteration of cellular deoxyribonucleic acid (DNA) by a carcinogen, a carcinogen being a substance that stimulates cancer. Carcinogens that cause the initiation of cancer can be environmental, viral or genetic. Smoked, cured, or barbecued foods or nitrate and nitrite preserved foods may act as carcinogens by increasing the risk of stomach and oesophageal lung cancers. This does not mean that all people who consume these foods will develop cancer (Cotugna & Vickery, 2003, p.8; Alberts, 1993, p.18).

The second step in cancer development is promotion, which involves the replication of the cancer cells. A high fat diet has been linked to the promotion of breast cancer. Promotion occurs over a long period of time, and the effect of promotion is, in fact, reversible. The period of time between exposure to a carcinogen and the development of a malignancy is termed the latent period, which can last from ten to 40 years (Cotugna & Vickery, 2003, p.8; Renneker, 1989).

The third step in cancer development is progression, which is also irreversible. This process involves malignant cell behaviour, invasion of adjacent tissues, malignant tumour growth, and metastasis (Cotugna & Vickery, 2003, p.8; Cassidy et al., 2002, p.19).

The American Joint Committee on Cancer (AJCC) has a four-step staging system, used after the diagnosis of breast cancer. AJCC provides a strategy for grouping patients with respect to prognosis. Therapeutic decisions regarding treatment methodologies are formulated according to the AJCC staging categories, as well as tumour size, lymph node status, estrogen-receptor and progesterone-receptor levels in tumour tissue, menopausal status and the general health of the patient (Singletary, Allred & Ashley, 2002). The AJCC staging of breast cancer can be viewed in Table 2.2 (Escott-Stump, 2002, p.539).

TABLE 2.2: AJCC Staging of breast cancer

Staging of breast cancer	
Stage 0	In situ
Stage I	Rarely metastasizing/non-invasive (less that 2.5 cm in diameter)
Stage II	Rarely metastasizing/invasive (2.5-5 cm in diameter)
Stage III	Moderately metastasizing/invasive (5 cm or larger in diameter)
Stage IV	Highly metastasizing/invasive

2.2.4 Mortality rates of cancer

Breast cancer is the most common cause of cancer death among women worldwide. Incidence rates are high in more developed countries, whereas rates in less developed countries are low, but increasing (Key et al., 2001). Cancer mortality rates in the United States have been declining slightly since 1990, according to the Department of Health and Human Services (Mettlin, 1996). Even though there has been a great improvement in the prevention, detection

and treatment of cancer, it is expected to remain the second leading cause of death for many more years.

2.3 NUTRITIONAL IMPLICATIONS OF CANCER

The adverse nutritional effects of cancer can be quite severe and are often compounded by the effects of the treatment regimens and the psychological impact of cancer (Eldridge, 2004, p.1004; Simpson, 1995, p.575). The result is often severe depletion of nutrient stores. Significant weight loss and poor nutritional status are documented in more than 50% of patients at the time of diagnosis and are associated with lower scores on quality of life measures. Early studies confirm that even a small amount of weight loss (<5% of body weight) before therapy is associated with a poor prognosis (Eldridge, 2004, p.1004; Gallagher-Allred, 1995, p.91).

2.3.1 Sensory changes due to cancer

Alterations in taste and smell are common among cancer patients, and can contribute to anorexia. Eldridge (2004, p.1008) states that studies of taste sensitivity in malignant disease have shown variable results. Taste alterations are associated with the disease, certain antineoplastic agents, and irradiation or surgery of the head and neck. Patients may also experience a heightened sense of smell that results in sensitivity to food preparation odours. Dietary interventions that decrease the aroma of foods, such as serving foods cold instead of hot, may be helpful. Sensation abnormalities do not consistently correlate with the tumour site, extent of tumour involvement, tumour response to therapy, or food preferences and intake (Eldridge, 2004, p.1008; Simpson, 1995, p.584).

2.3.2 Effect of cancer on energy metabolism

The presence of a tumour may affect the patient's biochemical and metabolic functions, possibly leading to increased morbidity and mortality (Nebeling, 2000, p.53). The malignant tumour may alter the body composition of the patient and initiate a sequence of events that could lead to altered carbohydrate, lipid and protein metabolism (Mutlu & Mobarhan, 2000). Standard nutritional support may not always be effective in significantly improving the outcome of malnourished cancer patients, due to changes in their metabolism (Eldridge, 2004, p.1007; Simpson, 1995, p.584). The tumour responsible for these changes can influence normal metabolism. Increased energy expenditure, as well as elevations in basal metabolism, along with alterations in enzyme activity and the immune system, occur in these patients. The end result is an alteration in energy requirements and the carbohydrate, lipid and protein metabolism (Eldridge, 2004, p.1007). Additional alterations can be seen in tissue water content, acid-base balance, and in the concentrations of electrolytes, vitamins or minerals. These metabolic abnormalities may impair nutritional status and contribute to cancer cachexia via the depletion of adipose tissue, protein, water and mineral stores (Nebeling, 2000, p.53).

Side effects of the different treatment modalities combine to further impair the nutritional status of the patient (Mutlu & Mobarhan, 2000; Nebeling, 2000, p.55). The overall impact of glucose intolerance, impaired insulin sensitivity, and increased energy expenditure, combined with reduced energy intake due to anorexia, further exacerbate alterations in energy metabolism initiated by the tumour (Simpson, 1995, p.584).

2.3.3 Effect of cancer on carbohydrate metabolism

A significant increase in the rate of glucose turnover, combined with increased energy demand by the tumour, contributes to increased energy expenditure and the depletion of body fat stores, as observed in some cancer patients (Eldridge,

2004, p.1007). Normal energy substrates that usually provide an alternative fuel supply during periods of stress or starvation are poorly metabolized by the tumour cells. Understanding the relationship between nutrient needs and tumour metabolism in the cancer patient is critical if nutrition intervention is to have a positive impact and improve the patient's outcome (Mutlu & Mobarhan, 2000).

Nebeling (2000, p.55) states that a well-nourished adult in the resting state will consume glucose at a rate of 140 g/day (2342 kJ). Under typical metabolic conditions, the oxidations of amino acids during normal tissue breakdown accounts for 75 g/day (1569 kJ), while oxidations of triglycerides at 130 g/day (4895 kJ) accounts for the rest in a well-nourished adult. In the resting state, approximately 20 g lactate are formed daily and normally re-synthesized back to glucose in an adult. This cyclic metabolic pathway, in which glucose is converted to lactic acid by glycolysis and then reconverted in the liver, is referred to as the Cori cycle (Nebeling, 2000, p.55).

TABLE 2.3: Carbohydrate metabolic abnormalities present in the cancer state

Carbohydrate metabolic abnormalities present in the cancer state
Increased gluconeogenesis from amino acid and lactate
Increased glucose disappearance and recycling
Insulin resistance
Increased glucose synthesis
Decreased glucose turnover
Increased Cori cycle activity (energy consuming futile cycling, which is estimated to lead to an approximate 0,9kg per month)
Increased glucose consumption by the tumour
Production of insulin or insulin-like substances by the tumour

Abnormal elevation in Cori cycle activity has been reported in malnourished cancer patients; this increased activity accounts for up to 1255 kJ/day loss of energy. The demand for glucose carbons by the tumour tissue can increase demand for glucose production by the liver, especially if glucose cannot be fully oxidized by the tumour tissue itself. This inability to effectively oxidize glucose may explain why some cancer patients exhibit an increase in Cori cycle activity and elevated glucose production (Nebeling, 2000, p.55). The changes in carbohydrate metabolism are displayed in Table 2.3.

During starvation or dietary deprivation, the body adapts. Inadequate dietary carbohydrate intake leads to the metabolization of triglycerides from adipose tissue (McCallum, 2003, p.37; Mutlu & Mobarhan, 2000). The triglycerides are broken down into glycerol and free fatty acids. These free fatty acids are used for energy by most of the body cells. As lipid mobilization is accelerated, upsetting the balance of lipogenesis and lipolysis, free fatty acids are released into the blood and generate ketone bodies. Ketones enter the Krebs cycle and slow glucose synthesis. The heart and skeletal muscles are able to use the ketones as energy, but not the brain. After a period of time, even the brain adapts and becomes able to convert ketones into ATP, but the liver cannot. During starvation, the plasma ketone concentration increases, as the production of ketones surpasses the level at which the heart and skeletal muscle can oxidize them (Nebeling, 2000, p.55).

2.3.4 Effect of cancer on lipid metabolism

Eldridge (2004, p.1007) states that alterations in lipid metabolism in cancer patients include an alteration in body composition and increased lipid mobilization (Table 2.4).

TABLE 2.4: Lipid metabolic abnormalities present in the cancer state

Lipid metabolic abnormalities present in the cancer state
Increased lipolysis
Increased glycerol turnover
Decreased lipogenesis and fat storage
Decreased lipoprotein lipase activity
Free fatty acid hyperlipidemia
Elevated triglycerides
Decreased high-density lipoproteins
Increased venous glycerol
Decreased plasma glycerol clearance
Increased lipid oxidation
Possible tumour dependence on specific fatty acids (linoleic and arachidonic)
Increased use of fatty acids as energy by the host tissue in the presence of certain tumours
Impaired suppression of lipid mobilization, in the presence of glucose administration
Increased metabolic rate secondary to increased gluconeogenesis from glycerol

Studies indicate that hypermetabolic cancer patients have increased rates of lipolysis, fatty acid and glycerol turnover, and fatty acid oxidation. Cancer is associated with increased plasma lipid concentrations, changes in the plasma lipoprotein composition, and plasma lipase activity. (Eldridge, 2004, p.1007; Mutlu & Mobarhan, 2000; Nebeling, 2000, p.55).

2.3.5 Effect of cancer on protein metabolism

Alterations in protein metabolism appear to be directed toward providing adequate amino acids for tumour growth (Eldridge, 2004, p.1007). Protein functions as a critical reserve of metabolic fuel and may become seriously depleted during tumour growth (Nebeling, 2000, p.57), specifically seen due to reduced skeletal muscle (Eldridge, 2004, p.1007). Various alterations in protein metabolism occur in cancer patients, including patient nitrogen depletion,

decreased muscle protein synthesis, increased protein catabolism in liver and skeletal muscle, and abnormal plasma amino acid levels. Studies on the dynamics of protein metabolism in humans have shown that muscle tissue degradation in the whole body is elevated in patients with various types of cancer, a response similar to other conditions such as infection or injury (Mutlu & Mobarhan, 2000). Abnormalities in protein metabolism of cancer patients are shown in Table 2.5.

TABLE 2.5: Protein metabolic abnormalities present in the cancer state

Protein metabolic abnormalities present in the cancer state
Increased protein catabolism
Increased whole body protein turnover
Increased protein synthesis
Decreased muscle protein synthesis
Increased hepatic synthesis of acute phase reactants
Increased hepatic and tumour protein synthesis
Decreased plasma concentrations of gluconeogenic amino acids
Abnormal serum proteins, similar to kwashiorkor or protein-energy malnutrition

Besides dietary factors, a malignant disease such as breast cancer could lower serum albumin concentrations as well as other nutrients (Frankmann, 2000; Robinson et al., 1990, p.391). Protein malnutrition could also cause reduced serum albumin concentrations. Hypoalbuminemia also occurs because of increased total body water associated with cancer cachexia (Eldridge, 2004, p.1007). Lowered serum albumin concentrations result in symptoms such as tiredness and weakness, as well as prolonged treatment time for medical conditions such as breast cancer (Robinson et al., 1990, p.391).

2.3.6 Other metabolic changes due to cancer

Fluid and electrolyte imbalances are seen in patients with advanced cancer (Eldridge, 2004, p.1007). Hypercalcemia may be seen in bone-metastasizing

tumours of the breast that induce parathyroid hormone-like peptides. Professionals do, however, agree that calcium should not be restricted in hypercalcemic patients. Severe fluids imbalances could also occur in patients with severe diarrhoea and vomiting (Mutlu & Mobarhan, 2000).

The activities of several enzyme systems can be affected, as well as certain endocrine functions. The nature of the alteration varies according to the tumour type. The patient's immunologic function can be impaired, apparently as a result of both the neoplasm and progressive malnutrition. In addition to the cancer induced metabolic effects, the mass of the tumour may anatomically alter the normal physiology of specific organ functions (Eldridge, 2004, p.1007).

2.3.7 Cancer cachexia in cancer patients

Cancer cachexia is characterized by extreme weight loss, with depletion of both lean body muscle mass and adipose tissue, anorexia, early satiety, anaemia, immunosuppression, altered metabolic rate, and abnormalities in fluid and energy metabolism that accompany advanced cancer, even with adequate nutrition (Eldridge, 2004, p.1006). The tumour's presence may also alter the patient's ability and desire to eat. The normal physiologic conservation mechanisms seen during periods of acute starvation do not occur in the presence of a malignant tumour (McCallum & Polisena, 2000, p.42). During periods of starvation, free fatty acids (FFA) from adipose tissue supply energy to the liver and muscle. The FFA is converted to ketones, which are then used by the body tissues. Acting as a glucose substrate, ketones signal the body to inhibit glucose usage and induce protein and adipose conservation mechanisms. Rates of gluconeogenesis and protein degradation from muscle mass decline, along with insulin levels. Ketones play an important role as an alternative energy source during periods of starvation.

The aetiology of cancer cachexia is, however, not entirely understood. Recent work has focused on the role of cytokines (Eldridge, 2004, p.1006; Simpson, 1995, p.580). A number of cytokines are suspected to have a role in cancer cachexia. These factors may well be specific to tumour types and may influence or be influenced by the metabolism of other substrates (McCallum, 2003, p.36). The cytokines have overlapping physiologic activities, which makes it unlikely that cytokines alone are responsible for the weight loss and cachexia associated with cancer (Key et al., 2001). Tumour necrosis factor (TNF)-alpha, interleukin 1 (IL-1), interleukin 6 (IL-6), and leukemia-inhibitory factor (LIF) are cytokines suspected of having a part in the development of cancer cachexia. The administration of thalidomide, an inhibitor of TNF-alpha, has resulted in weight gain in patients with human immunodeficiency virus (HIV), but when administered in therapeutic doses, it may cause significant and incapacitating drowsiness (Eldridge, 2004, p.1006). It is suggested that all cytokines inhibit lipoprotein lipase, preventing fatty acids from being freed from transport lipoproteins to allow lipid storage, though in varying degrees (McCallum, 2003, p.36).

Hormonal abnormalities, such as increased cortisol, decreased insulin/insulin resistance, and/or decreased testosterone are also seen in cachectic cancer patients. There are, however, few studies to substantiate any relationship between these abnormalities and cachexia (McCallum, 2003, p.36). Several studies have suggested that there may be catabolic factors beyond the cytokines that have a role in the development of cachexia and are specific to skeletal muscle and adipose tissue. Lipid-mobilizing factors (LMF) may promote lipolysis in the adipose tissue. LMF found in the sera of cancer patients have been shown to be proportional to the extent of weight loss. LMF was reduced in cases of tumour response to chemotherapy. It appears that eicosapentaenoic acid (EPA) docosahexaenoic acid (DHA), also found in fish oil and flaxseed, gamma linoleic acid (GLA) and linoleic acid (LA) are ineffective in inhibiting LMF. There may also

be a protein-mobilizing factor (PMF) present in weight loss in cancer patients. A proteoglycan, 24Kda, has been shown to induce muscle protein degradation. Interestingly, EPA was found to decrease protein degradation, as well as LMF-related weight loss (McCallum, 2003, p.37; Key et al., 2001).

2.4 NUTRITIONAL IMPLICATIONS OF CHEMOTHERAPY

People often automatically associate cancer treatment with chemotherapy, weight loss, nausea and hair loss. Many people with cancer are treated with chemotherapeutic agents; others receive radiation therapy; undergo surgery; or receive a combination of treatments. This section will review chemotherapeutic agents frequently used for breast cancer treatment, their related side effects and the nutritional implications of chemotherapy on the human body. Chemotherapeutic agents such as Docetaxel, CMF (Cyclophosphamide, Methotrexate and 5FU combination) and CAF (Cyclophosphamide, Adriamycin and 5FU combination) will be considered, seeing that they are the drugs of choice in the treatment of breast cancer at ECOC.

2.4.1 Chemotherapy agents

Cancer chemotherapy is, as the name implies, the use of chemical agents or drugs in the treatment of malignant disease, either as initial treatment, in conjunction with surgical procedures or radiotherapy, or when surgery or radiotherapy is not possible (Riccardi & Allen, 1999; Leon, de Jager & Toop, 1995, p.197). Chemotherapy is the common term used to describe any of three basic types of drug therapy used in cancer treatment. These include cytotoxins (cell-killers), biologics/immunologicals (stimulate the immune system), and hormonals (interfere with hormone production or action) (McCallum, 2003, p.44). While surgery and radiation are used to treat localized tumours, chemotherapy is

a systemic therapy that affects the entire body (Eldridge, 2000, p.61). Adjuvant chemotherapy is a common treatment, combining radiation and/or surgery with chemotherapy (McCallum, 2003, p.42). Only cytotoxins will be discussed in detail, as they were the chemotherapies used during this study.

TABLE 2.6: Cytotoxic agents

Cytotoxic agents			
Classification	**Description**	**Cell phase specificity**	**Examples**
Alkylating agents	Work on DNA to prevent cell division	Non phase-specific	Busulfan, Cisplatin, Cyclophosphamide, * Dacarbazine, Mechlorethamine
Nitrosoureas	Inhibit enzymes needed in DNA repair	Not phase-specific	Carmustine, Iomustine
Antimetabolites	Interfere with DNA and RNA growth	S phase	5-Fluorouracil, * Methotrexate, * Fludarabine, Cytarabine
Antitumor antibiotics	Antimicrobial/Cytotoxic Inhibit enzymes needed in DNA repair Inhibit mitosis by altering cellular membranes	Not phase-specific	Bleomycin, Dactinomycin, Daunorubicin, Doxorubicin
Mitotic inhibitors	Plant alkaloids and natural products Inhibit mitosis Inhibit enzymes needed for cell reproduction	M phase	Docetaxel, * Paclitaxel, Etoposide, Vinblastine, Vincristine

* Cytotoxic drugs used during this study

Cytotoxins can be toxic to normal cells as well as malignant cells, in particular those with a rapid turnover such as bone marrow, hair follicles, and oral and intestinal mucosa (Eldridge, 2000, p.61; Riccardi & Allen, 1999). Chemotherapy is curative in some neoplasms, while only palliative in others, where it will relieve symptoms and prolong life (Leon et al., 1995, p.199). Cytotoxic drugs used in

the treatment of breast cancer fall into several classifications, as displayed in Table 2.6. The toxicity of the drug may be reduced with careful control of the dose magnitude, administration time, and by using a combination of chemotherapy regimens (McCallum, 2003, p.45; Leon et al., 1995, p.199).

The chemotherapy agents commonly used in the treatment of breast cancer include Docetaxel, CMF and CAF (Cassidy et al., 2002, p.76). Of these three, Docetaxel is the most potent and causes the most significant side effects, as described in Section 2.4.3. The classification of Docetaxel, CMF and CAF as cytotoxic agents are described in Table 2.6.

2.4.2 Goals of chemotherapy treatment

Several factors need to be considered when evaluating a patient's response to chemotherapy. Important factors include how much tumour burden is present, the use of combined treatment modalities (surgery, radiation and/or chemotherapy), existing medical conditions, nutritional status and the goal of the planned therapy (Eldridge, 2000, p.61; Simpson, 1995, p.575).

The goals for antineoplastic treatment are (Eldridge, 2000, p.61):

Cure	–	to obtain a complete response to treatment of a specific cancer
Control	–	to extend the length of life when a cure is not possible
	–	to obscure microscopic metastases after tumours are surgically removed
	–	to shrink tumours before surgery or radiation therapy
Palliation	–	to provide comfort when cure or control is not possible
	–	to improve quality of life
	–	to reduce tumour burden, and relieve cancer-related symptoms such as pain and organ obstruction.

2.4.3 Nutritional and non-nutritional side effects of chemotherapy

Acute effects of chemotherapy, particularly Docetaxel, CMF and CAF, occur shortly after administering the drugs. The severity of the side effects experienced relates to single- or combination-agent therapy, dose administrations, planned number of cycles, individual response, medications and current health status (Eldridge, 2000, p.61). The long-term effects of chemotherapy may become evident only years after treatment and may include the suppression of ovarian function, resulting in the development of secondary carcinomas (Leon et al., 1995, p.199).

2.4.3.1 Systemic side effects of chemotherapy

Symptoms include allergic reactions such as skin rashes, thrombophlebitis with IV therapy, fever, headache, hypotension and weakness (Leon et al., 1995, p.199). Normal gut function may also be affected, due to damage to the cells lining the gastrointestinal tract, resulting in digestion and absorption changes that could compromise nutritional status even further. Gastrointestinal tract side effects include stomatitis, mouth ulcerations, esophagitis, abdominal pain, haemorrhage, diarrhoea, and intestinal ulceration and perforation (Key et al., 2001). Chemotherapy can adversely affect hepatic and renal function and cause chemotherapy-induced bone marrow suppression that causes anaemia, neutropenia and thrombocytopenia, involving antibody and cell-mediated immunity (Riccardi & Allen, 1999). Docetaxel causes neurosensory signs characterised by paraesthesia, dysesthesia or pain, including burning.

2.4.3.2 Nutritional side effects of chemotherapy

Cancer patients may experience a variety of symptoms that could have a significant effect on their nutritional status, regardless of their BMI status before diagnosis. Malnutrition occurs in the majority of patients with cancer, and is a major cause of morbidity and mortality in advanced disease (Van Cutsem &Aredns, 2005). It is not known whether loss of body fat or fat-free mass during

chemotherapy relates to diminished dietary intake, failure to meet elevated energy requirements, or to the presence of an acute-phase response (Harvie et al., 2005). Cancer-related malnutrition is the result of a combination of factors, including local tumour effects, the patient response to the tumour, and the effects of anticancer therapies. Although reduced food intake is an important cause of nutritional decline, disturbances in metabolism and changes in BEE may also contribute (Van Cutsem & Arends, 2005). The most important nutrition related side effects include nausea, vomiting, anorexia, mucositis, esophagitis, altered taste and early satiety (McCallum, 2003, p.44; Riccardi & Allen, 1999). Sore mouth and throat (stomatitis, mucositis, or esophagitis) result from mucosal irritation and lesions. Pain and inflammation is common, which affects dietary intake. Aversion to foods and specific tastes is also termed mouth blindness or dysgeusia. For many patients, the lower threshold of urea causes an aversion to meat, often also associated with a bad smell of the meat (Murphey, 1994, p.83).

