



## ➤ Product Review ◀

February 2020 #334

### ***NUTRITIONAL SUPPORT FOR CANCER PATIENTS – PART I***

#### ***INTRODUCTION***

As we all know, over the years there have been few subjects that have generated more controversy and criticism in the clinical nutrition community than the relationship between nutrition and cancer, whether the discussion revolves around optimal diets and/or nutritional supplements. Complicating the issue even more are the two very polarizing subsections of the controversy – prevention and treatment. While hundreds, if not thousands, of papers have been written about diets and dietary substances that potentially demonstrate efficacy in cancer prevention, consensus is not even close to universal. Furthermore, the same can be stated about supplements and cancer prevention. Want to turn up the heat even more? Consider the topic of using diet and supplements