TABLE 2.7: Nutritional implications of chemotherapy

Nutritional implications of chemotherapy	
Alkylating agents	Nausea, vomiting
Antibiotics	Anorexia, diarrhoea, nausea, vomiting, stomatitis
Antimetabolites	Diarrhoea, nausea, vomiting, stomatitis
Corticosteroids	Sodium and fluid retention, weight gain
Sex hormones	Anorexia, nausea, vomiting, fluid retention
Vinca alkaloids	Nausea, vomiting

With all types of chemotherapy, prompt and aggressive attention to side effects and the appropriate use of supportive care such as nutrition and medication is essential (Escott-Stump, 2002, p.528). Table 2.7 shows the nutritional implications of chemotherapy. Docetaxel, CMF and CAF, commonly used for breast cancer treatment, are alkylating agents and antimetabolites, causing nausea, vomiting, diarrhoea and stomatitis.

2.4.3.3 Effect of chemotherapy on body composition and serum albumin

Some cancers are associated with metabolic alterations that appetite stimulants are unable to overcome (McCallum, 2003, p.121). This condition leads to cachexia, which is the clinical consequence of chronic, systemic inflammatory response. Depletion of skeletal muscle and the redistribution of the body's protein are major changes that occur (Escott-Stump, 2002, p.527). *In vivo* and *in vitro* studies of breast cancer have established no changes in basal energy expenditure (BEE) during treatment, though most women seem to gain weight after treatment. These women also have increased fat stores, decreased lean body mass and decreased physical activity, which are contributing factors to weight gain, rather than decreased BEE (McCallum, 2003, p.94).

Docetaxel has been known to cause a drop in serum albumin concentrations during treatment, regardless of the patient's current BMI. Both CMF and CAF cause hyper pigmentation of the skin, especially on the palms and soles, and the nails (Reynolds, 1989, p.610). No studies on the significant drug effect of CAF have been reported on serum albumin concentrations. CMF has been reported to cause megaloblastic anaemia in the elderly, but no significant direct related drug effect on serum albumin concentrations has been reported. CAF causes pronounced bone-marrow depression with leucopenia, but blood counts recover about 21 days after a dose (Reynolds, 1989, p.626, 636).

2.5 EFFECT OF CANCER AND CHEMOTHERAPY ON QUALITY OF LIFE

A patient's general condition profoundly affects treatment decisions, and the patient's condition may be directly influenced by the underlying cancer or may

reflect another concomitant illness, age, chemo- and radiation therapy, nutritional status or mental condition (Cassidy et al., 2002, p.80). The advanced technology of modern cancer, as well as its potential dangers, renders patients extremely vulnerable and dependent on others. For many, this loss of control is overwhelming, and it contributes significantly to psychological distress. Most cancer treatment procedures release unwanted toxicities that interfere with the patient's quality of life. The question should be asked whether a small improvement in median survival compensates for additional discomfort that affects the patient's quality of life (Cassidy et al., 2002, p.224). Performance status scales and the Rotterdam Quality of Life Survey are used to determine the effect of cancer on the quality of life of breast cancer patients. Both methods are used, because it shows both the health professional and the individual's view on the patient's quality of life.

2.5.1 Performance status as measure of quality of life

Patients with a poor performance status tolerate therapy worse and respond less often than those with a good performance status (Cassidy et al., 2002, p.80). The ZUBROD-ECOG-WHO classification system displayed in Table 2.8 refers to the classification of the effect of the disease on the patient's daily ability to function.

TABLE 2.8: ZUBROD-ECOG-WHO performance status classification

(Mina, Higgens & Glatstein, 1984, p.536)

0	Normal activity
1	Symptoms, but fully ambulant
2	Symptomatic, but in bed <50% of the day.
3	Needs to be in bed >50% of the day, but not bedridden.
4	Unable to get out of bed.
5	Dead

Performance status does not necessarily parallel the stage of cancer. It does, however, provide additional prognostic information. The performance status is determined by the medical professional performing the test, on the basis of what is observed.

Performance status is a helpful tool to determine the patient's daily functioning. It is, however, subjective, seeing that it is done by the medical professional/researcher and therefore displays the medical professional/researcher's perception about the patient.

2.5.2 Rotterdam Quality of Life Survey

Several questionnaires for completion by patients have been developed. The Rotterdam Quality of Life Survey is a quality of life questionnaire that was specifically formulated for use with cancer patients. The Rotterdam Survey comprises 30 questions, with a scoring of zero to 90. A high score is associated with an impaired quality of life, while a low score is associated with a good quality of life. The Rotterdam Quality of Life Survey can be used as a two-factor measure for assessing psychological and physical morbidity. Watson, Law, Maguire, Robertson, Greer, Bliss & Ibbotson (1992) tested the validity of the Rotterdam Quality of Life Survey. A highly significant positive association was found between the Rotterdam Quality of Life Survey and other anxiety questionnaires frequently used (HADS and PAIS). Although the Rotterdam Quality of Life Survey does not measure all dimensions of psychosocial functioning, it is a helpful and brief method of assessing physical and psychosocial morbidity in cancer patients. The Rotterdam Quality of Life Survey is a questionnaire completed by the patient, reflecting the patient's perception of her quality of life status.

2.6 NUTRITIONAL REQUIREMENTS OF CANCER PATIENTS RECEIVING CHEMOTHERAPY

2.6.1 Introduction

Scientific evidence suggests that one third of the cancer deaths that occur each year in the United States can be attributed to nutritional and other life-style related factors (Key et al., 2001). While incidence in South Africa differs from that in Europe and the United States, breast cancer is the most common cancer diagnosis made in South African women (Alberts, 1993, p.14). The primary reasons are the differences in the composition of the population, different causative factors that have a role to play, and the fact that diagnoses are made more accurately and on a more regular basis in the United States. Evidence suggests that millions of cases of human cancers could be prevented worldwide by changes in eating, weight control, physical activity and smoking or tobacco habits (Eldridge, 2004, p.1000; Key et al., 2001). Nutrition is an important part of the care and management of a patient, whether the patient is newly diagnosed, undergoing active therapy, recovering from treatment or in remission and trying to prevent cancer recurrence (Eldridge, 2004, p.1008; Rock & Denmark-Wahnefried, 2002). The role of nutrition is complex and often subject to misinterpretation, because of the fact that the energy we consume comes from three macronutrients: fat, carbohydrates and protein. Examining the effects of their independent effects is difficult in human populations, because we eat such mixed diets (Eldridge, 2004, p.1000; Cotugna & Vickery, 2003, p.39). The goals of nutrition in cancer care are to reverse or prevent nutritional deficiencies, to preserve lean body muscle, to minimize nutrition related side effects and to improve quality of life (Eldridge, 2004, p.1008; Willett, 2001). Early nutritional assessment and intervention as preventative measures are imperative.

Breast cancer is one of the more common cancers, but does not present the more "typical" nutrition-related symptoms one usually associates with cancer, as mentioned previously. Symptoms may be dependent on the stage of the disease, sites of metastasis, course of treatment, and menopausal status of the patient (Eldridge, 2004, p.1008). Generally, breast cancer itself does not present with any nutrition related symptoms. Breast cancer chemotherapy can cause nausea, vomiting, fatigue and mouth sores. Advanced breast cancer poses more difficult nutritional issues (Mattison et al., 2004; McCallum, 2003, p.29). Bone metastasis is common and painful. The narcotics used to treat pain could cause constipation, which could lead to a multitude of other problems. Gastrointestinal metastases can complicate breast cancer further with nausea, vomiting, diarrhoea, constipation, bowel obstruction, early satiety, anorexia, and weight loss. Pain and swelling associated with brain and spinal metastases are often treated with corticosteroids, leading to weight gain and hyperglycemia (McCallum, 2003, p.29).

Dietary modulations may be beneficial, but the possibility exists that by improving nutrition, tumour growth will also be stimulated (Nebeling, 2000, 53). In an attempt to identify the ideal nutrition for the patient, without stimulating the tumour, the following has been reported in clinical trials:

- Supplementation of arginine may potentially stimulate the immune system, enhance wound healing, improve recovery time from trauma, and inhibit tumour growth rates.
- Supplementation of ketones, as the primary energy source, may reduce the fall in urinary nitrogen levels and initiate protein conservation in the patient.

A number of tumours specifically metabolize glucose, so the administration of a concentrated lipid source of energy may reduce the glucose substrate available to the tumour. Supplying adequate energy substrates to the patient in a form

that cannot be used by the tumour may inhibit tumour growth by decreasing catabolism of the patient's body stores (Nebeling, 2000, p.53; Alberts, 1993, p.18).

Estimating nutrient requirements in a clinical oncology setting is merely an estimate. There are so many variables involved in adequate nutritional support for the cancer patient that the best route to follow is to choose a reasonably simple and accurate formula and provide careful and consistent follow-up to determine if the patient's needs are adequately met.

In the following section, the nutritional requirements of cancer patients will be discussed in more detail.

2.6.2 Energy requirements

The association between energy intake and breast cancer has received much attention. The significance of data on energy intake and cancer risk in humans remains unclear. The relationship between body weight, body mass index (BMI) or relative body weight and site-specific cancer has been widely investigated, and in most epidemiologic studies, a positive association has been seen with cancers of the breast, endometrium and kidney (Eldridge, 2004, p.1000; Willett, 2001). Miller and colleagues (1978, as referred to by Cotugna & Vickery, 2003) conducted a case-control investigation, estimating a number of dietary variables for individuals with breast cancer. In that study, no association with energy intake was noted. Holmberg, Ohlander, Byers, Zack, Wolk, Bergstrom, Bergkvist, Thurfjell, Bruce & Adami (1994, p.1805) completed a case-control analysis of the relationship between current diet and breast cancer risk on 380 cases and 525 control subjects. Risks did not change appreciably with adjustment for total energy intake or known breast cancer risk factors. Assessing energy intake as a possible risk factor for the development of breast cancer is important; some literature suggests it is not the total energy intake that is significant, but the diet

composition and the effect of the diet on body composition (Willett, 2001). Unfortunately, assessing associations based on past dietary intake of individuals diagnosed with cancer carries the possibility of biased reporting, based on the patient's difficulty in remembering previous intake, as well as the impact of the cancer diagnosis itself.

To assess the risk of postmenopausal breast-cancer patients, Barret-Connor and Friedlander (1993) conducted a cohort study in 1993, including 50 women aged from 40 to 79 years of age. Over the 15-year duration of the study, 15 women were diagnosed with breast cancer. They concluded that the strongest risk factors for developing breast cancer were the total energy intake as well as the total dietary fat intake. If fat and energy intake are risk factors, maintaining the same energy intake and substituting fat energy with carbohydrate energy may not necessarily be protective against the development of breast cancer. In the mentioned study, the type of fat was not significantly associated with the breast cancer risk.

Energy requirements in patients with cancer in general, have been shown to vary, depending on disease site and level of stress. In clinical settings, the Harris Benedict equation has been found to be a more practical, reliable and effective method for measuring BEE, seeing that it takes into account gender, age, height and weight. Table 2.9 shows the calculation of the Harris-Benedict formula (Riccardi & Allen, 1999). BEE is multiplied by an activity and stress factor to calculate total energy expenditure (TEE). The intake of energy for a cancer patient should be adequate, 105 to 146kJ/kg body weight to maintain and 146 to 209kJ/kg body weight to replete body stores (McCallum & Polisena, 2000, p.45). Reeves et al. (2006) states that BEE in cancer patients undergoing anticancer therapies does not appear to be as high as commonly thought. Saxton et al. (2006) states that individual energy requirements for breast cancer patients, that have shown to gain weight during breast cancer treatment, should

be estimated from a formulae of basal metabolic rate and physical activity level . The aim of this strategy should be to induce a steady weight loss of up to 0.5 kg each week. Recently, the use of weight loss algorithms proven successful in other clinical settings that incorporate dietary therapy, physical activity, and ongoing behaviour therapy have been endorsed by the National Institutes of Health and other health agencies (Chlebowski et al., 2002). Factors between 15% and 30% above basal energy expenditure are indicated for weight maintenance and anabolism, while increases of 10% to 80% above basal energy expenditure are used for postoperative septic patients. A stress factor of 1.1 to 1.3 BEE is recommended for cancer patients. Because these calculations are an estimate and not based on actual measurements of energy expenditure, the monitoring of patient response to the nutrition regimen and adjustments in energy goals are necessary (Riccardi & Allen, 1999). The monitoring of body weight and energy intake during treatment, is especially important for breast cancer patients seeing that an increase in body weight causes and increased risk for breast cancer recurrence (Krebs et al., 2006). Limitations of the Harris-Benedict formula is that it does not consider body composition (except for gender differences) and that the standard stress factors for cancer are too generic to be applicable to all cancer patients. Although definitive weight loss intervention trials in breast cancer patients remain to be conducted, the current evidence relating increased body weight to adverse breast cancer outcome and the documented favourable effects of weight loss on clinical outcome in other co morbid conditions, support consideration of programs for weight loss or at least weight maintenance in breast cancer patients (Chlebowski et al., 2002).

Some cancers are hypermetabolic and some hypometabolic, while others have a very small effect on metabolism, if any at all. The published standard stress factors for cancer are general guidelines, and are likely based on cancers known to be hypermetabolic. There are no specific stress factors for individual cancer diagnoses. Other than for bone marrow transplantation, all other cancers have a

generalized stress factor. More advanced cancers may present greater metabolic stress, due to a greater tumour burden or inflammatory response (McCallum, 2003).

TABLE 2.9: Harris-Benedict formula with activity and stress factors (McCallum, 2003, p.92)

Harris-Benedict formula with activity and stress factors

Basal energy expenditure (BEE) for females
= 655.1 + (9.6 x Weight) + (1.8 x Height) – (4.7 x Age)]

BEE is expressed in kcal per 24 hours
Weight is actual weight in kilograms
Height is measured in centimetres
Age is measured in years

Total Energy Expenditure (TEE) = BEE X Activity Factor X Stress Factor

Activity	Factor
Immobilized	1
Bed bound	1.2
Moderately Active	1.3

Stress	Factor
Starvation	0.8 – 1
Elective surgery	1 - 1.1
Infection	1.05 - 1.25
Sepsis	1.3 - 1.8
Acute renal failure	1.3 - 1.55
Liver failure	1.3 - 1.55
Bone marrow transplant	1.2 - 1.7
Cancer	1.1 - 1.3

Some controversy exists among practitioners as to whether ideal body weight (IBW), actual weight (AW) or adjusted ideal body weight should be used to calculate energy requirements for overweight patients, with a body weight greater than 125% of IBW. It is assumed that overweight patients have an increased body fat content and that, since fat is metabolically less active than

lean muscle, using AW for these calculations will result in an overestimation of energy needs. Ireton-Jones and Turner (1991) found that AW was in fact a more accurate estimation of energy requirements than IBW. If patients are obese, then an adjustment for weight may be made, since fat is not as metabolically active as lean muscle. Weight can be adjusted as follows:

Adjusted IBW = ([{actual weight – IBW} X 0.25] + IBW)

This formula adjusts IBW for obesity, allowing for some metabolic activity from the additional weight, but not as much as if the additional weight were only lean body mass (McCallum, 2003, p.92). This formula, even though widely used, has not been validated, and was therefore not used during this study. Other methods of estimating energy requirements are also available, and are based on energy/kg body weight estimation. The same issue whether IBW or AW should be used, applies, even with these calculations.

The metabolic changes that occur in cancer patients are not consistent. It is therefore important to make well-founded estimates of the patient's energy requirements, but even more important to evaluate whether the patient is receiving the recommended energy intake, and whether the estimated energy intake is in fact accurate (McCallum, 2003, p.93). The energy intake recommended for breast cancer patients is the use of the Harris-Benedict formula using AW, an activity factor of 1.3, and a stress factor of 1.1 to 1.3.

2.6.3 Protein requirements

The role of protein in cancer development is complicated, seeing that most diets high in protein are also high in red meat and low in fibre (Eldridge, 2004, p.1001; Willett, 2001). Diets containing a substantial amount of red meat may increase the risk of colorectal, renal, pancreatic, breast and prostate cancer. For this reason, the recommendation of "eat a variety of healthful foods, with an

emphasis on plant sources" was formulated (Cotugna & Vickery, 2003, p.50; Alberts, 1993, p.18).

TABLE 2.10: Estimated protein requirements for cancer patients (McCallum, 2003, p.96)

Estimating protein requirements for cancer patients		
Disease state	**Example**	**Protein requirements (g/kg IBW / day)**
Normal, non-stressed		0.8
Mild metabolic stress	Elective hospitalization	1.0 - 1.1
Moderate metabolic stress	Infection/complicated post-operative care	1.2 - 1.4
Severe metabolic stress	Sepsis	1.5 - 2.5
Bone marrow transplant		1.4 - 1.5
Liver/kidney compromise		0.5 - 0.8
Majority of cancer patients		1.0 - 1.5 (higher end for patients with depleted visceral proteins)
Malnourished cancer patient		1.5 – 2

Creasay (1985, as referred to by Cotugna & Vickery, 2003) identified two major considerations in 1985, when attempting to establish a relationship between protein intake and cancer. Firstly, a minimum protein intake of approximately five percent of the diet is essential for health and growth. Secondly, protein does not stand alone. Other components accompany this nutrient and some of them, such as fat, are suspected of being carcinogenic (Cotugna & Vickery, 2003, p.49). According to Toniolo and coworkers (1994, as referred to by Cotugna & Vickery, 2003) no association between protein intake and breast cancer risk was found in a prospective cohort study of 14291 women. The intake of meat was, however, elevated in those subjects who eventually

developed the disease. This was not true for other forms of animal products such as poultry, fish or dairy products. Tumour development is suppressed by diets that contain levels of protein below that required for optimal growth, and is enhanced by protein levels two to three times the amount that is required (Eldridge, 2004, p.1001; Rock & Denmark-Wahnefried, 2002). A high intake of soy products, which are rich in fibre and phytoestrogens such as genistein, has been shown to be associated with decreased breast cancer risk (Cotugna & Vickery, 2003, p. 61; Willett, 2001).

Increased protein turnover is seen in patients with cancer. Protein requirements can be calculated in various ways. Table 2.10 provides some methods of calculating protein requirements for cancer patients (McCallum, 2003, p.95). According to Escott-Stump (2002, p.540), the intake of protein should be high, that is, 1 to 1,5g/kg body weight to maintain and 1,5 to 2,0g/kg AW to replete losses. Nitrogen balance can also be used as an index of protein requirements. Nitrogen balance is calculated by using the following formula:

Nitrogen balance = (24 hour nitrogen intake in grams – 24 hour total urine nitrogen in grams) + 2 grams (McCallum, 2003, p.96).

The 24-hour nitrogen intake in grams is multiplied by 0.16 to give the dietary protein requirement in gram. This is where nitrogen intake consists of 16% of dietary protein and the two grams nitrogen added, indicates the grams of nitrogen lost during usual skin sloughing and from faecal loss. The equation assumes no diarrhoea and no excessive loss via other routes. In the event of these disorders, direct measurement of nitrogen loss should be performed. To perform the test, a 24-hour urine specimen collection is more accurate than extrapolates from shorter urine collections. The total urine nitrogen should be measured directly, when possible, while the total nitrogen can be approximated from the urine urea nitrogen. About 80% of total nitrogen is urea nitrogen, but

this could be misleading in critically ill patients. A positive nitrogen balance of 3 to 5g/day can be interpreted as sufficient for anabolism and wound healing, and a negative balance often occurs for several days after an acute injury (McCallum, 2003, p.96).

As with energy requirements, follow-up and re-evaluation of the recommended protein requirement is essential for good patient care. It is important to provide adequate energy to ensure that protein is used for tissue synthesis, rather than for energy requirements (McCallum, 2003, p.94).

The recommended protein intake should be 1.5g/kg AW per day for cancer patients.

2.6.4 Dietary fat guidelines

Altogether 250 cases and 219 control subjects, part of a case-control Taiwanese study, indicated the harmful effect of dietary fat intake on the risk of breast cancer development (Lee, Chang, Horng, Chang, Cheng & Huang, 2005). McCann, Ip, Ip, McGuire, Muti, Edge, Trevisan & Freudenheim (2004) found no significance between the intake of conjugated linoleic acid and overall breast cancer risk in a trial involving 1122 subjects and 2036 controls. Recent research has suggested that an increased (n-3) fatty acid intake and/or increased (n-3)/(n-6) PUFA ratio in the diet is associated with a lower breast cancer risk. A case-control study by Goodstine and coworkers investigated the association between the intake of (n-3) and other fatty acids and the (n-3)/ (n-6) PUFA ratio and breast cancer risk. In this study, premenopausal women showed a 41% non-significant lowered risk for the development of breast cancer, with an increased intake of PUFA (Goodstine et al., 2003).

Bloch and Eldridge (2002, p.540) recommend that fat intake should constitute 20% of total energy intake, with a decrease in saturated fatty acids (SFA) to

seven percent. Fat intake during adulthood does not seem to be associated with the overall risk of breast cancer, except in women with no history of benign breast disease, where the intake of unsaturated fats appears to be a risk for breast cancer. SFA intake has not yet been proven to be a definite risk for breast cancer development. In the Nurses Health Study, no association was found between the type and amount of fat consumed and the risk of breast cancer (Bloch & Eldridge, 2002, p.539).

Recommended fat intake is as low as 20% of total energy intake daily, with a decrease in SFA to less than seven percent of total energy.

2.6.5 Carbohydrate requirements

Prudent dietary guidelines suggest that 50 to 60% of daily energy should come from carbohydrates (Yale, 1992, p.41). The intake of complex carbohydrates should be increased. To achieve this, one must consume five or more servings of a combination of fruit and vegetables, especially green and yellow vegetables and citrus fruits, al well as six or more servings of a combination of breads, cereals and legumes.

Greater than 60% total energy from carbohydrate intake has been hypothesized to be a risk factor for breast cancer, possibly mediated by elevated levels of free insulin, estrogen and insulin-growth factor-1. Few epidemiologic studies have investigated the intake of carbohydrate in relation to the risk of breast cancer, and results are inconsistent. In a population-based case-control study conducted by Romieu, Luzcano-Ponce, Sanchez-Zamorano, Willett & Hernandez-Avila (2004), a positive association was found between carbohydrate intake and breast cancer risk. This association was present in both premenopausal and postmenopausal women. Among carbohydrate components, the strongest associations were observed for sucrose and fructose (Romieu et al., 2004). In a case-control study conducted in South-East England, no association was reported

between sugar intake and breast cancer risk. In a large Italian case-control study, greater carbohydrate consumption was significantly associated with a higher risk of breast cancer; starch was the main contributor to the increase, while no increased risk was observed for sugar. Witte et al. (2004, as referred to by Romieu et al., 2004) reported that carbohydrate intake was associated with the risk of premenopausal bilateral breast cancer. This recent case-control study suggests an association between sweet intake, expressed as a percentage of energy, and the risk of breast cancer among premenopausal women.

Carbohydrate recommendations are to adhere to prudent dietary guidelines and to have 50 to 60% daily energy from carbohydrates, preferably complex carbohydrates.

2.6.6 Dietary fibre

There are two major classifications of dietary fibre: the polysaccharides and the lignins (Mattisson, Wirfalt, Johansson, Gullberg, Olsson & Berglund, 2004). The polysaccharides include cellulose, hemicelluloses, pectins, gums and mucilages. Legnins are polymers of aromatic alcohols. Dietary fibres are also divided into two categories, based on their solubility in water. The fibres that are structural in nature are called water-insoluble fibres. They are cellulose, lignins, and some hemicelluloses. The gel-forming fibres, known as water-soluble fibres, include pectins, gums, mucilages and some hemicelluloses. Foods differ in both the amount and type of fibre they contain. Table 2.11 summarizes the components of dietary fibre, their functions as well as good food sources (Cotugna & Vickery, 2003, p. 58).

Early studies focused on the possible protective role of fibre in preventing cancer of the colon, rectum, breast and ovaries (Eldridge, 2004, p.1001). The intake of fibre influences the intake of meat, fat and refined carbohydrates. A number of observational and case-control studies indicate that fibre-rich diets are associated

with a protective effect in colon cancer. Some evidence exists that dietary fibre may also have a protective effect on breast cancer (Cotugna & Vickery, 2003, p.61; Mattisson et al., 2004). It is suggested that fibre-mediated changes in intestinal bacteria lead to a reduction in the deconjugation and reabsorption of estrogens, or that fibre may directly bind with estrogens. Compounds such as phytoestrogens found in fibre-containing foods may compete with estradiol for estrogen receptors in breast tissue and in that way beneficially affect breast cancer risk (Cotugna & Vickery, 2003, p.61).

TABLE 2.11: Fibre characteristics (Cotugna & Vickery, 2003, p.61)

Fibre characteristics		
Component / Type	**Functions**	**Good Sources**
Cellulose (Insoluble)	Structural material of cell wall	Wheat bran, whole grains, vegetables
Lignins (Insoluble)	Cell wall component	Wheat, carrots, potatoes, strawberries
Hemicelluloses (Insoluble and soluble)	Cell wall component; cement between wall	Wheat bran, whole grains
Pectins (Soluble)	Binds cell wall; holds water	Apples, citrus fruit
Gums (Soluble)	Part of secretory cells	Oatmeal, legumes
Mucilages (Soluble)	Water-holding properties	Seeds, seaweed

The association between fibre and cancer risk remains inconclusive. However, the consumption of high fibre foods should still be recommended, because of

their overall health benefit and because they contain other substances that contribute to cancer risk reduction (Eldridge, 2004, p.1001). It is recommended that 25 to 30 g fibre be consumed daily for all types of cancer.

2.6.7 Miscellaneous substances

Epidemiologic studies indicate that alcohol has a causal role in carcinogenesis, especially for cancers of the mouth, pharynx, larynx, oesophagus, lung, colon, rectum, liver and breast (Eldridge, 2004, p.1003; Key et al., 2001). Alcohol appears to have an increased effect on those tissues directly exposed to it during consumption (Simpson, 1995, p.573).

Coffee and tea has been investigated as a possible risk factor for a variety of cancers. The findings are that the regular consumption of both coffee and tea has no significant relationship to the risk of cancer at any known site (Eldridge, 2004, p.1003; Willett, 2001).

Artificial sweeteners have been investigated as a risk for the development of bladder cancer. The majority of evidence from metabolic studies and epidemiologic studies indicates that cyclamate itself is not carcinogenic and that no measurable increase in the risk of bladder cancer has been noted in individuals who have used the non-nutritive sweeteners cyclamate and saccharin (Eldridge, 2004, p.1003; Willett, 2001).

2.6.8 Vitamin and mineral requirements

McDermott (2000, as referred to by McCallum, 2003) states that an estimated 40% of the US population take vitamin and mineral supplements. There is growing public interest in the use of vitamins, minerals and other micronutrients in the prevention and treatment of cancer. The most commonly used supplements in attempts to prevent or treat cancer are the antioxidants, including Vitamins C and E, selenium, the carotenoids, copper, manganese, zinc,

flavonoids, and coenzyme 10 (Cotugna & Vickery, 2003, p.71; Willett, 2001). Antioxidants function by scavenging free radicals, stopping lipid per oxidation that can cause DNA damage, and possibly lead to cancer (McCallum, 2002, p.97; La Vecchia, Altieri & Tavani, 2001). Mattisson et al. (2004) is inconclusive about the use of specific nutrients as supplements in the prevention or treatment of cancer, but is highly supportive of a diet rich in a wide variety of fruits and vegetables, because of their high vitamin and mineral content.

Vitamin A consists of preformed vitamin A (retinol, retinyl esters and related compounds) from animal sources, and certain carotenoids, found primarily in fruits and vegetables, that are partially converted to retinol in the intestinal epithelium. Vitamin A regulates cell differentiation and may prevent the emergence of cells with a malignant phenotype (Potischman, Swanson, Coates, Gammon, Brogan, Curtin & Briton, 1999). The loss of differentiation is a basic feature of cancer cells. The role of vitamin A in maintaining epithelial tissue may be important, since many cancers arise from rapidly dividing epithelial cells. Vitamin A may thus provide a cellular defence against reactive oxygen species that damage DNA (Willett, 2001). Vitamin A is also important in immune function (Cotugna & Vickery, 2003, p.74). Retinol inhibits the growth of human breast carcinoma cells *in vitro,* while retinyl acetate reduced breast cancer incidence in some rodent models (Willett, 2001). Many investigations concerning vitamin A intake and breast cancer have been case-control studies; thus, their interpretation is limited by the potential for selection and recall bias. In a meta-analysis of nine case-control studies with data on vitamin A intake, a significant protective association between total vitamin A and breast cancer was reported. However, when preformed vitamin A and carotenoids were examined separately, the data from these case-control studies was more strongly supportive of a protective association for carotenoid vitamin A than for preformed vitamin A (Willett, 2001).

Vitamin E, also an anti-oxidant, has inhibited breast cancer tumours in some, but not all, rodent experiments (Willett, 2001). Relatively few studies are available to assess the association between dietary vitamin E intake and breast cancer, while none of the published prospective studies have reported a significant inverse association. Willett (2001) states that there is no evidence of a protective effect with the use of vitamin E supplements, even at high doses for a long duration.

Vitamin C is also an anti-oxidant and can block the formation of carcinogenic nitrosamines. Medical literature indicates that a high vitamin C intake significantly reduces the risk of cancer (La Vecchia et al., 2001; Simpson, 1995, p.573). The protective role was especially strong for cancers of the oral cavity, oesophagus and stomach, but there was also a substantial risk-reducing effect at cervical, rectal and breast sites (Cotugna & Vickery, 2003, p.79). Evidence from population studies indicates the strong protective effect of vitamin C on the development of breast cancer (Yuan, Wang, Ross, Henderson & Yu, 1995). Few animal studies have assessed the effect of vitamin C on breast cancer. In the largest case-control study reported, no association was observed for vitamin C. However, in a subsequent study by the same group, a significant protective association was present. In a meta-analysis of nine other case-control studies with data on vitamin C, a significant inverse association was observed. In the 14-year follow-up of the Nurses' Health Study, no evidence of any reduction was seen with the long-term use of vitamin C supplements. The existing data on the intake of vitamin C and breast cancer risk is inconsistent, but the available prospective data does not support any benefits from high vitamin C intake in reducing breast cancer risk (Willett, 2001; Howe, Tomio & Gregory, 1990).

Selenium is an important component of the anti-oxidant enzyme glutathione peroxides. It inhibits cell proliferation, and in animal studies, has been found to protect against a variety of cancers, although usually at high levels of intake.

Although there is a rapidly increasing body of literature on selenium and cancer, the role of this mineral in cancer risk is far from clearly defined. There are plausible biologic mechanisms for anticarcinogenic activity. The most obvious is protection against oxidative damage, although this is not thought to be the primary mechanism (Cotugna & Vickery, 2003, p.84). Ecological studies have shown strong inverse associations between country-specific and national measures of selenium exposure and breast cancer rates. Selenium intake cannot be measured accurately by means of dietary intake assessment, because of the high variability in the selenium content of individual foods, depending on the geographical area in which the foods were grown. However, tissues such as blood and toenails do reflect selenium intake and thus provide an informative measure of diet. Several studies using these biomarkers of selenium intake have been conducted (Willett, 2001). In the largest study, Hunter, Morris, Stampfer, Colditz, Speizer & Willet (1990) observed no association between toenail selenium and risk of breast cancer during four years of follow-up studies (Hunter et al. 1990). Of the other prospective studies, only the study of Knekt et al. (1990) from Finland showed any evidence of an increased risk amongst women in the lowest category of selenium (Knekt, Aromaa & Maatela, 1990). All this data suggests that increases in selenium intake are unlikely to reduce the risk of breast cancer for most women in countries with existing moderate or high levels of selenium intake (Willett, 2001; Simpson, 1995, p.573).

Lycopene, found in tomatoes, may be protective against the development of breast cancer. Vitamin C, alpha-tocopherol, Folate, beta carotene, zeaxanthin, and dietary fibre from fruits and vegetables are most protective against cancer development (Block, Patterson & Subar, 1992).

Folate is involved in DNA synthesis, repair and methylation. It has been hypothesized that a high intake of folate may reduce the risk of human cancers, including breast cancer (Shrubsole, Jin, Dai, Shu, Potter, Herbert, Gao and

Zheng, 2001). Shrubsole et al. (2001) support the protective role of dietary folate in breast carcinogenesis. In a trial conducted in urban Shanghai, they found dietary folate to have an inverse association with breast cancer risk. A more pronounced inverse association between folate intake and breast cancer risk was observed among women who consumed high levels of folate cofactors (methionine, vitamin B12 and vitamin B6) than those whose intake levels of these nutrients were low (Shrubsole et al., 2001). Potischman et al. (1999) also confirm that cancer risk is not associated with the intake of folate.

It appears that the combination of nutrients found in the presence of a low-fat plant-based diet is the key to the prevention of both primary and secondary cancer (McCallum, 2003, p.98). Dietary sources of vitamins and minerals that meet the Dietary Reference Intake (DRI) and Recommended Dietary Allowances (RDA) levels are usually adequate, but a general supplement may be safely recommended. Demographic and personal characteristics, time passed since diagnosis, and stage of cancer at time of diagnosis, are predictive of dietary supplements used by women at risk of breast cancer recurrence (Block et al., 1992).

Dietary sources of vitamins and minerals that meet the RDA and Adequate Intake (AI) levels of the DRI are recommended and are usually adequate, but a general multi-supplement may be safely recommended (Willett, 2001, 396).

2.7 SUMMARY

The relationship between diet and cancer is a complex issue. In recent years, there has been a growing awareness among the public as well as scientific researchers of the association between cancer and nutrition, both as a means of

prevention and treatment. Many controversial issues surround the area of cancer prevention through dietary means, as many combining factors could play an influential role. Prompt and appropriate nutritional management of the cancer patient may help to improve the patient's outcome, tolerance to treatment and quality of life.

Besides dietary factors, malignant diseases such as breast cancer could lower serum albumin concentrations as well as other nutrients, which could compromise a patient's outcome. Nutrition plays an important role in the management of patients with cancer, from diagnosis through treatment and recovery. Patients have different needs and challenges with regard to their nutritional management, and providing individual nutritional advice is an important part of treatment.

Cancer patients may experience a variety of symptoms and metabolic changes during their treatment time that could have a significant effect on their nutritional status including serum albumin concentrations and body composition, and that need to be addressed as soon as they appear, or they could affect the patients' quality of life.

CHAPTER 3

METHODOLOGY

The methodology and techniques used for the study will be discussed in this chapter in the following order: study design; ethical approval; sample; terms and definitions; techniques; dietary intervention programme; study proceedings; statistical analysis; and problems encountered.

3.1 STUDY DESIGN

A three month randomized clinical trial was performed.

3.2 ETHICAL APPROVAL

Ethical considerations were applied throughout the duration of the study. Before the start of the study, ethical approval was obtained from the Ethical Committee of the Faculty of Health Science at the University of the Free State. Approval was also obtained from the management of St. George's Hospital in Nelson Mandela Bay (previously Port Elizabeth) (Annexure A) and the ECOC. Each patient gave written consent for her participation in the study (Annexure B).

3.3 SAMPLE

Convenience sampling was used, in terms of which all consecutive patients complying with the inclusion criteria for a period of 19 months were included. Patients were assigned to either the experimental group (E) or control group (C), using a randomized list. This selection method was chosen as the most effective, seeing that a database of a large number of subjects was not available.

3.3.1 Population

The study population consisted of female first- or second-line breast cancer patients diagnosed and treated at the ECOC at St. George's Hospital in Nelson Mandela Bay (previously known as Port Elizabeth).

3.3.2 Inclusion criteria

Patients between the ages of 18 and 60 years, with a performance status of zero, one or two, were included in the study. Performance status (see 3.4.3.1) was used as a screening measure and a quality of life measure during the study.

3.3.3 Exclusion criteria

Patients with existing complications at the start of chemotherapy, such as endocrine abnormalities, including diabetes mellitus and obstruction of the upper or lower digestive tract, a performance status of three, four or five, and patients already participating in existing trials in the Unit, were excluded.

3.3.4 Sample size and selection

Brink (1992, p.38) states that the sample size should mainly be determined by the purpose of the study. The level of accuracy needed, the size of the population, the nature of the research design (qualitative research requires a smaller sample size), methods of data collection and financial resources are also

determining factors. However, other researchers are of opinion that despite the type of research, the bigger the sample size, the more accurate the collected data (McCallum & Polisena, 2000, p.4). Furthermore, Brink (1992, p.39) suggests that one should aim for a manageable sample size. Other researchers also recommend that for in-depth studies in which time-consuming techniques are employed, a smaller sample size is often more practical (Compton & Hall, 1972, p.190; McCallum, 2003, p.27). It was impossible to determine beforehand what the availability and willingness of suitable patients would be to take part in such a fairly intensive study. Therefore, the sample size for this study was mainly determined by the availability and willingness of suitable patients.

The admittance statistics of the ECOC showed that four newly diagnosed breast cancer patients were admitted each month. Based on the ECOC patient statistics, it was estimated that 60 patients could possibly be recruited in 15 to 18 months. It was therefore decided on a sample size of 60 patients in total; 30 patients in each group. This sample size is supported by Brink (1992, p.38), who states that it is preferable to have a minimum of 30 patients per variable or group. On the other hand, Henquin, Navivi, Reshef, Barak & Horn (1989) used a total of 19 cancer patients only to determine the effect of nutritional support during chemotherapy. This group of 19 patients was then divided into three smaller subgroups to perform the study. Because of such a small sample size, the results found were used to show tendencies only. A small sample size could also be used as a pilot for further research. Therefore, a total sample size of 19 to 60 could be regarded as suitable for this present study.

Due to factors such as the deceased frequency of breast cancer diagnosis and the discontinued use of Docetaxel chemotherapy in the Oncology Unit, only 13 patients could be recruited to the E-group, and 14 patients to the C-group, thus 27 in total. The patients were recruited over the 19 months' duration of the study. Although the total sample recruited was small, it was within the Henquin

et al. (1989) sample of 19 and the Brink et al. (1992, p.38) acceptable sample size of 60 patients. According to Brink (1992, p.38), because of the small number of patients included in this study, the results of the study would have a preliminary meaning and would show tendencies only.

3.4 DIETARY INTERVENTION PROGRAMME

The diet intervention programme refers to an individualized diet, with an optimal energy (calculated on the patient's ideal body weight to prevent weight gain in overweight and obese patients), and increased protein (OEIP) content of 1.5g protein/kg ideal body weight per day (McCallum & Polisena, 2000, p.47). By prescribing an energy intake to maintain ideal body weight for an overweight or obese patient it will precipitate a slow and ongoing weight loss, which would be beneficial for the long term risk of breast cancer recurrence (Eng et al., 2005). Weight loss per se was not calculated into the dietary prescription, because no studies could be found encouraging strict weight loss during chemotherapy treatment to show a beneficial effect on long term breast cancer risk. Energy calculations were adjusted for underweight patients by using an increased activity factor.

3.4.1 Energy requirements

Energy requirements were determined by using the Harris Benedict formula for women, that determines BEE [BEE = 655.1 + (9.6 x W) + (1.8 x H) – (4.7 x A) x 4.184]; W, referring to ideal body weight measured in kg; H, referring to height measured in cm; and A, referring to age measured in years. To adjust energy requirements, an activity factor of BEE x 1.3 was used for all patients that were not bedridden. Further energy adjustments of BEE x 1.5 were made, for patients that needed weight gain. No energy deductions to cause a specific weight loss was made for overweight or obese patients, but their BEE requirements were

calculated using their ideal body weight and not their actual body weight, in an attempt to prevent further weight gain and possibly cause a slow and steady weight loss. Research done by Reeves et al. (2006) stated that BEE in cancer patients undergoing chemotherapy does not appear to be as high as commonly thought. It was decided to not give a restricted energy with calculated weight loss dietary program, because such a restricted energy intake would cause the body to use the increased protein intake as a source of energy and not to maintain serum albumin levels, as required (Hammond, 2004, p.431). It was important to only supply optimal energy for the patient's ideal body weight, to ensure optimal use of dietary protein and to not cause any further weight gain, which will further increase breast cancer risk and risk of recurrence (Krebs et al., 2006). Weight gain in breast cancer patients is considered an indicator of poor prognosis, even after the administration of chemotherapy (McCallum, 2000, p.49).

3.4.2 Protein requirements

Protein requirements were calculated for the experimental group at 1.5g/kg ideal body weight per day.

3.4.3 Individualized eating plan

The diet treatment consisted of three main meals per day, as well as a nutritional supplementary shake as a mid-morning and mid-afternoon snack, and a small snack before bedtime. The nutrients in the supplementary shake were calculated as part of the daily nutritional requirements and not as an additional intake. The shakes were introduced to make the consumption of the required energy and nutrients easier, taking into account the patients' altered appetites. The nutritional supplementary shake, a powder that had to be mixed with water, contained 1046 kJ, 10.13 g protein, 9.38 g fat, 31.5 g carbohydrates and small

amounts of various vitamins and minerals. The complete nutritional analysis of the nutritional supplement is presented in Annexure F.

To ensure better compliance and to make the diet treatment as easy as possible, theoretical calculated dietary requirements were converted to the different food groups and explained to each patient, with her own individualized, easy-to-use eating plan. An example of an eating plan is presented in Annexure G.

3.5 TERMS AND DEFINITIONS

The variables measured for this study included serum albumin concentrations, anthropometrical status, quality of life, and dietary intake.

3.5.1 Serum albumin concentrations

Serum albumin concentrations refer to concentrations at the baseline visit, at the three-weekly visits, as well as at the end of the treatment period. The normal reference range for serum albumin of 35 to 50 g/dL was used, and a value below 35g/dL was considered inadequate.

3.5.2 Anthropometrical status

Anthropometrical status included current weight, height, mid-upper arm circumference (MUAC), and triceps skin fold (TSF) measurements. Anthropometrical status refers to calculated BMI, mid-arm fat area (MAFA), mid-arm muscle area (MAMA) and body composition measurements.

3.5.2.1 Weight

Actual body weight refers to measured body weight at the baseline visit, at the three-weekly visits, and end of treatment body weight.

3.5.2.2 Height

Height refers to measured body height in meters obtained at baseline visit.

3.5.2.3 Body Mass Index

BMI (kg/m^2) refers to the calculated BMI, using measured weight and height measurements obtained at the baseline visit, at the three-weekly visits, and at the end of treatment.

BMI is categorized as (Hammond, 2004, p.424):

Underweight	<18.5 kg/m^2
Healthy	18.5–25 kg/m^2
Overweight	25–29 kg/m^2
Obese	>30 kg/m^2

3.5.2.4 Mid-upper arm circumference

MUAC refers to the measurement, expressed in cm, taken at baseline, during three-weekly visits, and at the end of the treatment period.

3.5.2.5 Triceps skin fold

The TSF measurement refers to the measured triceps skin fold thickness at baseline, expressed in mm, during three-weekly visits, and at the end of treatment.

TABLE 3.1: Categories for interpretation of TSF and MAFA percentiles (Lee & Nieman, 2003, p.226)

≤ 5th percentile	Lean
> 5th but ≤ 15th percentile	Below average
> 15th but ≤ 75th percentile	Average
> 75th but ≤ 85th percentile	Above average
> 85th percentile	Excess fat

The categories for the interpretation of TSF percentiles are displayed in Table 3.1 (Lee & Nieman, 2003, p.226). TSF measurements are categorized according to gender and age and the National Health and Nutrition Examination Survey (NHANES) percentiles, as displayed in Table 3.2.

3.5.2.6 Mid-arm fat area

MAFA refers to the calculated body fat (BF), using the MUAC and TSF measurements, expressed in cm^2, obtained at baseline, during three-weekly visits, and at the end of treatment. The categories for the interpretation of MAFA percentiles are displayed in Table 3.1. MAFA measurements are categorized according to gender and age and the NHANES percentiles, as displayed in Table 3.2.

TABLE 3.2: Female NHANES percentile classifications of TSF, MAFA and MAMA used for this study (Mahan & Escott-Stump, 2004)

Age (years)	TSF percentiles		MAFA percentiles		MAMA percentiles	
	15th	75th	15th	75th	15th	85th
18-24.9	12	24.5	13.5	30.6	43	67
25-29.9	13	26.5	15.1	34.8	48.4	72.8
30-34.9	15	29.5	17.2	39	49.2	75.3
35-39.9	15.5	30	18	41.7	48.9	76.6
40-44.9	16	30.5	19.2	42.6	49.6	74.4
45-49.9	16.5	32	19.8	44.4	48.1	71.1
50-54.9	18.3	32.1	21.4	45.6	47.8	72.5
55-59.9	18.3	32.1	20.7	46.4	47.9	71.8

3.5.2.7 Mid-arm muscle area

MAMA refers to the calculated lean muscle (LM), using the MUAC and TSF measurements, expressed in cm^2, obtained at baseline, during three-weekly visits, and at the end of treatment. The categories for the interpretation of MAMA percentiles are displayed in Table 3.3 (Lee & Nieman, 2003, p.228). MAMA

measurements are categorized according to gender and age and the NHANES percentiles, as displayed in Table 3.2.

TABLE 3.3: Categories for interpretation of MAMA percentiles (Lee & Nieman, 2003, p.226)

≤ 5th percentile	Wasted
> 5th but ≤ 15th percentile	Below average
> 15th but ≤ 85th percentile	Average
> 85th but ≤ 95th percentile	Above average
> 95th percentile	High muscle

3.5.2.8 Body composition

Body composition refers to BF% and LM% analysis by means of bio-electrical impedance (BEI) analysis at baseline, during three-weekly visits, as well as at the end of the treatment period. A BF% of between 21% and 31% was considered normal for the subjects of this study, while a LM% of between 69% and 79% was considered normal for the subjects of this study.

3.5.3 Quality of life

Quality of life refers to performance status, as well as the Rotterdam Quality of Life Survey.

3.5.3.1 Performance status

Performance status refers to the health professional's interpretation and classification of the patient, based on the effects of the disease and the level of daily functioning. For the purpose of this study, the ZUBROD-ECOG-WHO classification system was used. The ZUBROD-ECOG-WHO classification system is displayed in Table 3.4 (Mina et al., 1984; Oken et al., 1982).

TABLE 3.4: ZUBROD-ECOG-WHO performance status classification

(Mina et al., 1984, p.536)

ZUBROD-ECOG-WHO performance status classification	
0	Normal activity
1	Symptoms, but fully ambulant
2	Symptomatic, but in bed <50% of the day.
3	Needs to be in bed >50% of the day, but not bedridden.
4	Unable to get out of bed.
5	Deceased

3.5.3.2 Rotterdam Quality of Life Survey

The Rotterdam Quality of Life Survey includes changes in physical as well as psychological symptoms, manifested in good or poor appetite, irritability, tiredness, worrying, painful muscles, depressive mood, lack of energy, lower back pain, nervousness, nausea, desperate feelings about the future, difficulty in sleeping, headaches, vomiting, dizziness, lack of sexual interest, tenseness, stomach pains, anxiety, constipation, diarrhoea, heartburn, shivering, tingling hands, difficulty in concentrating, sore mouth/swallowing, loss of hair, burning/sore eyes, shortness of breath, and dry mouth. The Rotterdam Quality of Life Survey reflects the patient's perception of her own quality of life. In this study, quality of life was determined at baseline, during three-weekly visits as well as at the end of the trial. A scoring of between zero and 90 was given, with a lower score indicating a better quality of life and a higher score indicating a poor quality of life.

3.5.4 Dietary intake

Dietary intake refers to habitual energy and protein intake as at baseline, as well as the median energy, macro and micronutrient intake during the three-months' of the study. The energy and protein intake of the E-group were compared to individualised calculated values. The other macro- and micronutrients of the E-

group and the energy, macro- and micronutrient intakes of the C-group were compared to Recommended Dietary Allowances (RDA) and Adequate Intake (AI) levels for healthy individuals (Earl, 2004, pp. 364). RDA refers to the amount of a nutrient needed to meet the requirements of 97% to 98% of the healthy population. AI is the recommended daily intake level based on observed or experimentally determined estimates of a nutrient by a group of healthy individuals. AI is used when a RDA cannot be determined (Earl, 2004, pp. 363). Comparing nutritional intake data of cancer patients to RDA/AI for healthy individuals may not fully meet the increased requirements of cancer patients. RDA/AI levels were however used because of a lack of nutrient recommendations for breast cancer patients receiving chemotherapy. Because no dietary recommendations are available for breast cancer patients, the nutritional adequacy of dietary intake data must be interpreted carefully.

3.6 TECHNIQUES

In this study, techniques chosen to determine serum albumin concentrations, anthropometrical status, quality of life and dietary intake will be described. Validity of measuring techniques and reliability of data are important aspects of the data collection process (Neuman, 1997, p.192). Validity is the ability of the instrument to measure the phenomenon it intends to measure, while reliability is the dependability of the measure to consistently give the same results, stable over time (Monsen & Cheney, 1992, p.13).

3.6.1 Serum albumin concentrations

The laboratory used for measuring serum albumin concentrations has a South African National Accreditation System (SANAS) ranking and its testing complies

with IFO-IEC17025 standardized techniques. Serum albumin concentrations were reported in Annexure D.

3.6.2 Anthropometry

Standard anthropometrical techniques were used (Hammond, 2000, p.353, 369-373). The anthropometrical data was reported in Annexure C.

3.6.2.1 Weight

A Seca Digital scale was used to determine the patient's actual body weight, to the closest 100 gram. The weight limit was set at 150.0kg body weight. Patients were weighed without their shoes, wearing light clothing, at approximately the same time of the day, and after empting their bladders. Patients were weighed on the same scale throughout the duration of the study, by the same researcher. The reliability of the measuring technique was ensured by compliance with the above-mentioned requirements. Furthermore, the reliability of the measuring instrument was ensured by having the measuring instrument periodically calibrated for accuracy by using weights with known weights.

3.6.2.2 Height

A Seca stadiometer, securely mounted on a flat surface, was used to determine the patients' height, to the closest millimetre. To ensure the reliability of the measuring technique, all patients were measured without shoes, hair coverings, hair bands or combed-up hair. The patients stood with their arms at their sides, looking straight ahead, breathing normally, feet flat, legs straight, with knees and heels together. Their heels, buttocks and upper backs all touched the wall. The head was in a visual horizontal position, with the upper part of the ear and the exterior corner of the eye forming a parallel line with the floor. The measurement was taken at maximum inspiration to the nearest mm, when the Frankfurt lines formed a 90° angle to the measuring stick. Reliability was further

ensured by compliance with the above-mentioned requirements, and all measurements were performed by the same researcher, as recommended by Gibson (1990).

3.6.2.3 Body Mass Index

BMI is considered a validated measure, indicating overnutrition or undernutrition (Hammond, 2004, p.424). BMI was used to determine the patient's level of adiposity according to the relationship between measured weight and height. BMI was calculated, using the following formula:

$$BMI = \frac{\text{Weight (kg)}}{\text{Height}^2\ (m^2)}$$

3.6.2.4 Mid-upper arm circumference

The middle point of the dominant arm was determined by measuring the distance between the acromion process of the scapula and the tip of the elbow. This point was marked with a skin pencil. The MUAC was then measured by using a metal measuring tape, to the closest millimetre, while the dominant arm was stretched along the patient's side, but yet relaxed. Reliability was ensured by compliance with the above-mentioned guidelines.

3.6.2.5 Triceps skin fold

A Harpenden skin fold calliper was used to determine TSF thickness. The patient stood upright, with the dominant arm relaxed along the same side. A double layer skin was taken between the thumb and index finger of the researcher's left hand, and slightly pulled away from the underlying tissue (Hammond, 2004, p.425). With obese patients the amount of tissue grasped was enough to forma fold with approximately parallel sides (Lee & Nieman, 2003, p.186). TSF measurement was taken on the same level as the MUAC, at the back of the arm,

parallel with the length of the arm, to the closest 0.2 mm. Three consecutive TSF measurements were taken, from which an average was determined and used as a result. The validity of this measurement depends on the accuracy of the measuring technique. Accuracy decreases with increasing obesity (Hammond, 2004, p.425). To ensure improved accuracy, only one researcher did all the measurements and caution was taken in interpreting the results to avoid possible reading error due to the high incidence of overweight and obesity among breast cancer patients (Lee & Nieman, 2003, p.186). To improve reliability of TSF thickness measurements especially in overweight or obese patients, BEI was also measured seeing that BMI does not have a significant impact on the accuracy of its readings. BEI was found to be an even better determinant of body fat percentage than skinfold measurements (Lee & Nieman, 2003, p.203).

3.6.2.6 Mid-arm fat area

MAFA was indirectly determined by using MUAC and TSF measurements. MAFA is used as an indication of body fat mass. The formula used to determine MAFA is (Hammond, 2004, p.427):

$$\text{MAFA } (cm^2) = \frac{\text{TSF (cm) x MUAC (cm)}}{2} - \frac{\pi \text{ x (TSF (cm))}^2}{4\pi}$$

3.6.2.7 Mid-arm muscle area

MAMA was indirectly determined by using MUAC and TSF measurements. MAMA is a good indication of lean body mass and thus an individual's skeletal protein reserves (Hammond, 2004, p.426). The formula used to determine MAMA is (Lee & Nieman, 2003, p.228):

$$\text{MAMA } (cm^2) = \frac{[\text{MUAC (cm)} - (\pi \text{ x TSF (cm)}]^2}{4\pi}$$

3.6.2.8 Body composition

BF% and LM% were determined by BEI, using a hand-held Bodystat® 1500 single frequency meter. BEI involves attaching electrodes to the extremities of a patient and passing a small electrical current of 50 kHz through the electrodes to obtain electrical and resistance measurements. The following precautions were taken: the patients were well hydrated, had not exercised in the previous four to six hours, and had not consumed alcohol in the previous 24 hours. With compliance to above mentioned precautions, BEI has been found to be a more reliable measurement of body composition, compared to BMI, skin-fold measures, height and weight (Hammond, 2004, p.428). BEI has also been used in other breast cancer research to determine body composition (Turner et al., 2004). To ensure the reliability of the readings, all metal objects such as jewelry and watches were removed beforehand.

3.6.3 Quality of life

Quality of life was determined by using a performance status scale and the Rotterdam Quality of Life Survey.

3.6.3.1 Performance status scale

Performance status was determined by scoring each patient on a quality of life/activity scale by the researcher, during each visit. The performance status scale is based on the interpretation of the researcher. The validity of this measuring technique has been proven and it is accepted as a standard quality of life measure for all types of cancer patients.

3.6.3.2 Rotterdam Quality of Life Survey

The Rotterdam Quality of Life Survey is a questionnaire that was completed by each patient at each visit. The Rotterdam questionnaire constitutes an interpretation by the patient of her own quality of life. A scoring of between zero and 90 was given, with a lower score indicating a better quality of life and a

higher score indicating a poor quality of life. The validity of this questionnaire has been proven previously as an existing standardized quality of life questionnaire, specifically formulated for all types of cancer patients, therefore also considered valid for the population group in the present study. The reliability of the measure is dependent on the accurate interpretation by the patient of her own quality of life. An example of the Rotterdam quality of life questionnaire is displayed in Annexure D.

3.6.4 Dietary intake

Dietary intake data was collected by using a diet history and a food diary.

3.6.4.1 Diet history

A Burke-type diet history, that included a 24-hour recall, a food frequency questionnaire and other information such as weight history, previous dietary changes, use of supplements, and food intolerances, was used to determine the habitual dietary intake patterns of patients prior to the start of the study. This information was not used as part of the scientific diet calculation or the results. The diet history was only used as a tool to socially individualize the meal patterns and personal preferences in the diet prescription for the E-group. Calculation of the diet prescription is discussed in 3.6.

3.6.4.2 Food diary

A food diary was used by all patients to record their exact daily dietary intake for the three month duration of the study, which included foods, drinks, vitamin and mineral supplements. Herbal supplements were not included in the analysis of this study. The food diary was used to determine whether the E-group complied with the dietary intervention program. For the purpose of this study, a special food diary form was compiled, to facilitate and ensure more accurate completion (Annexure E). This method was chosen to obtain data on daily intake and is regarded as a valid method of dietary recall by Earl and Borra (2000, p.338).

The validity of a food diary is dependent on the accuracy of the kept data. A food diary is usually kept for three to seven days to ensure accuracy of data (Hammond, 2004, p.418). In this study it was decided that both the E- and C-group keep a food diary for the full three month duration of the study, to monitor possible dietary changes over the treatment period. To improve accuracy of data, the food diary was discussed at length with each patient at the three weekly visits. Overweight and obese patients also tend to underreport dietary intake data. These limiting factors that could affect the accuracy of the dietary intake data was kept in mind during interpretation of the data. To improve the reliability of the data, each subject was supplied with standard measuring cups for standardized measurements, to ensure an accurate recall of daily dietary intake, as recommended by Pervan et al. (1995, p.124). Each patient was also asked to update the food diary with each intake, and not to rely on memory. The reliability of the measuring instrument was determined by the accuracy by which the subjects measured and supplied dietary intake data. To further improve reliability, the food diary was discussed with each patient during each three-weekly visit to ensure that she was still using the measuring cups and giving an accurate recall of daily intake.

3.7 STUDY PROCEDURES

3.7.1 Recruitment and randomizing

Female breast cancer patients that met the inclusion and exclusion criteria of the study and had given written consent were randomly assigned to either an E-group or a C-group and then initiated into the study.

The study procedures are shown in Figure 3.1.

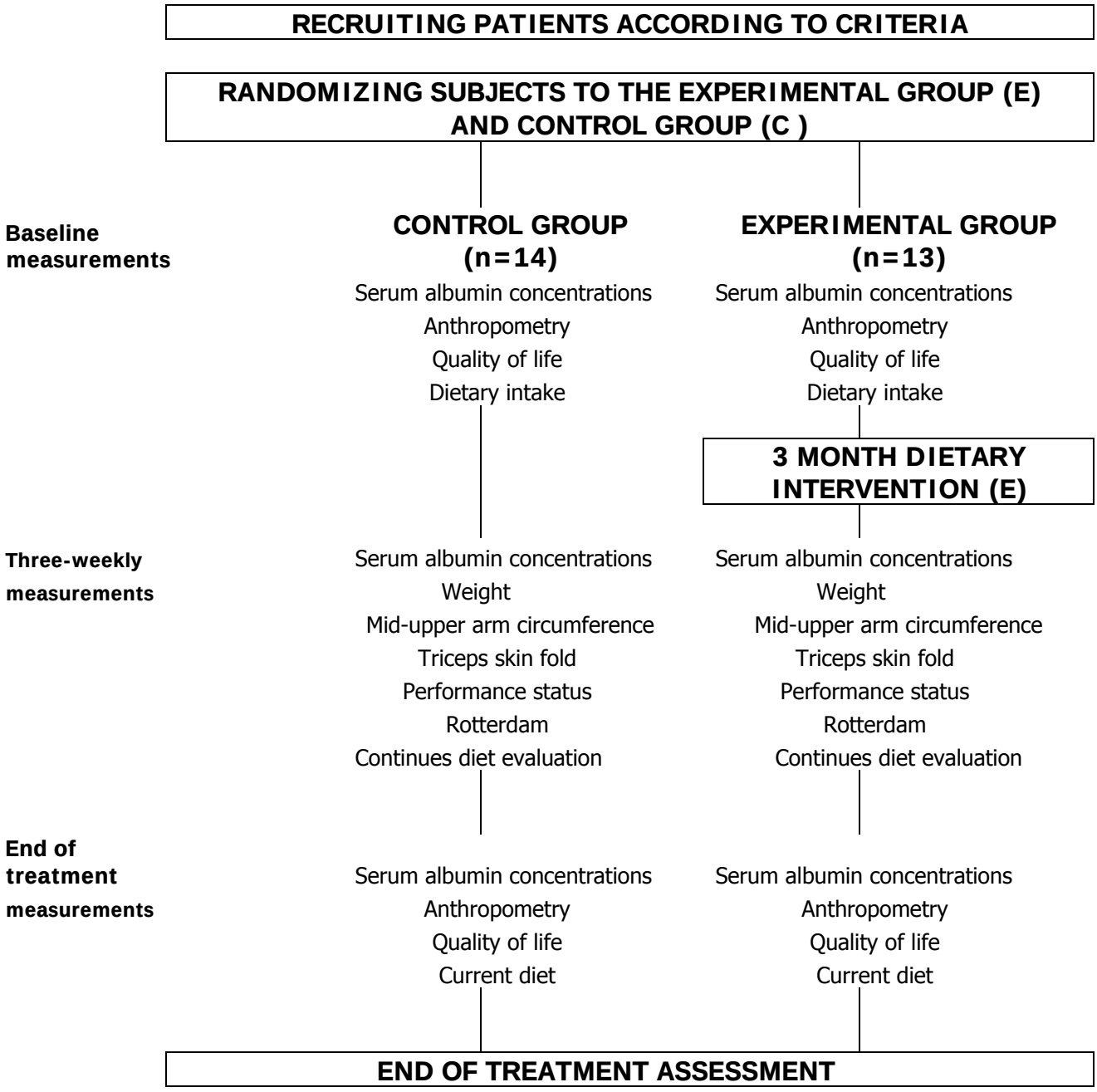


FIGURE 3.1: Schematic flow diagram of the procedures of study

3.7.2 Procedures at baseline

During the baseline visit, the patient's serum albumin concentrations, anthropometrical status, quality of life and current dietary intake were

determined (Figure 3.1). An individualized calculated eating plan, that included a nutritional supplement, was given to each patient in the E-group, while patients in the C-group received no such intervention.

3.7.3 Procedures during three-weekly visits

During the three-weekly follow-up visits, the following procedures were performed: serum albumin concentrations; body weight measurement; MUAC; TSF; performance status; and the Rotterdam Quality of Life Survey. Each patient in both the E- and C-groups kept a food diary. This food diary was discussed during each visit of the patients in the E-group and adjustments to dietary intake were made, if necessary. The three-weekly control of the food diaries served to ensure compliance with the dietary intervention by the E-group throughout the duration of the study.

3.7.4 Procedures at end of treatment

After the three-month duration of the study, each patient's serum albumin concentration, anthropometric status, current dietary intake and quality of life were determined and compared to that of the C-group, to determine the effect of the dietary intervention programme.

3.8 STATISTICAL ANALYSIS

Values at baseline were calculated per group by using median and percentiles for continuous data and frequencies and percentages for categorical data. The changes in baseline data, three-weekly measurements and end of treatment results were summarized by using median and percentiles, as appropriate, with a 95% CI for median differences between the E- and C-groups. Means and standard deviations were not used to describe the results, because they would

give a skewed reflection of the results due to the small sample size. The above mentioned statistical parameters are believed to be more reliable if such a small sample size, such as this study, is involved.

Nutritional intake per person was analyzed by using the MRC food composition tables and Foodfundi® software.

3.9 PROBLEMS ENCOUNTERED

The small sample size, due to the discontinued used of Docetaxel chemotherapy, initially a part of the inclusion criteria, was considered a major problem. Docetaxel was the chemotherapy of choice and frequently used at the start of the study. It was noted that breast cancer patients receiving Docetaxel chemotherapy often presented with a lowered serum albumin concentration. Therefore, it was decided to select breast cancer patients on Docetaxel treatment for the study. Due to a decline in the number of diagnosed breast cancer patients in the Unit, as well as a change in medical aid legislation in terms of which the frequent use of Docetaxel chemotherapy was disallowed due to the cost thereof, the number of patients actually enrolled in the study drastically declined. After 12 months, only ten patients could be recruited to the study. The population was accordingly expanded from breast cancer patients using Docetaxel chemotherapy only, to breast cancer patients receiving Docetaxel, CMF and CAF chemotherapy. No studies on the significant drug effect of CAF or CMF have been reported on serum albumin concentrations. In the following nine months, the sample size could be increased to 27 patients in total. This meant that the sample size was increased from ten to 27 patients over a nine months' period. Although a sample size of 30 in each of the E- and C-groups would have been ideal, this study ended with a much smaller sample size (E: n=13; C:

n=14). Due to the small sample size, the results have to be interpreted with caution: they have a preliminary meaning and show tendencies only.

The three month duration of the study is a limiting factor. To effectively determine the effect of an OEIP dietary implementation on anthropometrical measures and quality of life, the study should be extended over a longer period of time.

A further possible limitation is the accuracy of keeping a food diary for the three month duration of the study. Food diaries are usually kept for three to seven days to ensure optimal accuracy. By keeping a food diary for such an extended period of time, there is a tendency of accuracy to decrease. To improve the reliability of the data, control measures were taken as discussed in Section 3.5.4.2.

Another limitation of the study is the use of skinfold calliper in overweight and obese patients. With increased obesity the accuracy of skin fold calliper measurements reduces. To ensure improved measurements and accuracy, several measures were taken as discussed in Section 3.5.2.5.

CHAPTER 4

RESULTS

4.1 INTRODUCTION

The aim of the study was to determine the effect of an OEIP diet intervention programme on the serum albumin concentrations, anthropometrical status, quality of life and current nutritional intake of breast cancer patients receiving chemotherapy, the E-group, compared to those of a C-group that were not administered such a programme.

The results of the clinical findings will be described in the following order: baseline characteristics of each group; dietary intakes; changes in serum albumin concentrations; anthropometrical measures, and quality of life surveys, using median and percentiles for continuous data and frequencies and percentages for categorical data, with 95% CI. Means and SD were not used due to the small sample size of the study.

4.2 BASELINE CHARACTERISTICS OF STUDY POPULATION

The final study included 27 female breast cancer patients between the ages of 29 and 59 years (E: n=13; C: n=14). The median age of the E-group was 52.6 years, with a minimum age of 27 years and a maximum age of 59.7 years, while the median age for the C-group was 51.2 years, with a minimum age of 36.8 years and a maximum age of 59.8 years.

In the E-group, two patients had been diagnosed with liver metastases, two with brain metastases, and nine with other or unknown metastases. The C-group presented with one patient each diagnosed with bone, lung, liver and brain metastases, and ten with unknown metastases.

At baseline the habitual energy and protein intake of both the E- and C-groups were very similar. The E-group had a habitual energy intake of 6703.6 kJ and 67.92 g protein daily, while the C-group had a habitual energy intake of 6030.7kJ and 58.59 g protein per day.

4.3 DIETARY INTAKE DURING TREATMENT PERIOD

A daily food diary was kept by each patient for the duration of the study. The macro- and micronutrient intake of the E- and C-groups was determined and compared. The dietary intake data was used as a control to determine whether the E-group was complying with the dietary intervention programme and to determine whether the E-group had an improved dietary intake compared to that of the C-group. The three months' dietary intake data of the E- and C-groups are displayed in Table 4.1. The E-group, received a dietary intervention in an attempt to achieve their optimal energy and increased protein intake, (for this study specifically calculated in terms of energy and protein) and the C-group receiving no dietary intervention. The RDA/AI was considered for the other macronutrients of the E-group, the energy and macronutrient intake of the C-group and the micronutrient intake for both the E- and C-groups.

TABLE 4.1: Median three months' dietary intake and median percentage of the RDA/AI of E- and C-groups

Nutrients (RDA units)	RDA/ AI	Experimental group		Control group		95% CI for median difference
		Median	Median % RDA	Median	Median % RDA	
Energy (kJ)	** 10093	6722	109.95	4790.5	68.3	[862 ; 3188] *
Protein (g)	***RDA=46 CPR=82	75.15	150.3	51.95	104	[14.9 ; 40.5] *
CHO (g/day)	130	211.6	113	152.35	72.7	[22.8; 93.9] *
Sugar (g)	-	44.9	112.9	31.8	80.7	[-5.6; 23.5]
Fibre (g/day)	25	13.7	54.85	12.7	50.8	[-3.7; 4.1]
Total fat (g)	30%TE	49.3	107.3	34.3	67.3	[7.0 ; 26.4] *
SFA (g)	<10%TE	15.85	97.6	12.45	70	[1.3 ; 7.6] *
MUFA (g)	10%TE	16.05	99.5	11	57.3	[2.4 ; 9.3] *
PUFA (g)	10%TE	13.75	86.35	6.65	34.7	[5.4 ; 10.8] *
Cholesterol (mg)	300	265	88.3	133.5	44.6	[73 ; 202] *
Vit A (RE)	800	1232.5	154	617.5	77.2	[-135; 1398] *
Vit B1 (mg)	1	1.6	153.7	0.925	84.1	[0.32; 0.87] *
Vit B2 (mg)	1.2	2.06	168.9	1.29	103.1	[0.31; 1.12]*
Niacin (mg)	13	22.9	171.1	15.2	107.3	[4.7; 12.7] *
Vit B6 (mg)	1.6	2.065	129.1	1.25	78.1	[0.5; 1.38] *
Folic Acid (ug)	180	265.4	147.4	166.15	92.4	[31.3; 153.2] *
Vit B12 (ug)	2	6.535	327.9	3.075	153.8	[2.69; 4.71] *
Vit C (mg)	60	164.6	247.3	55.45	92.4	[59.3; 139.7] *
Pan. Acid (mg)	5.5	5.655	102.8	2.945	53.5	[2.06; 3.77] *
Biotin (ug)	65	92.15	141.8	14.7	22.7	[61.0; 81.3] *
Vit D (ug)	5	5.535	110.8	1.72	34.4	[2.24; 4.98] *
Vit E (mg)	8	11.315	141.4	5.665	70.8	[1.9; 8.31] *
Calcium (mg)	800	772	96.5	536.5	67.1	[134; 436] *
Iron (mg)	10	12.3	113.7	9.7	66.5	[-1.9; 6.4]
Magnesium (mg)	280	306	109.2	219.5	78.4	[35; 165] *
Phosphorus (mg)	800	1185.5	148.2	902.5	112.8	[118; 562] *
Potassium (mg)	2000	2582	129.2	1947	97.4	[317; 1465] *
Sodium (mg)	3000	1697	56.6	1361	45.4	[-106; 634]
Zinc (mg)	12	14.2	118.4	6.7	56.1	[6.2; 9.5] *
Copper (mg)	2.2	1.39	63.1	0.885	40.2	[0.21; 0.69] *
Manganese (mg)	3.5	3.025	86.4	2.04	58.4	[0.39; 1.91] *

* Statistically significant difference

** Energy requirements were determined individually for the E-group using the Harris Benedict formula

*** Protein requirements for the E-group was individually determined using 1.5 g protein per kg ideal body weight, approximately 82 g/day, while the RDA for protein is 0.8 g/kg, thus at least 46 g/d for women of 19 to > 70 years of age.

CPR (Calculated Protein Requirement), CHO (carbohydrate), TE (total energy), SFA (saturated fatty acids), MUFA (mono-unsaturated fatty acids), PUFA (polu-unsaturated fatty acids), Vit (vitamin), Pan. Acid (panthothenic acid).

The median protein intake for the E-group was 75.2 g/day and 52 g/day for the C-group. The E-group showed a statistically significant higher intake of protein compared to that of the C-group, with the 95% confidence interval (CI) of [14.9; 40.5] confirming this result. A protein intake of 1.5 g protein/kg body weight per day was aimed for in this study. The E-group had an actual median protein intake of 1.04 g/kg baseline body weight, compared to 0.72 g/kg median protein intake for the C-group.

The E-group consistently showed a statistically significant higher intake of all the macro- and micronutrients, with the exception of sugar, fibre, iron and sodium (Table 4.1), and all essential amino acids (Table 4.2) compared to that of the C-group for the three months' duration of the study, with the 95% CI for median differences confirming these results. This improved nutritional intake confirms the effect of the dietary intervention seeing that the C-group's dietary intake data was comparable to the E-groups baseline dietary intake patterns.

TABLE 4.2: Median three months' essential amino acid intake and median percentage of RDA/AI of E- and C-groups

Essential amino acids	Experimental group			Control group			95% CI for median difference
	25%	Median (g)	75%	25%	Median (g)	75%	
Ioleucine	3.346	3.566	3.7755	1.69	2.11	2.556	[0.99; 1.98] *
Leucine	5.79	6.06	6.44	2.92	3.611	4.34	[1.72; 3.36] *
Lysine	4.93	5.48	5.77	2.436	3.068	3.78	[1.47; 3.16] *
Methionine	1.79	1.9	1.97	0.82	1.044	1.28	[0.61; 1.12] *
Phenylalanine	3.17	3.27	3.48	1.65	2.095	2.322	[0.94; 1.82] *
Treonine	2.78	3	3.18	1.426	1.784	2.18	[0.79; 1.65] *
Tryptophan	0.85	0.87	0.94	0.435	0.5885	0.6385	[0.23; 0.49] *
Valine	3.897	4.12	4.33	1.99	2.44	2.85	[1.24; 2.24] *
Arginine	3.55	3.85	4.13	2.12	2.56	2.99	[0.73; 1.98] *
Histidine	1.94	2.13	2.31	1.053	1.339	1.585	[0.51; 1.13] *

* Statistically significant difference

4.4 CHANGES IN SERUM ALBUMIN CONCENTRATIONS

The changes in data between baseline and three-weekly visits were calculated per group by means of median values, and percentiles with 95% CI for the median difference between the groups. The results between different visits were also compared. Comparisons were made between visit 2 and baseline (Visits 2:B), visit 3 and visit 2 (Visits 3:2), visit 4 and visit 3 (Visits 4:3), visit 5 and visit 4 (Visits 5:4), and, finally, visit 5 and baseline (Visits 5:B).

The median serum albumin concentrations for the E-group varied from 37g/dL at baseline, to 39g/dL at visit 5 (Table 4.3), while the serum albumin concentrations for the C-group varied from 38g/dL at baseline, to 36.5g/dL at visit 5. Even though a positive change in the E-group and a negative change in the C-group were noted, the changes were not significant, by means of 95% CI for the median difference.

TABLE 4.3: Serum albumin concentrations per visit for E- and C-groups

Visit	Experimental group			Control group			95% CI for median difference
	25%	Median (g/dL)	75%	25%	Median (g/dL)	75%	
1	37	37	39	37	38	40	[-3 ; 1]
2	37	38	39	37	38	38	[-1 ; 2]
3	38	38.5	39.5	35	37	38	[0 ; 4]
4	38	39	40	33	37	38.5	[0 ; 6]
5	38.5	39	40	34	36.5	38	[0 ; 6]

Changes in serum albumin concentrations were compared between different visits, as reflected in Table 4.4. No statistically significant changes were noted in either the E- or C-groups for Visits 2:B, Visits 3:2, Visits 4:3 or Visits 5:4.

However, the median change in serum albumin concentration for the E-group at visits 5:B was an increase of 1.5g/dL, compared to a decrease of 3.0g/dL for the C-group. The serum albumin concentrations of the E-group in Visits 5:B compared to that of the C-group during the same period showed a statistically significant positive change, with a 95% CI for the median difference of [2; 6]. The improvement in serum albumin concentration of the E-group resulted in the non-postponement of chemotherapy cycles.

Spearman correlation was used to determine the correlation between serum albumin concentrations at Visit 5 and baseline. In the E-group, the serum albumin concentrations at Visit 5 showed a significant correlation with baseline, with a value of 0,82 and a p-value of 0.0011. No significant correlation could be found between the serum albumin concentrations of the C-group for the same period, with p=0.002.

TABLE 4.4: Change in serum albumin concentrations compared between different visits for E- and C-groups respectively

	Experimental group			Control group			
Visit	**25%**	**Median** (g/dL)	**75%**	**25%**	**Median** (g/dL)	**75%**	**95% CI for median difference**
Visits 2:B	-0.5	0	1	-3	0	0	[0 ; 3]
Visits 3:2	1	1	1	-2	0	0	[0 ; 3]
Visits 4:3	0	0.5	1	-2	-1	0	[0 ; 3]
Visits 5:4	-1	0	1	-0.5	0	1	[-1 ; 1]
Visits 5:B	0	1.5	2.5	-4	-3	-1.5	[2 ; 6] *

* Statistically significant difference; B = Baseline visit

4.5 CHANGES IN ANTHROPOMETRICAL MEASUREMENTS

Anthropometrical measurements included current body weight, BMI, TSF, MUAC, MAFA, MAMA, BF% and LM%.

4.5.1 Body weight

Changes in body weight, measured in kilogram (kg) at the baseline visit and on the subsequent three-weekly visits, were compared between the different visits for the E- and the C-groups (Table 4.5). In this study, the E-group had three patients that were classified as normal body weight, seven as overweight and two as obese, compared to the C-group that had five normal body weight patients, six overweight and four obese patients. 17% of the E-group and 27% of the C-group were found to be obese. No statistically significant changes in body weight were noted in either the E- or C-groups between Visit 2 and the baseline visit (Visits 2:B), Visits 3:2, Visits 4:3, Visits 5:4; or Visits 5:B.

TABLE 4.5: Changes in body weight compared between different visits for E- and C-groups respectively

Visit	Experimental group			Control group			95% CI for median difference
	25%	Median (kg)	75%	25%	Median (kg)	75%	
Visits 2:B	-0.85	-0.2	-0.3	-0.6	0	0.3	[-1.4 ; 0.5]
Visits 3:2	-0.65	0.65	1.5	-0.8	0.2	0.9	[-0.9 ; 1.6]
Visits 4:3	-1.2	-0.2	0.7	-0.25	0.1	1.45	[-1.9 ; 0.4]
Visits 5:4	-0.5	0.05	0.45	-0.6	0.51	1	[-0.9 ; 0.9]
Visits 5:B	-3	-0.15	2.7	-1.45	0.7	3.4	[-4.5 ; 2.3]

B = Baseline visit

4.5.2 Body Mass Index

The median BMI for the E-group varied from 26.9 kg/m^2 at the baseline visit, to 27.4 kg/m^2 at Visit 5, and from 25.3 kg/m^2 at the baseline visit, to 26.8 kg/m^2 at Visit 5 for the C-group (Table 4.6). Even though positive changes in BMI in both the E- and C-groups were noted, no statistical significant changes in BMI were found, by means of 95% CI for the median difference.

TABLE 4.6: BMI per visit for E- and C- groups

Visit	Experimental group			Control group			95% CI for median difference
	25%	Median (kg/m^2)	75%	25%	Median (kg/m^2)	75%	
1	25.99	26.93	30.37	22.56	25.32	28.43	[-2.0 ; 5.9]
2	25.61	27.59	30.25	22.39	24.93	28.35	[-2.1 ; 5.9]
3	25.2	27.74	30.53	22.2	25.08	28.35	[-1.9 ; 6.2]
4	24.64	27.43	30.64	21.97	26.49	29.93	[-2.9 ; 5.4]
5	24.4	27.4	30.61	21.86	26.79	29.9	[-3.3 ; 5.7]

4.5.3 Mid-upper arm circumference

The median MUAC for the E-group varied from 31.5 cm at the baseline visit, to 31 cm at Visit 5; for the C-group, the median MUAC varied from 29.1 cm at the baseline visit, to 31.5 cm at Visit 5 (Table 4.7). Even though these opposite changes in MUAC measurements were observed, no statistically significant changes in MUAC were found by means of 95% CI for the median difference, even though a negative change in the E-group and a positive change in the C-group were noted.

TABLE 4.7: MUAC per visit for E- and C-groups

Visit	Experimental group			Control group			95% CI for median difference
	25%	Median (cm)	75%	25%	Median (cm)	75%	
1	27.1	31.5	32.5	28	29.1	33.1	[-2.6 ; 3.3]
2	27.3	31.2	32.05	28	29.4	33.2	[-3.2 ; 2.9]
3	27.3	31.1	32.55	27.2	29.5	33.3	[-3.1 ; 3.4]
4	27.6	30.95	32.6	26.85	31.2	34.1	[-4.5 ; 2.9]
5	27.7	31	32.8	27.2	31.5	33.75	[-4.3 ; 2.8]

TABLE 4.8: Change in MUAC compared between different visits for E- and C-groups respectively

Visit	Experimental group			Control group			95% CI for median difference
	25%	Median (cm)	75%	25%	Median (cm)	75%	
Visits 2:B	-0.25	-0.05	0.1	-0.1	0.1	0.1	[-0.5 ; 0.2]
Visits 3:2	-0.05	0.15	0.4	-0.2	-0.2	0.1	[-0.1 ; 0.9]
Visits 4:3	-0.2	-0.05	0	-0.2	0.05	0.45	[-0.4 ; 0.4]
Visits 5:4	-0.15	0.05	0.2	-0.4	-0.2	0.2	[-0.3 ; 0.5]
Visits 5:B	-0.45	0.1	0.85	-0.7	-0.15	1.05	[-0.9 ; 1.0]

B = Baseline visit

The MUAC between the different visits showed no statistically significant changes in either the E- or C-groups for Visits 2:B, Visits 3:2, Visits 4:3, Visits 5:4 or Visits 5:B (Table 4.8).

4.5.4 Triceps skin folds

Even though the patients in the study had a median baseline BMI of 25.32 and higher, no problems were encountered with measuring TSF. Caution was taken in interpreting the results of the 22% of the total population being obese (two

patients in the E-group and four patients in the C-group), due to possible reading error because of obesity. The median TSF measurements for the E-group varied from 23.1 mm at the baseline visit, 21.9 mm at the second visit, to 21.6 mm at Visit 5 while the median TSF measurements for the C-group varied from 23.6 mm at the baseline visit to 26.3 mm at Visit 5, all of which showed no statistical significance. TSF measurements for visits 1 to 5 are reflected in Table 4.9.

Even though a negative change in TSF measurements was recorded for the E-group, and a positive change in TSF measurements was seen for the C-group during the same period, no statistically significant changes in TSF measurements were found, by means of 95% CI for the median difference for the duration of the study. When TSF measurements were compared to TSF percentiles, the median TSF measurements for both the E-and the C-groups were consistently between the 15th and the 75th percentile for fat. TSF measurements were classified as average for both the E- and C-groups, with no significant differences found either within or between the two groups.

TABLE 4.9: TSF measurements per visit for E- and C-groups

Visit	Experimental group			Control group			95% CI for median difference
	25%	Median (mm)	75%	25%	Median (mm)	75%	
1	19.4	23.1	27	16.8	23.6	32.2	[-7.4 ; 6.3]
2	19.5	21.9	31.7	17	24.1	33.1	[-7.8 ; 7.8]
3	19.2	21.35	29.3	17.2	22.9	34.4	[-9.6 ; 7.4]
4	20.6	22.6	32.15	15.2	25.05	36.55	[-10.7 ; 7.8]
5	19.7	21.6	32.45	15.25	26.3	36	[-12.0 ; 7.8]

TSF measurements compared between the different visits displayed no statistically significant changes for either the E- or C-groups, namely Visits 2:B, Visits 3:2, Visits 4:3, Visits 5:4 or Visits 5:B (Table 4.10).

TABLE 4.10: Change in TSF measurements compared between different visits for E- and C- groups respectively

Visit	Experimental group			Control group			95% CI for median difference
	25%	Median (mm)	75%	25%	Median (mm)	75%	
Visits 2:B	-0.45	0.3	1.55	-0.1	0.2	0.9	[-1.2 ; 1.3]
Visits 3:2	-0.25	0.35	1.05	-1	-0.2	2.6	[-2.6 ; 1.3]
Visits 4:3	-0.25	0.65	2.7	0	0.55	1.3	[-0.9 ; 2.0]
Visits 5:4	-0.5	0	0.4	-1.25	-0.45	1.1	[-1.8 ; 1.3]
Visits 5:B	-1.65	1.7	3.65	-1.45	0.85	4.85	[-3.1 ; 2.9]

B = Baseline visit

4.5.5 Mid-arm fat area

The median MAFA for the E-group varied from 33.5 cm^2 at the baseline visit, to 29.8 cm^2 at Visit 5, while the median MAFA for the C-group varied from 28.9 cm^2 at the baseline visit, to 35.9 cm^2 at Visit 5 (Table 4.11).

TABLE 4.11: MAFA per visit for E- and C-groups

Visit	Experimental group			Control group			95% CI for median difference
	25%	Median (cm^2)	75%	25%	Median (cm^2)	75%	
1	22.8	33.5	38.1	20.9	28.9	45	[-11.21; 10.79]
2	23	30.7	44.9	21.7	28.3	46	[-14.92; 10.93]
3	24.3	28.3	42.6	21.2	28.6	47.5	[-17.54; 11.28]
4	26.1	29.1	44.5	18.6	34.3	50.9	[18.37; 14.28]
5	23.9	29.8	45.1	18.7	35.9	51.7	[-16.31; 14.29]

Even though a negative change in the E-group and a positive change in the C-group were noted, no statistically significant changes in MAFA were found, by

means of 95% CI for the median difference at the different visits. MAFA compared to percentiles showed that all the median MAFAs for both the E- and the C-groups were between the 15th and the 75th percentile for fat. No significant differences were found either within or between the E- or C-group.

4.5.6 Mid-arm muscle area

The median MAMA for the E-group varied from 40.7 cm^2 at the baseline visit, to 39.9 cm^2 at Visit 5, while the median MAMA for the C-group varied from 42.7 cm^2 at the baseline visit, to 41.6 cm^2 at Visit 5 (Table 4.12).

Even though negative changes in MAMA were noted in both the E- and C-groups, no statistically significant changes in MAMA were found, by means of 95% CI for the median difference at the different visits. MAMA compared to percentiles showed that the median MAMAs of both the E- and C-groups were considered normal, at between the 15th and the 85th percentiles, both within and between the two groups.

TABLE 4.12: MAMA per visit for E- and C-groups

	Experimental group			Control group			
Visit	25%	Median (cm^2)	75%	25%	Median (cm^2)	75%	95% CI for median difference
1	36.3	40.7	45.9	38.5	42.7	44.2	[-6.9; 6.36]
2	34.2	38.8	45.1	37.6	41.6	43.2	[-7.76; 4.04]
3	35.4	40	44.96	38.2	40.6	43.9	[-5.92; 5.94]
4	34.9	39.7	43.9	37.8	40.7	45.3	[-6.88; 5.96]
5	35.3	39.9	43.9	38.1	41.6	44.3	[-6.08; 6.04]

4.5.7 Body composition

Body composition was determined with BEI and described by means of BF% and LM%.

4.5.7.1 Change in body fat percentage

The median BF% for the E-group varied from 39.3% at the baseline visit, to 42% at Visit 5, while the median BF% for the C-group varied from 35.8% at the baseline visit, to 34.9% at Visit 5 (Table 4.13).

Even though a positive change in the E-group and a negative change in the C-group were noted, no statistically significant changes in BF% were found, by means of 95% CI for the median difference at the different visits. For this study, a BF% of 21% to 31% is considered normal.

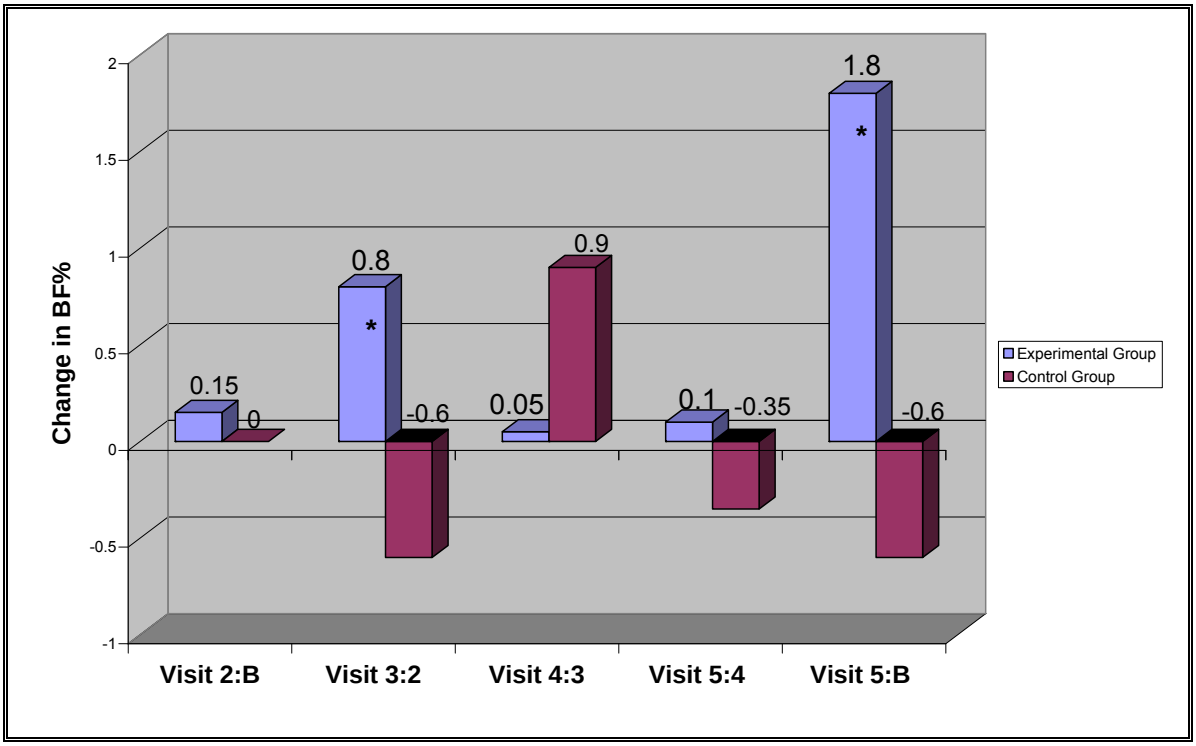
TABLE 4.13: BF% per visit for E- and C- groups

Visit	Experimental group			Control group			95% CI for median difference
	25%	Median (%)	75%	25%	Median (%)	75%	
1	36.1	39.3	41.5	30.9	35.75	39.5	[-3.7 ; 9.1]
2	36.25	40.45	42.3	30.6	35.6	37.8	[-4.0 ; 9.8]
3	39.35	40.55	44.25	30.1	33.6	37	[-1.3 ; 11.1]
4	39.75	41.85	44.55	31	35.6	40.4	[-2.2 ; 11.2]
5	39.55	42	44.2	29.3	34.9	40.15	[-2.5 ; 12.5]

With a median BF% of 39.3% and 35.8% respectively at the baseline visit, both the E- and the C-groups, were above the upper limit of normal for BF%. BF% increased throughout the study, with end of treatment BF% being higher than the values recorded at the baseline visit. Changes in BF% showed no statistically significant changes for either the E- or C-groups for Visits 2:B, Visits 4:3 or Visits

5:4. Statistically significant changes in BF% were, however observed between the E- and C-groups for Visits 3:2 and Visits 5:B (Figure 4.1).

The median change in BF% for the E-group at Visits 3:2 showed an increase of 0.8%, but a decrease of 0.6% for the same period for the C-group (Figure 4.1). The median change in BF% for the E-group at Visits 5:B showed an increase of 1.8%, but a decrease of 0.6% for the C-group during the same period, with the 95% CI for the median difference of [0.2; 4.7] confirming the statistical significance.



* Statistically significant difference; B = Baseline visit

FIGURE 4.1: Change in BF% between different visits for E- and C-groups respectively

4.5.7.2 Change in lean muscle percentage

The median LM% for the E-group varied from 60.7% at the baseline visit, to 58% at Visit 5, and the median LM% for the C-group varied from 64.3% at the

baseline visit, to 65.1% at Visit 5 (Table 4.14). No statistically significant changes in LM% were found using 95% CI for the median difference in either the E- or C-group.

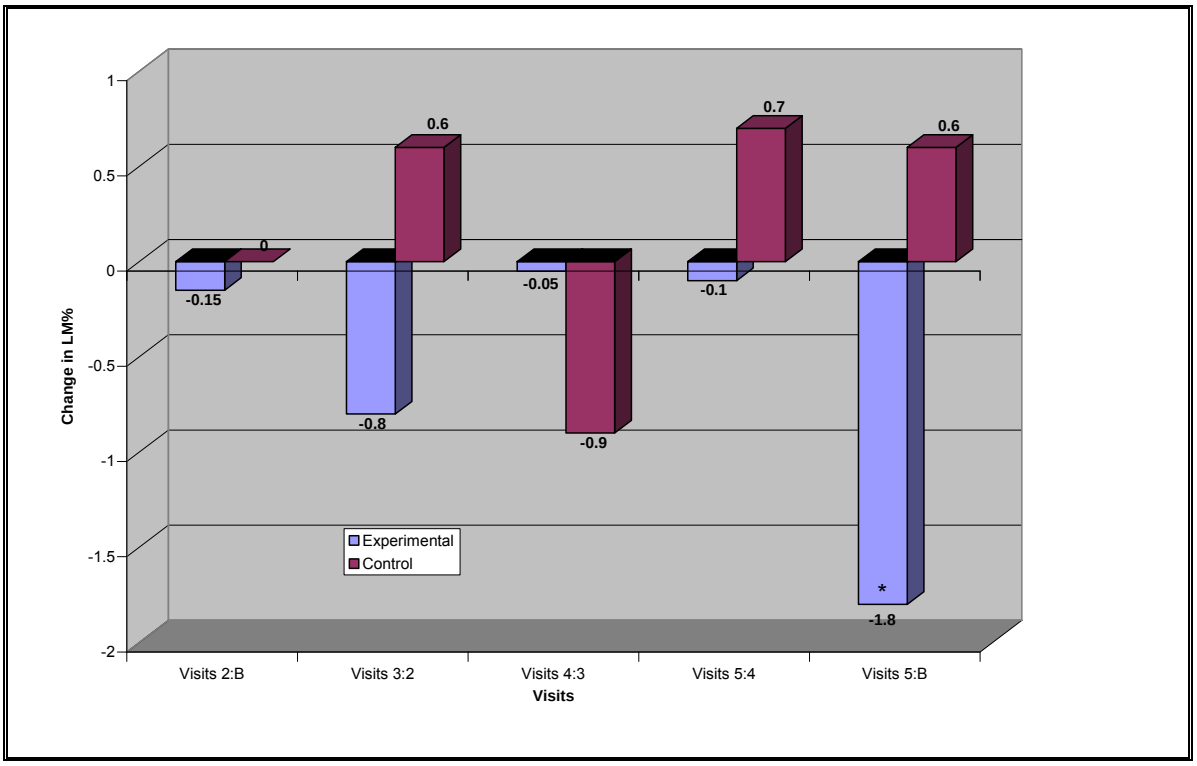
Both the E-group which, recorded a LM% of 60.7% at the baseline visit and of 58% at Visit 5, and the C-group, which recorded a LM% of 64.3% at the baseline visit and of 65.1% at Visit 5 presented with a LM% lower than normal (69% to 79%) throughout the duration of the study. No statistically significant differences were found between the E and C-group's LM% between the different visits.

TABLE 4.14: LM% per visit for E- and C-groups

Visit	Experimental group			Control group			95% CI for median difference
	25%	Median (%)	75%	25%	Median (%)	75%	
1	58.5	60.7	63.9	60.5	64.25	69.1	[-9.1 ; 3.7]
2	57.7	59.56	63.75	62.2	64.4	69.4	[-9.8 ; 4.0]
3	55.75	59.45	60.65	63	66.4	69.9	[-11.1 ; 1.3]
4	55.45	58.15	60.25	59.6	64.4	69	[-11.2 ; 2.2]
5	55.8	58	60.45	59.85	65.1	70.7	[-12.5 ; 2.5]

LM% showed no statistically significant changes for either the E- or C-groups for Visits 2:B, Visits 3:2, Visits 4:3 or Visits 5:4 (Figure 4.2).

The E-group showed a statistically significant reduced LM% (95% CI of [-4.9; -0.3]) at Visit 5B, compared to that of the C-group. The median change in LM% for the E-group at Visits 5:B was a decrease of 1.8%, while the median change in LM% for the C-group during the same time was an increase of 0.6%.



* Statistically significant difference; B = baseline visit

FIGURE 4.2: Change in LM% between different visits for E- and C-groups

4.6 CHANGE IN QUALITY OF LIFE MEASUREMENTS

Quality of life was determined by means of a performance status scoring and Rotterdam Quality of Life Questionnaire during each visit. The scoring of both measurements was done individually. The results that describe quality of life will be discussed in the following section.

4.6.1 Performance status

Performance status was a scoring given by the researcher on the apparent quality of life enjoyed by the patient. Change in performance status showed no statistically significant changes in either the E- or C-groups for Visits 2:B, Visits 3:2, Visits 4:3, Visits 5:4 or Visits 5:B (Table 4.15).

TABLE 4.15: Comparison of performance status between different visits for E- and C- groups

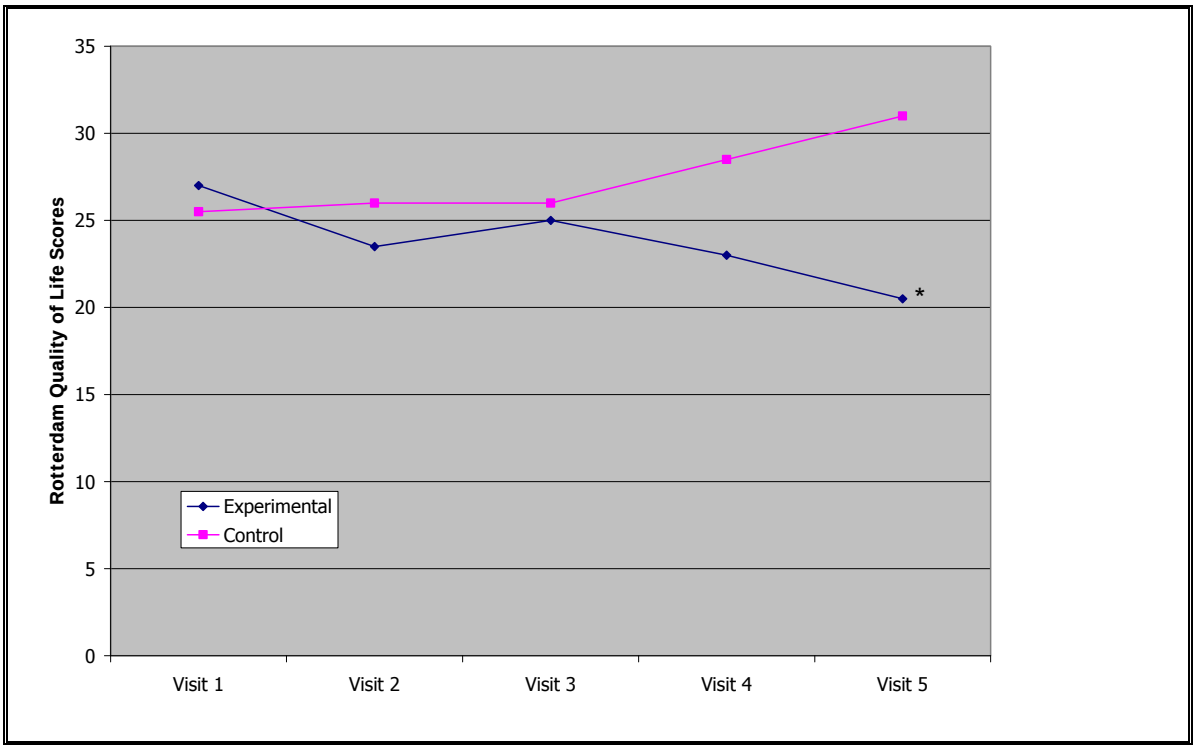
Comparison of performance status between visits			
	Experimental group	**Control group**	**95% Confidence for the median difference**
Visits 2:B	0%	30.80%	[-57.6%; -0.5%]
Visits 3:2	16.70%	61.50%	[-38.8%; -6.6%]
Visits 4:3	41.70%	25%	[-19.3%; 47.6%]
Visits 5:4	25%	33.30%	[-40.3%; 26.0%]
Visits 5:B	83.30%	100%	[-44.8%; 10.4%]

B = Baseline visit

4.6.2 Rotterdam Quality of Life Survey data

The Rotterdam Quality of Life Survey is a questionnaire that was completed by each patient during each visit. The Rotterdam questionnaire constitutes an interpretation by the patient of her quality of life and consisted of 30 questions. The median Rotterdam quality of life measurement for the E-group varied from 27 at the baseline visit, to 23 at Visit 4, while it varied from 25.5 at the baseline visit, to 28.4 at Visit 4 for the C-group (Figure 4.3). Even though an improvement in quality of life was noted for the E-group and negative change in quality of life was noted for the C-group, no statistically significant changes were found, using 95% CI for Visits 1 to 4.

A statistically significant improvement in the Rotterdam Quality of Life Survey results was recorded for the E-group during Visit 5, compared to that of the C-group in the same period. The median Rotterdam quality of life measurement for the E-group at Visit 5 was 20.5, as compared to the 31 recorded for the C-group for the same period, confirmed by the 95% CI for the median difference of [-20; -1].



* Statistically Significant Difference

FIGURE 4.3: Quality of life scoring per visit for E- and C-groups determined through Rotterdam Quality of Life Questionnaire

No statistically significant changes were evident in the Rotterdam quality of life measurements in either the E- or C-groups on Visits 2:B, Visits 3:2, Visits 4:3 or Visits 5:B (Table 4.16). The median change in Rotterdam quality of life measurement for the E-group at Visits 5:4 indicated an improvement of 3.5, while an increase of 2 was recorded for the C-group during the same period (reduced quality of life), confirming the statistical significance using the 95% CI for median difference of [-10; -2].

TABLE 4.16: Change in quality of life, determined by Rotterdam Quality of Life Questionnaire, compared between different visits for E- and C-groups respectively

Visit	Experimental group			Control group			95% CI for median difference
	25%	Median	75%	25%	Median	75%	
Visits 2:B	-9.5	-2.5	5	-4	0	2	[-9; 6]
Visits 3:2	-3.5	-1.5	4	-1	2	6	[-8; 3]
Visits 4:3	-5	-1	2.5	-3.5	1	4	[-5; 3]
Visits 5:4	-7.5	-3.5	1	0.5	2	5.5	[-10; -2] *
Visits 5:B	-11.5	-9.5	-1.5	-5.5	4.5	10.5	[-20; 0]

* Statistically significant difference; B = Baseline visit

4.7 SUMMARY

Dietary intake data for the duration of the study showed that the E-group had a statistically significant improved intake of energy as well as all macronutrients, all vitamins and all minerals, with the exception of sugar, fibre, iron and sodium, compared to the C-group.

Serum albumin concentrations showed a statistically significant improvement in the E-group for the three months' intervention period, significantly so that the postponement of chemotherapy cycles due to a reduced serum albumin concentration was not necessary for the E-group. An increase in serum albumin concentrations of 1.5g/dL was observed from the baseline visit to visit 5, while the C-group showed a drop in serum albumin concentrations of 3g/dL during the same period. The C-group showed a tendency towards an increased BMI, MUAC, TSF, and MAFA, and a decrease in MAMA. The E-group, on the other hand

showed a tendency towards an increased BMI and decreased TSF, MAFA and MAMA. No significant changes were, however, observed between the E- and C-groups in regards to weight, BMI, MUAC, TSF, MAFA or MAMA for the duration of the study.

The E-group showed an increased 1.8% BF% when baseline and end of treatment data were compared, in contrast with a decrease in BF% of 0.6% for the C-group. This change in BF% was a statistically significant improvement of BF for the E-group. The C-group showed a statistically significant improved LM% of 0.6% at Visits 5:B compared to a loss of 1.8% LM% in the E-group during the same period.

No significant changes in performance status (researcher's perception) were observed between the E-or C-groups during the treatment time. The E-group showed a tendency to have a more consistent performance status than that of the C-group. The Rotterdam quality of life survey (patient's own perception of quality of life) showed a statistically significant improved quality of life for the E-group at Visits 5:4, compared to that of the C-group, but no statistically significant change for either the E-or C-group from baseline to visit 5.

CHAPTER 5

DISCUSSION

Few studies have investigated the impact of nutrition intervention on the serum albumin concentrations, anthropometrical status and quality of life of breast cancer patients receiving chemotherapy.

5.1 LIMITATIONS OF THE STUDY

As explained in Chapter 3, the small sample size is a limiting factor that needs to be kept in mind when interpreting the data and making recommendations. The small sample size was due to the discontinued used of Docetaxel chemotherapy, initially a part of the inclusion criteria. Due to a decline in the number of diagnosed breast cancer patients in the ECOC, as well as a decline in the use of Docetaxel chemotherapy, the population was accordingly expanded from breast cancer patients using Docetaxel chemotherapy only, to breast cancer patients receiving Docetaxel, CMF and CAF chemotherapy, thus could the sample size be increased to 27 patients in total. Due to the small sample size, the results have to be interpreted with caution: they have a preliminary meaning and show tendencies only.

The short three month duration of the study is a limiting factor. To effectively determine the effect of an OEIP dietary implementation on anthropometrical measures and quality of life, the study should be extended over a longer period

of time. The short duration period of the OEIP dietary implementation, should be considered as the results are interpreted.

Another limiting factor is the use of RDA/ AI for healthy individuals to assess dietary intake data of breast cancer patients, because no specialized dietary intake guidelines are available for breast cancer patients while receiving chemotherapy. The accuracy of nutritional intake data is of concern, because it is dependant on the accuracy of data kept by each patient, for a long period of three months. It is suggested to collect the most accurate dietary intake data a three to seven day period is more effective. The problem of underreporting of dietary intake data by overweight and obese patients should also be considered when interpreting dietary intake data.

A further possible limitation is the accuracy of keeping a food diary for the three month duration of the study. Food diaries are usually kept for three to seven days to ensure optimal accuracy. By keeping a food diary for such an extended period of time, there is a tendency of accuracy to decrease and the patient burden is high. A further accuracy problem is the tendency for overweight and obese patients to underreport their dietary intake in a food diary. The possibility of underreporting should also be kept in mind when interpreting the results, however both the E-and C-groups had a comparable number of overweight and obese patients and both groups therefore have a similar margin of reporting error.

Another limitation of the study is the use of skin fold callipers in overweight and obese patients. With increased obesity the accuracy of skin fold calliper measurements reduces. To ensure improved measurements and accuracy, several measures were taken as discussed in Section 3.5.2.5.

A final limitation of the study was the questionable energy and protein requirements of breast cancer patients during chemotherapy treatment, seeing that no conclusive evidence exists. The adequacy of giving an energy intake to only maintain a patient's ideal body weight, to not cause any further weight gain and subsequently further increase breast cancer risk should be evaluated. The efficacy of limiting energy intake in an attempt to maintain ideal body weight and increase protein intake to ensure improved serum albumin concentrations should be evaluated.

5.2 DIETARY INTAKE AND CHARACTERISTICS OF E- AND C-GROUPS

The OEIP dietary intervention programme implemented in the study improved the overall nutrient intake of the patients. Improved intake was accomplished by means of a nutritional supplement on a daily basis and ongoing nutritional advice during each three-weekly visit. The purpose of the dietary intervention programme was to determine the impact thereof on the serum albumin concentrations, anthropometrical status and quality of life of breast cancer patients receiving chemotherapy. It is believed that the three month duration of the study is very short and the results are interpreted with caution. The accuracy of the food diary over a three month period is also questionable. To improve the accuracy of dietary intake data, precautions were taken, as mentioned in Section 3.5.4.2.

The median energy intake of the E-group (110% of the RDA) was significantly more than the median energy intake of the C-group (68.3% of the RDA) [862; 3188]. The median energy intake of the E-group was, however, only 81% of calculated requirements. A target protein intake of 1.5 g protein/kg body weight per day was set for this study. The E-group had an actual protein intake

of 1.04 g/kg/day baseline body weight, compared to the C-group's 0.72 g/kg/day for the duration of the study. The E-group consumed less protein than planned, possibly due to reduced intake because of nausea during the first week following chemotherapy. The intake of the nutritional supplement was also reduced to one glass instead of two glasses per day during the first week following chemotherapy. Despite the reduced intakes in both the E- and C-groups during the first week after chemotherapy, the median consumption of both groups exceeded the RDA for protein: 150.3% for the E-group and 104% for the C-group. Although the protein intake of the E-group was significantly more, the patients were not able to consume the full dietary intervention of 1.5 g/kg body weight per day. Martin (2000, p.47) suggests that an energy to protein ratio in healthy individuals should be 125:1 to 150:1, and 100:1 in malnourished patients. Septic patients may even approach 80:1. Although not septic, in this study the E-group had an energy to protein ratio of 89:1, while the ratio in the C-group was 92:1. The median total fat intake expressed as a percentage of total energy intake for the E-group was 107.3% RDA, which was significantly better than the 67.3% RDA for the C-group.

The E-group showed a statistically significant higher intake of all measured vitamins and minerals compared to the C-group, with the exception of iron and sodium. In their report on the Women's Healthy Eating and Living (WHEL) study, Rock and Denmark-Wahnefried (2002) emphasize the potential importance of adequate multiple vitamin and mineral intake in influencing the progression of breast cancer. It appears, however, that no single dietary factor explains the protective effect. Compounds found together in vegetables may have a synergistic effect on breast cancer risk (Freudenheim, Marshall, Vena, Laughlin, Brasure, Swanson, Nemoto & Graham, 1996). Even though vitamins and minerals could possibly have a protective effect against breast cancer development, the results of current and other studies have not proven that an

increased intake of vitamins and minerals is beneficial in improving serum albumin concentrations or anthropometrical measures.

The goal of the dietary intervention program, namely to significantly improve the nutritional intake of the E-group with a nutritional supplement, was met. The nutritional intake of the E-group was consistently significantly better than that of the C-group. The adequacy of the nutritional intake of the E-group is not conclusive, seeing that their nutritional intake was compared to RDA/ AI for healthy individuals due to a lack of nutritional intake guidelines for breast cancer patients during chemotherapy treatment.

5.3 EFFECT OF DIET INTERVENTION PROGRAMME ON SERUM ALBUMIN CONCENTRATIONS

Albumin is a non-specific biomarker for malnutrition and should be evaluated in its clinical context. Albumin is usually an indicator for longer periods of malnutrition and for that reason it was decided to treat and monitor patients for a period of three months. The impact of the medical condition and the effect of chemotherapy on the serum albumin concentrations of breast cancer patients should first be interpreted before the effect of a diet intervention programme can be assessed. Various alterations in protein metabolism occur in cancer patients, as discussed in Section 2.3.5. Serum albumin concentrations can also be affected by the nutrition related side-effects of chemotherapy, as mentioned in Section 2.4.3. It is important to maintain an adequate serum albumin concentration, for albumin stabilizes the distribution of water in body compartments. Albumin is a carrier of several plasma components in the body. Albumin is essential in blood clotting and also serves as an emergency reserve of protein in times of starvation (Meyer & Grey, 1988, p.224). The rate of decrease

of serum albumin concentrations is not proportional to the degree of malnutrition. However, in the absence of acute stress, low levels of serum albumin concentrations are predictive of a poor prognosis in cancer patients. Serum albumin concentrations of less than 35g/dL indicate protein depletion (Mutlu & Mobarhan, 2000).

McCarthy and Weihofen (1999) monitored a sample of 40 newly diagnosed cancer patients that were encouraged to use a nutritional supplemental shake between meals to improve their nutritional intake. Similar to the present study, they found that the total energy and protein intake of the experimental group was significantly higher than that of the control group. They did, however, not determine the effect of improved nutritional intake on serum albumin concentrations.

In the present study, the C-group, that had no dietary intervention, showed a significant drop of 3 g/dL in serum albumin concentrations. These results agree with those Bozzetti, Cozzaglio, Gavazzi, Bidoli, Bonfanti, Montalto, Soto, Valente & Zucali (1998), that also recorded significantly reduced serum albumin concentrations in a control group of cancer patients receiving no dietary intervention. The E-group, that received the OEIP diet, showed a significant increase of 1.5 g/dL in serum albumin concentrations [2; 6] during the treatment time, in contrast with Bozzetti et al. (1998), that recorded unchanged serum albumin concentrations in a group of cancer patients receiving standard nutritional supplementation. The improvement recorded in the E-group's serum albumin concentrations in the present study occurred despite the use of three different chemotherapy regimens and the levels of acute stress and inflammation present in both groups. This improvement in serum albumin concentrations suggests that the diet intervention succeeded in improving serum albumin concentrations during chemotherapy treatment over three months, and the

postponement of chemotherapy cycles for the patients in the E-group was not necessary.

Epidemiologic data is limited and contradictory regarding the potential benefit of an increased intake of protein on serum albumin concentrations. Although some literature suggest that tumour growth is suppressed by diets that contain levels of protein below that required for optimal growth (McCallum, 2003, p.91), it has also been shown that tumour growth is enhanced only with excessive intake of protein, at levels two to three times the required amounts (Eldridge, 2004, p.1001). The solution would probably be to find a level of protein intake that does not enhance tumour growth, but is still sufficient to maintain optimal serum albumin concentrations. Literature suggest an adequate protein intake for cancer patients of 1 to 1.5 g/kg/day (McCallum & Polisena, 2000, p.47), therefore the author assumed that an intake of 1 to 1.5 g/kg/day would not enhance tumour growth in patients.

Based on the present and other studies, it seems that a high protein intake of 1 to 1.5 g/kg/day and an optimal energy intake, could possibly have a positive effect on the serum albumin concentrations of breast cancer patients receiving chemotherapy, where an optimal energy intake is calculated to maintain a patient's ideal body weight and not actual body weight. Optimal energy intake would therefore gradually increase body weight in the case of underweight patients and cause a slow weight loss in the case of overweight and obesity.

5.4 EFFECT OF DIET INTERVENTION PROGRAMME ON ANTHROPOMETRICAL STATUS

Increased BMI or body weight was found to be a significant risk factor for recurrent disease, decreased survival, or both, in a review of 26 studies by Rock

and Denmark-Wahnefried (2002). Women with higher levels of obesity exhibited a 30% to 540% increased risk of death (Ziegler et al., 1996). These findings were confirmed by the Breast Cancer Detection Demonstration Project in which 226 pre-menopausal women and 1198 post-menopausal women participated (Yong et al., 1996). The present study shows the same tendencies, seeing that the median age for the E- and C-groups were 51 and 52 years respectively (post-menopausal women), and both groups started the study at baseline with an overweight BMI of 26.9 and 25.3 respectively. In line with Rock and Denmark-Wahnefried's (2002) findings, it would mean that the patients in both the E- and C-groups would be at increased risk for disease recurrence due to their relative high BMI from the baseline visit to the end of the study (E: 26.9 – 27.4; C: 25.3 – 26.8).

After a diagnosis of breast cancer, weight gain often occurs in women during their treatment (Willett, 2001). Such weight gain usually ranges from 2.5 to 6.2 kg (Rock and Denmark-Wahnefried, 2002). During their study, Cohn et al. (1982) recorded a weight gain in all patients receiving nutritional support. In the present study, the C-group showed a similar tendency towards weight gain. In contrast with the study by Cohn et al., (1982) the E-group showed a tendency towards weight loss, seeing that each patient's energy intake was calculated to maintain their ideal body weight, and not their increased actual body weight. Because it has been shown that weight gain after diagnosis adversely affects disease-free survival, breast cancer patients receiving treatment should be monitored closely to ensure that they maintain their body weight (Rock and Denmark-Wahnefried, 2002).

In this study, the E-group showed a tendency towards a decreased TSF and MAFA, while the C-group a tendency towards an increased TSF and MAFA; even though these opposite changes were noted, no significant changes were observed between the E- and C-groups in regards to TSF or MAFA for the

duration of the study. The opposite changes in TSF measurements could possible be explained by measuring error and inaccuracy, due to the large percentage of over weight and obese patients in the study.

Comparing results from BF% and MAFA calculations, some discrepancies were found. The use of skin fold thickness in overweight and obese patients is however not recommended due to lack of accuracy. Lee and Nieman (2003, p.228) state that discrepancies in calculated and measured body composition analysis could be ascribable to errors in measurements or possible electrolyte imbalances affecting BEI readings. BEI is considered an accurate measure of body composition (Hammond, 2004, p.428). Based on the discrepancies observed, BEI was considered the more accurate measuring instrument for body composition in this study. Despite the possibility of researcher measuring error, and the difficulty in using calipers in overweight and obese patients, calipers were used in this study to possibly confirm results found by means of BEI. When skin fold measurements are correctly done, they provide estimates of body composition that correlate well with those derived from hydrostatic weighing, the most widely used laboratory method used for determining body composition (Lee and Nieman, 2003, p.185).

Kutynec and colleagues (1999, as referred to by McCallum, 2003), cite a study where patients did not gain weight during treatment, but changes in body composition were observed (McCallum, 2003, p.29). Cohn et al. (1982) confirm these findings despite no change in body weight, cancer patients presented with an increased BF% when receiving nutritional intervention. The same tendencies were observed in the present study. No statistically significant changes in actual weight were found, but the E-group presented with a statistically significant increase in BF%, and the C-group with a statistically significant decrease in BF%. The difference in BF% between the E- and C-groups in the present study could

possibly be explained by the significantly higher intake of energy and fat by the E-group for the duration of the study.

Comparing the results of LM% and MAMA calculations, discrepancies were found regarding readings for the C-group. MAMA calculations for the C-group showed a decrease in LM, while LM% showed an increase for the same period. Lee and Nieman (2003, p.228) describe this phenomenon, namely that MAMA overestimates the amount of LM due to several measurements that could be sources of error, as common. As BEI are considered the more accurate measure of body composition (Hammond, 2004, p.428), LM% measured with BEI was also considered the more accurate measure of LM in this study.

Studies on the dynamics of protein metabolism in humans have established that muscle tissue degradation in the entire body is elevated in patients with various types of cancer (Nebeling, 2000, p.57). Although typical weight gain in healthy individuals is characterized by a gain in lean tissue as well as adipose tissue, all clinical studies on cancer patients that have measured body composition change, have consistently found either no gains in lean tissue mass or actual losses in lean tissue mass as weight and adipose tissue increase (Rock & Denmark-Wahnefried, 2002). This phenomenon has been confirmed by the present study, where the E-group recorded a significant loss in LM% and increase in BF%. The findings of the present study are, however, in contrast with a study by Bozzetti et al. (1998), that described unchanged levels of LM% despite the administration of enteral nutrition support to a group of cancer patients receiving chemotherapy, while patients not receiving enteral nutrition recorded a decrease in total LM%. The significant loss of LM% in the E-group in the present study could probably be ascribed to changes in protein metabolism and increased protein needs of the body. Decreases in lean body mass during treatment may be a factor in post-treatment weight gain (McCallum, 2003, p.29).

Patients in the present study tended to present with an increased BMI and a statistically significant increased BF%, together with a statistically significant decrease in LM%. From the results of the present study and current literature, it seems that breast cancer patients tend not to show significant changes in body weight with dietary interventions; their BF% may increase, while, according to the present study, their LM% may decrease. The effect of diet in this small study seems to show a tendency to contribute to the maintenance of body weight, while BF% may increase and LM% may decrease.

5.5 EFFECT OF DIET INTERVENTION PROGRAMME ON QUALITY OF LIFE

Performance status and the Rotterdam Quality of Life Survey were used to determine patients' quality of life. No statistically significant changes were noted in either the E- or C-group's performance status scoring in this study. With a statistically significant improvement in serum albumin levels, an improvement in the E-group's quality of life scores was expected, seeing that serum albumin levels affect symptoms such as tiredness and weakness. Performance status is mainly determined by the researcher's perception of the level of physical activity and tiredness of the patient. Altogether 83% of patients in the E-group had a lowered performance status, from the baseline visit to end of treatment, compared to a 100% lowered performance status scoring for the C-group during the same period.

Using the Rotterdam quality of life measurement, which represents the patient's perception of her quality of life, it was found that the E-group had a significantly improved quality of life scoring at the end of the diet intervention compared to that of the C-group for the same period. The Rotterdam questionnaire measures

quality of life aspects such as irritability, worrying, painful muscle, depressive mood, nausea, to name but a few. No other studies could be found that specified the use of the Rotterdam Questionnaire as a tool to determine the effect of dietary intervention on patients' quality of life. The findings from the present study are, however, consistent with the three months' dietary and supplement intervention study conducted by Ravasco et al. (2005) on colorectal cancer patients using an unidentified quality of life questionnaire. Ravasco et al. (2005) reported a proportional improvement in quality of life scores for both groups in their study, receiving either dietary or supplement treatment. The Rotterdam Quality of Life Survey is frequently used as a tool among oncology patients. However, for the purpose of the study, it should be noted that of the 30 questions posed, only 16% were related to nutrition and the ability to eat. Dietary change would require a longer implementation period to have a possible positive effect on a patient's perception of her quality of life.

The Performance status scale and Rotterdam Quality of Life Survey are both quality of life measures, but determine completely different aspects of quality of life. Both the E-and C-groups showed a drop in performance status scoring, without, however, a statistically significant difference. The Rotterdam Quality of Life Survey showed a statistically significant improvement in patients' perceptions of their quality of life, in the E-group, compared to those of the C-group. It appears that the effect of diet in this study has shown a significant improvement in the E–group regarding quality of life measures, which is in line with other studies, where an improvement in quality of life has been reported in cancer patients after dietary intervention.

CHAPTER 6

CONCLUSIONS AND RECOMMENDATIONS

Current literature is not clear about the specific role and benefit of nutrition in breast cancer treatment (Rock & Denmark-Wahnefried, 2002). The role of specific dietary factors in breast cancer causation has not been completely resolved (Willett, 2001). Epidemiological data and prospective studies do not support each other's findings.

6.1 CONCLUSIONS

From this study, it would appear that an OEIP diet intervention programme does not have a significant effect on most measured anthropometrical and quality of life measures.

The nutritional intake of the E-group was statistically significantly better (median protein 1.04 g/kg; energy 6722 kJ/day) than the C-group (median protein 0.72 g/kg; energy 4790 kJ/day) for the duration of the study, including all other macro- and micronutrient intake. Even though non-nutrition related factors also affect serum albumin concentrations during chronic disease (Carlson, 2004, p.440), implementing an OEIP diet treatment had a significant positive outcome on the serum albumin concentrations of the E-group, ensuring that their chemotherapy cycles did not have to be postponed because of lowered serum albumin concentrations. From the findings of the present study, it may therefore be concluded that an OEIP dietary intervention could possibly be successful in

improving serum albumin concentrations of breast cancer patients during treatment.

Regardless of a nutritional intake more that 67% of the RDA for healthy individuals, no statistically significant weight or BMI changes could be established during the three months' treatment period, which is in line with research conducted by Willett (2001). The clinical adequacy of the E-group's nutritional intake is still a matter of concern. The problem of underreporting dietary intake data by patients for a three month period, could affect the accuracy of the reported intakes. Dietary intake data was also compared to RDA/AI for healthy individuals seeing that no specialized guidelines are available for breast cancer patients during chemotherapy treatment. The importance of limiting energy intake to prevent weight gain in overweight and obese patients, to not further increase breast cancer risk is also important. Breast cancer patients receiving chemotherapy seem to maintain or show slight increases in weight and BMI during treatment. It seems that dietary intake is not the only weight contributing factor involved in breast cancer treatment, seeing that the E-group in the present study recorded a slight, but non significant weight loss during the three month treatment time, despite optimal energy and increased protein intake, while the C-group showed a non significant slight increase in body weight despite their statistically significantly lower energy and protein intake.

No significant changes were found in MUAC, TSF, MAFA or MAMA between the two groups after implementing a high-energy, high-protein dietary intervention programme. The measurements in respect of MUAC, TSF, MAFA or MAMA were used to establish tendencies only, but BF% and LM% were used as the more reliable results for the present study.

The E-group showed a significant increase in BF%, compared to a significant decrease in BF% for the C-group. From this study, one can conclude that the

optimal energy, higher fat intake could have been a contributing factor in increasing the E-group's BF%. McCallum (2003) confirms this phenomenon as common in breast cancer treatment. The OEIP dietary intervention did, however, not have an effect on the patients' LM%. The E-group showed a statistically significant reduced LM%, compared to the C-group's increased LM%. Although the protein intake of the E-group was sufficient to improve serum albumin concentrations, it did not prevent muscle wasting. Changes in the protein metabolism and the increased protein needs of the body could explain the changes in LM%. Another factor that could have contributed to the change in LM% could have been the disease itself.

The dietary intervention programme had no significant effect on the performance status scoring. At the end of treatment, the perceptions of patients in the E-group regarding quality of life, as measured by the Rotterdam Quality of Life Survey, were significantly improved. The OEIP dietary intervention programme appeared to have a positive effect on the patients' perceptions of quality of life. The small sample size the short intervention period could have had an effect on the changes in quality of life measures.

6.2 RECOMMENDATIONS

- Breast cancer patients receiving chemotherapy treatment should aim to achieve an optimal nutritional intake without increasing their body weight if they are already overweight or obese.
- Breast cancer patients should use a daily nutritional supplement during chemotherapy treatment, to achieve adequate, individualized nutritional intake, only if their nutritional needs are not fully met by their food intake. Their total daily energy intake should however be monitored closely when

adding a nutritional supplement to avoid weight gain in the overweight and obese patients.

- An OEIP dietary intervention with an energy intake to maintain an ideal body weight and a protein intake of 1 to 1.5 g/kg per day could be used to successfully increase serum albumin concentrations of breast cancer patients during treatment, without causing weight gain.
- The Rotterdam Quality of Life Survey showed an improved quality of life for the E-group at the end of treatment as compared to the C-group. It is recommended that nutritional intervention be introduced earlier and continued for a period longer than three months to determine the true effect of such dietary intervention programme. It is also recommended that the Rotterdam Quality of Life Survey be divided into nutrition and non-nutrition related questions to determine if the dietary treatment affected any measured part of quality of life.
- It is recommended that the study be repeated with a larger sample size, to produce more decisive data and more definite results. By increasing the sample size, tendencies established in the present study could possibly be confirmed and better explained.
- It is recommended the individual effects of Docetaxel, CMF and CAF be determined on serum albumin concentrations of breast cancer patients receiving chemotherapy.
- From the present study, it is clear that more detailed information is needed in regard to the long-term effect of an OEIP diet treatment on the serum albumin concentrations, anthropometrical status and quality of life measures of breast cancer patients receiving chemotherapy. Cancer patients might benefit from intensive ongoing personal nutritional monitoring and counselling, but this field needs more detailed and intensive investigation.

Although the study group was small, this study can be regarded as unique in that it demonstrated the possible positive effect of an optimal energy (calculated according to the patients' increased requirements) increased protein (1.5 g/kg/day) dietary intervention programme on the serum albumin concentrations of breast cancer patients receiving chemotherapy. Nutritional intake can be significantly improved to adequate levels, by using a nutritional supplemental shake. Furthermore, the study revealed that improved nutritional intake through OEIP dietary intervention could possibly contribute to the maintenance of body weight, increased BF% and improved Rotterdam quality of life measures. LM% unfortunately decreased, while no significant change was recorded in performance status. Because of the limiting factors in the study, the results only show tendencies. Further long term OEIP dietary intervention is needed to determine possible long term benefits.

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ANNEXURE A
CONCENT LETTER FROM ST. GEORGE'S HOSPITAL

ST GEORGE'S HOSPITAL

St George's Hospital
40 Park Drive
Port Elizabeth 6001
PO Box 12051
Moffat Place 6002

Telephone 041 392-611
Accounts 041 501-180
Facsimile 041 392-600

Etiekkomitee van die Fakulteit Geneeskunde UV 28/8/03

Aangaande: Onkologie Navorsingsprojek te St.George's Hospitaal
ETOVS NR 148/03

Hiermee gee ek toestemming vir die uitvoering van die navorsingsprojek (IMPAK VAN 'N DIEETBEHANDELINGSPROGRAM OP DIE SERUMALBUMIENKONSENTRASIES, ANTROPOMETRIESE STATUS EN LEWENSKWALITEIT VAN PASIëNTE MET MAMMAKARSINOOM TYDENS CHEMOTERAPIE BEHANDELING), beplan deur René Smalberger IN DIE Onkologie eenheid van St. George's Hospitaal, Port Elizabeth.

Vriendelike Groete

Mnr. Beau Barfknecht (Hospitaal Bestuurder)

ANNEXURE B
INFORMED CONCENT FORM

INGELIGTE TOESTEMMING

Hiermee verklaar ek .....
dat ek my toestemming tot deelname aan die projek soos aan my verduidelik verleen.

Ek is ten volle ingelig deur die dieetkundige René Smalberger aangaande die waarskynlike voordelige, asook die waarskynlike nadelige gevolge wat uit die behandeling vir my kan voortspruit. Die behandeling sal bestaan uit 'n dieetbehandelingsprogram wat met hoë proteïen, hoë energie supplemente, 'n drie weeklikse ondersoek om liggaamsmates te bepaal sowel as 'n bloedtoets vir die bepaling van serumalbumienkonsentrasies. Die totale behandelingsperiode sal drie maande wees. Ek is ten volle bewus dat ek lukraak tot 'n eksperimentele of kontrolegroep ingedeel kan word, maar dat daar tot dusver geen mediese bewyse is dat die dieetbehandeling wel 'n betekenisvolle voordeel vir my sal inhou nie. Die behandeling sal uitgevoer word deur René Smalberger, of 'n ander gekwalifiseerde dieetkundige van haar praktyk.

My toestemming word uit vrye wil verleen en ek besef ook dat ek my toestemming te eniger tyd kan herroep.

GETEKEN (Pasiënt)

....

.....

(Persoon wat die behandeling gaan uitvoer)

INFORMED CONCENT

I,……agree to take part in the study as explained to me.

I was fully informed by the dietitian, René Smalberger regarding the possible advantages and disadvantages resulting from this proposed study. The treatment will entail a diet treatment of high protein, high energy supplements, a three weekly consultation to perform several body measurements and blood calculation to determine serum albumin concentrations. The duration of the study will be three months. I am fully aware that I will randomly be assigned to an experimental or control group, and that there is no evidence, thus far, that the proposed treatment will in fact be better. The treatment will be performed by René Smalberger, or another qualified dietitian from her practice.

I give my concent out of free will, and I am aware that I can withdraw from the study at any time.

SIGNED (Patient)

……. …….

…….

(Person performing the treatment)

ANNEXURE C
DATA RECORD FORM

VOEDINGSTATUSEVALUERING

		1-3
Pasiënt nommer (persoonlik):		
Respondent nommer:		4-5
Naam en Van:		
Adres:		
		D D M M Y Y
Geboortedatum:		6-11
Ouderdom:		12-13
Diagnose:		14

1. Borskanker met Been Metastate
2. Borskanker met Long Metastase
3. Borskanker met Lewer Metastase
4. Borskanker met Brein Metastase
5. Borskanker met Vel Metastase
6. Ander

Lengte:	cm	15-19
Skeletgrootte:	Gemiddeld:	20
	Meting 1:	
	Meting 2:	

1. Klein Liggaamsbou
2. Medium liggaamsbou
3. Groot Liggaamsbou

		D D M M Y Y
Basislyn Datum:		21 - 26
Massa:	kg	27-31
"Performance Status"		32
Bo-armomtrek	cm	33-37
Trisepsvelvou	Gemiddeld: cm	38-42

Rotterdam Vraelys Evaluering | | 43-44

S.Albumien | | 45-48
Liggaamsvetarea (%) | | 49-52
Liggaamspierarea (%) | | 53-56

Sessie Twee:

Massa: ..... kg | | 57-61
"Performance Status" ..... | | 62

Bo-armomtrek ..... cm | | 63-67
Trisepsvelvou Gemiddeld: ..... cm | | 68-72

Rotterdam Vraelys Evaluering | | 73-74

S.Albumien | | 75-78
Liggaamsvetarea (%) | | 1-4
Liggaamspierarea (%) | | 5-8

Sessie Drie:

Massa: ..... kg | | 9-13
"Performance Status" ..... | | 14

Bo-armomtrek ..... cm | | 15-19
Trisepsvelvou Gemiddeld: ..... cm | | 20-24

Rotterdam Vraelys Evaluering | | 25-26

S.Albumien | | 27-30
Liggaamsvetarea (%) | | 31-34
Liggaamspierarea (%) | | 35-38

Sessie Vier:

Massa:	kg	39-43
"Performance Status"		44
Bo-armomtrek	cm	45-49
Trisepsvelvou	Gemiddeld: cm	50-54
Rotterdam Vraelys Evaluering		55-56
S.Albumien		57-60
Liggaamsvetarea (%)		61-64
Liggaamspierarea (%)		65-68

Sessie Vyf:

Massa:	kg	69-73
"Performance Status"		74
Bo-armomtrek	cm	75-79
Trisepsvelvou	Gemiddeld: cm	1-5
Rotterdam Vraelys Evaluering		6-7
S.Albumien		8-11
Liggaamsvetarea (%)		12-15
Liggaamspierarea (%)		16-19

ANNEXURE D
ROTTERDAM QUALITY OF LIFE QUESTIONNAIRE

NAME : ……. FILE NO : ……

D.O.B.: ……. DATE : …….

DIAGNOSIS : ……..

In this questionnaire you will be asked about your symptoms. Read each item and place a tick in the circle opposite the reply which comes closest to how you have been feeling during the past week.

1. Lack of appetite

Not at all □
A little □
Quite a lot □
Very much □

2. Irritability

Not at all □
A little □
Quite a lot □
Very much □

3. Tiredness

Not at all □
A little □
Quite a lot □
Very much □

4. Worrying

Not at all □
A little □
Quite a lot □
Very much □

5. **Sore Muscles**

Not at all □
A little □
Quite a lot □
Very much □

6. **Depressed mood**

Not at all □
A little □
Quite a lot □
Very much □

7. Lack of energy

Not at all □
A little □
Quite a lot □
Very much □

8. Low back pain

Not at all □
A little □
Quite a lot □
Very much □

9. Nervousness

Not at all □
A little □
Quite a lot □
Very much □

10. Nausea

Not at all □
A little □
Quite a lot □
Very much □

11. Desperate feelings about the future

Not at all □
A little □
Quite a lot □
Very much □

12. Difficulty with sleeping

Not at all □
A little □
Quite a lot □
Very much □

13. Headaches

Not at all □
A little □
Quite a lot □
Very much □

14. Vomiting

Not at all □
A little □
Quite a lot □
Very much □

15. Dizziness

Not at all □
A little □
Quite a lot □
Very much □

16. Lack of sexual interest

Not at all □
A little □
Quite a lot □
Very much □

17. Feel tense

Not at all □
A little □
Quite a lot □
Very much □

18. Stomach pains

Not at all □
A little □
Quite a lot □
Very much □

19. Anxiety

Not at all □
A little □
Quite a lot □
Very much □

20. Constipation

Not at all □
A little □
Quite a lot □
Very much □

21. Diarrhoea

Not at all □
A little □
Quite a lot □
Very much □

22. Heartburn/ repeating

Not at all □
A little □
Quite a lot □
Very much □

23. Shivering

Not at all □
A little □
Quite a lot □
Very much □

24. Tingling hands

Not at all □
A little □
Quite a lot □
Very much □

25. Difficulty concentrating

Not at all □
A little □
Quite a lot □
Very much □

26. Sore mouth/swallowing

Not at all □
A little □
Quite a lot □
Very much □

27. Loss of Hair

Not at all □
A little □
Quite a lot □
Very much □

28. Burning/sore eyes

Not at all □
A little □
Quite a lot □
Very much □

29. Shortness of breath

Not at all □
A little □
Quite a lot □
Very much □

30. Dry mouth

Not at all □
A little □
Quite a lot □
Very much □

ANNEXURE E
FOOD DIARY FORM

Respondent Nommer: | | | 1-2

	D	D	M	M	Y	Y	
Datum:							3-8

Time **Tyd**	**Tipe of Food and additives** **Tipe voedsel met byvoegings**	**Quantity Consumed (ml)** **Hoeveelheid ingeneem (ml)**	(Kode)				(Hoeveelheid)				
											9-16
											17-24
											25-32
											33-40
											41-48
											49-56
											57-64
											65-72
											73-80
											1-8
											9-16
											17-24
											25-32
											33-40
											41-48
											49-56
											57-64
											65-72
											73-80
											1-8
											9-16
											17-24
											25-32
											33-40
											41-48
											49-56
											57-64
											65-72
											73-80
											1-8

ANNEXURE F
NUTRI-MIL NUTRITIONAL SUPPLEMENT PROFILE:

		Per 100 g	Per 250 ml (55 g)	% RDA** per 250 ml (Adults & children > 10 years)
Protein	g	18.4	10.1	
Carbohydrates	g	57.4	31.5	
Fat	g	17	9.4	
Energy	kJ	1941	1068	
Vitamin A	mcg RE	363	199.5	20
Vitamin D	mcg	1.8	0.99	20
Vitamin E	mg TE	3.6	2	20
Ascorbic acid	mg	21.8	12	20
Vitamin B1	mg	0.51	0.3	20
Vitamin B2	mg	0.58	0.3	20
Nicotinamide	mg	6.55	3.6	20
Vitamin B6	mg	0.73	0.4	20
Folic acid	mcg	72.73	40	20
Vitamin B12	mcg	0.45	0.25	25
Biotin	mcg	36.36	20	20
Pantothenic acid	mg	2.18	1.2	20
Choline	mg	140	77	*
Calcium	mg	290	159.5	20
Phosphorus	mg	290	159.5	20
Sulphur	mg	50	27.5	*
Iron	mg	5.09	2.8	20
Magnesium	mg	109	60	20
Zinc	mg	5.45	3	21.5
Iodine	mcg	55	30.25	10
Sodium	mg	408	224.4	*
Chloride	mg	633	348.2	*
Potassium	mg	620	341	*
Manganese	mg	1.3	0.7	14.2
Copper	mg	0.55	0.3	*
Selenium	mcg	21	11.6	16.5
Chromium	mcg	21	11.6	11.6
Molybdenum	mcg	40	22	22
Isoflavones	mg	32	17.6	*

** Recommended dietary allowance for persons 10 years and older, Foodstuffs, Cosmetics and Disinfectant Act,
28-Nov-97
RDA's Food and Nutrition Board, National Academy of Sciences, 1989.
** No RDA available*

ANNEXURE G
EXAMPLE OF E-GROUP INDIVIDUALIZED EATING PLAN

This is a personalized eating plan for _____ based on personal body compositions.

*CHOOSE **ONE** FOOD ITEM FOR EACH **

BREAKFAST:

*

_____cup Cooked Oats or
_____cup All Bran or
_____cup Cooked Porridge or
_____Weetbix or
_____Slice Brown Bread or
_____Cup Corn Flakes.

*

_____cup Low fat Milk or
_____cup Low fat Yoghurt or
_____cup Cultured Milk

*

_____g Low Fat Cheese or
_____T.spoon Peanut Butter or
_____T.spoon Cheese Spread or
_____Boiled Egg

MID-MORNING SNACK:

*

250 ml Nutri-mil Supplement

*

_____Fresh Fruit or
_____cup Mixed Fruit Salad or
_____ml Fresh Fruit juice

LUNCH:

*

_____Fresh Fruit or
_____cup Fruit Salad or
_____ml Fresh Fruit juice

*

_____Slices Brown Bread or
_____Provitas or
_____Crackers or
_____Rusks or
_____Slice bread and 1 cup soup or
_____Slice bread and 1 Fresh Fruit or
_____Cups Pop Corn or
_____Packet 2 Minute Noodles or
_____g Boiled Potato

*

_____g Low Fat Cheese or
_____T.spoon Peanut Butter or
_____T.spoon Cheese Spread or
_____g Chicken or Fish or
_____Boiled Egg

MID-AFTERNOON SNACK:

*

250 ml Nutri-mil Supplement

*

_____Fresh Fruit or
_____cup Fruit Salad or
_____ml Fresh Fruit juice

SUPPER:

*

_____Cup Cooked Rice or
_____Cup Boiled Potato or
_____Cup Cooked Pasta or
_____Cup Cooked Corn or
_____Cup Cooked Sweet Potato or
_____Cup Baked Beans or
_____Cup Cooked Beans / Lentils or
_____Slices Bread or
_____Bread Roll or
_____Pita Bread

*

_____g Chicken (without the skin) or
_____g Lean Red Meat or Ostrich or
_____g Fish or shellfish or
_____g Pork (no fat) or
_____g Chicken and 30g Cheese or
_____Grilled Fish fingers or
_____Grilled Fish Cakes

*

½ Cup Carrots or
½ Cup Peas or
½ Cup Beetroot or
½ Cup Onions or
½ Cup Mixed Vegetables or
½ Cup Butternut

LATE NIGHT SNACK:

*

_____Fresh Fruit or
_____Marie Biscuits or
_____Hard Boiled Sweets or
_____Cup Fruit Salad or
_____ml Fruit Juice or
_____Scoop Ice Cream

EXTRAS PER DAY:

*

_____Cup Low fat Milk

*

_____t.spoon Margarine or
_____t.spoon Butter or
_____t.spoon Oil or
_____t.spoon Mayonnaise or
_____t.spoon Salad Dressing or
_____Avocado or
_____Olives or
_____Nuts

*

_____teaspoons Sugar or
_____teaspoons Honey or
_____teaspoons Jam or
_____Hard Boiled Sweets

*

_____Single tots Whiskey or
_____ml dry wine or
_____ml Beer

USE FREELY:

Broccoli	Cauliflower
Cabbage	Celery
Tomatoes	Cucumber
Lettuce	Brussels Sprouts
Baby Marrows	Green Peppers
Mushrooms	Patty Pans
Gems	Green Beans
Spinach	Brinjals

Marmite	Bovril
Fish Paste	Naturlite Fruit Spread

Tea

Herbs and Spices

SUMMARY

Breast cancer patients receiving chemotherapy at ECOC, often present with lowered serum albumin concentrations, so much so that the lowered serum albumin concentrations first has to be treated before the next cycle of chemotherapy can be administered. The delay in chemotherapy treatment had financial, medical and emotional effects on the patients.

The objective of this study was to determine the effect of an optimal energy increased protein (OEIP) dietary treatment on serum albumin concentrations, anthropometrical status and quality of life of breast cancer patients receiving chemotherapy. In a clinical trial, 27 female breast cancer patients were randomised to an experimental group (E) (n=13), receiving an individualized OEIP diet consisting of food and a nutritional supplement, or a control group (C) (n=14), receiving no dietary intervention. Baseline and three-weekly visits involved determining serum albumin concentrations; anthropometrical assessment, including body weight; BMI, MUAC, TSF, MAFA, MAMA, BF% and LM%; and the completion of a quality of life questionnaire. Both groups kept a food diary for the duration of the study.

Median ages of the E-and C-groups were 52.62 and 51.19 years respectively, ranging from 29 to 59 years. Statistical analysis included, median and percentiles for continuous data, and frequencies and percentages for categorical data, with 95% CI for median differences. Due to the small sample size, non-parametric statistics were used to compare results.

By taking a daily nutritional supplement, the E-group was able to consume a significantly better amount of all macro- and micronutrients. The C-group showed a median drop of 3 g/dL in serum albumin concentrations with a median end value of 36.5 g/dL, while the E-group showed a statistically significant [2; 6]

median increase of 1.5 g/dL, with a median end value of 39 g/dL, suggesting that the dietary intervention had been successful in improving serum albumin concentrations over the treatment period.

No statistically significant changes were noted in either the E- or C- group's performance status scoring. The Rotterdam Quality of Life Survey found the E-group had a significant improved quality of life scoring during Visits 5:B, compared to the C-group for the same period. Other studies have also shown an improvement in quality of life measurement after the implementation of a dietary intervention programme in cancer patients.

An optimal energy diet, sufficient to maintain the patient's ideal body weight and not actual body weight, with a protein intake of 1.04 g/kg/day was sufficient to significantly improve serum albumin concentrations, to such an extent, that chemotherapy cycles did not have to be postponed. Regardless of nutritional intake, no statistically significant changes were found in weight, BMI, MUAC, TSF, MAFA or MAMA. The E-group showed a significant increase in BF% and a decrease in LM% for the duration of the study, compared to the C-group. The increase in BF% could possibly be explained by the high-energy, increased fat intake of the E-group. Changes in protein metabolism and the increased protein needs of the body could possibly explain the changes in LM%. From this study it may be concluded that an OEIP diet is not effective in preventing LM wasting.

An OEIP (1-1.5 g/kg/day) dietary intervention, is therefore recommended for breast cancer patients receiving chemotherapy. Nutritional intervention should commence at an earlier point to determine the effect of such intervention on patients' quality of life. It is recommended that the study be repeated with a larger sample size, to confirm tendencies found in the present study and to determine the long-term effect of an OEIP diet intervention on serum albumin

concentrations, the anthropometrical status, and the quality of life of breast cancer patients receiving chemotherapy.

KEY TERMS

Cancer - General term frequently used to indicate any of various types of malignant neoplasms, most of which invade surrounding tissues, may metastasize to several sites, and are likely to recur after attempt removal and to cause death of a patient unless adequately treated.

Chemotherapy - Treatment of disease by means of chemical substance or drugs; usually used in reference to cancer treatment.

Serum albumin - Serum albumin concentrations refer to concentrations at the baseline visit, at the three-weekly visits, as well as at the end of the treatment period. The normal reference range for serum albumin of 35 to 50 g/dL was used, and a value below 35g/dL was considered inadequate.

Anthropometrical status - Anthropometrical status included current weight, height, mid-upper arm circumference (MUAC), and triceps skin fold (TSF) measurements. Anthropometrical status refers to calculated BMI, mid-arm fat area (MAFA), mid-arm muscle area (MAMA) and body composition measurements.

Quality of Life - Quality of life refers to performance status, as well as the Rotterdam Quality of Life Survey.

Performance status - Performance status refers to the health professional's interpretation and classification of the patient, based on the effects of the disease and the level of daily functioning.

Rotterdam quality of life survey - The Rotterdam Quality of Life Survey includes changes in physical as well as psychological symptoms. The Rotterdam Quality of Life Survey reflects the patient's perception of her own quality of life.

Dietary intake - Dietary intake refers to habitual intake at baseline, as well as the three-months' duration of the study.

Nutrition – The study of the food and liquid requirements for normal physiologic function, including need, maintenance, growth, activity factor and stressors.

Diet intervention programme – The diet intervention programme refers to an individualized diet, with a optimal energy, increased protein content of 1.5g protein/kg bodyweight per day.

OPSOMMING

Borskankerpasiënte wat chemoterapie by ECOC ontvang, presenteer dikwels met verlaagde serumalbumienkonsentrasie, dermate dat die verlaagde serumalbumienkonsentrasie eers behandel moet word voordat die volgende siklus chemoterapie toegedien kan word, met 'n finansiële, mediese en emosionele uitwerking op die pasiënte.

Die doel van dié studie was om die uitwerking van 'n optimale energie, hoë-proteïen (OEIP) (1,5 g/kg) dieetbehandeling op die serumalbumienkonsentrasies, antropometriese status en lewenskwalitieit van borskankerpasiënte wat

chemoterapie ontvang, te bepaal. In ‘n kliniese ewekansigheidsproef, is 27 vroulike borskankerpasiënte ingedeel in ‘n eksperimentele groep (E) (n=13) wat ‘n geïndividualiseerde OEIP dieet, bestaande uit voedsel en ‘n voedingsaanvulling ontvang het, of in ‘n kontrolegroep (K) (n=14), met geen dieetintervensie nie. Die basislyn- en drieweeklikse besoeke het die volgende behels: die bepaling van serumalbumienkonsentrasies; antropometriese evaluering, insluitende massa, lengte, ; liggaamsmassa indeks (LMI); bo-arm-omtrek (BAO); triseps-velvou (TSV); boarm-vetarea (BAVA); bo-armspierarea (BASA); persentasie liggaamsvet (LV%); en persentasie liggaamspiere (LS%); asook die invul van ‘n lewenskwaliteitsvraelys. Beide groepe het ‘n voedseldagboek gehou vir die duur van die studie.

Die mediane ouderdom van die E- en die K-groep was onderskeidelik 52.62 en 51.19 jaar, en het van 29 tot 59 jaar gewissel. Statistiese ontleding het mediane en persentiele vir voortgesette data behels, en frekwensies en persentasies vir kategoriese data, met ’n vertrouens interval (VI) van 95% vir mediaanverskille. Weens die klein steekproefgrootte is nie-parametriese statistieke gebruik om resultate te vergelyk.

Pasiënte in die E-groep wat ‘n daaglikse voedingsaanvulling geneem het, het ’n statisties betekenisvolle verbeterde mikro- en makrovoedingstof inname getoon. ‘n Mediaandaling van 3 g/dL in serumalbumienkonsentrasies is vir die K-groep aangeteken, met ‘n mediaaneindwaarde van 36.5 g/dL, terwyl die E-groep ’n statisties betekenisvolle mediaanstyging [2; 6] van 1.5 g/dL getoon het, met ‘n mediaan-eindwaarde van 39 g/dL, wat daarop dui dat die dieetintervensie daarin geslaag het om die serumalbumienkonsentrasies oor die behandelingstydperk te verbeter.

Geen statisties beduidende verskille is in óf die E- óf die K-groep se prestasiestatus-puntetelling bemerk nie. By gebruik van die Rotterdam

Lewenskwaliteit-opname, is daar gevind dat die E-groep ‘n aanmerkbaar verbeterde lewenskwaliteit-puntetelling gedurende Besoeke 5:B aangeteken het, vergeleke met die K-groep vir dieselfde tydperk. Ander studies het ook ‘n verbetering in die gemete lewenskwaliteit getoon na die implementering van ’n dieetintervensieprogram.

’n Optimale energie dieet, wat genoegname energie voorsien om die pasiënt se ideale massa in stand te hou en nie haar werklike massa nie, met ‘n proteïeninname van 1,04 g/kg/dag was genoeg om serumalbumienkonsentrasies aansienlik te verbeter, in so ‘n mate dat dit nie nodig was om chemoterapiesiklusse uit te stel nie. Ongeag die voedingsinname, is geen statisties beduidende verskille in gewig, LMI, BAO, TSV, BAVA of BASA aangeteken nie. Die E-groep het ’n betekenisvolle toename in BF% en verlaging in LS% vir die duur van die studie getoon, vergeleke met die K-groep. Die toename in LV% kan moontlik deur die hoë energie- en verhoogde vetinname van die E-groep verduidelik word. Veranderinge in proteïenmetabolisme en die verhoogde proteïenbehoeftes van die liggaam kan moontlik die veranderings in LS% verduidelik. Uit dié studie kan die gevolgtrekking gemaak word dat ’n OEIP dieet nie LS-uittering verhoed nie.

’n OEIP (1-1.5 g/kg/dag) dieetintervensie, word aanbeveel vir borskankerpasiënte wat chemoterapie ontvang. Voedingsintervensie moet op ‘n vroeër stadium begin word om die uitwerking van sodanige intervensie op lewenskwaliteit te bepaal. Daar word aanbeveel dat die studie met ‘n groter steekproefgrootte herhaal word, om tendense wat in die huidige studie aangetref is, te bevestig en om die langtermynuitwerking van ’n OEIP dieet op serumalbumienkonsentrasies te bepaal, asook op die antropometriese status en die lewensgehalte van borskankerpasiënte wat chemoterapie ontvang.

SLEUTELTERME

Kanker- ‘n Term wat algemeen gebruik word om ‘n verskeidenheid maligniteite te beskryf, waarvan meeste die omringende weefsel binnedring, metastase mag voorkom, en selfs die dood van die pasiënt veroorsaak.

Chemotherapy – Die behandeling van ‘n maligne toestand deur middel van ‘n chemiese substans of middel.

Serumalbumien - Serumsalbumienkonsentrasie verwys na die konsentrasie van serumalbumien tydens basislyn, drieweeklikse besoeke en aan die einde van die studie periode. Normaalwaardes wissel van 35 tot 50 g/dL, en ‘n waarde onder 35g/dL was as ontoereikend beskou.

Antropometriese status - Antropometriese status verwys na massa, lengte, liggaamsmassa indeks, bo-arm-omtrek, triseps-velvou, boarm-vetarea, bo-armspierarea, persentasie liggaamsvet en persentasie liggaamspiere.

Lewenskwaliteit – Lewenskwaliteit verwys na prestasiestatus, sowel as die Rotterdam Lewenskwaliteit vraelys.

Prestasiestatus - Prestasiestatus verwys na die gesondheidswerker se persepsie en klassifikasie van die pasiënt, met betrekking tot die effek van die siektetoestand op die liggaam se funksionering.

Rotterdam Lewenskwaliteit Vraelys - Die Rotterdam Lewenskwaliteit Vraelys behels die pasiënt se persepsie aangaande veranderinge in fisiese en psigologiese simptome.

Dieet inname - Dieet inname verwys na die gewoontlike diet inname tydens die basislyn besoek, sowel as die drie maande duur van die studie.

Voeding – Die studie van voedsel en vloeistof behoeftes vir normale fisiologies funksionering met inagneming van instandhouding, groei, aktiwiteit- en stresfaktore.

Dieet intervensie program – Die dieet intervensie program verwys na ‘n geïndividualiseerde diet, met ’n optimale energie en ’n verhoogde proteïen inhoud, van 1.5g proteïen/kg liggaamsmassa per dag.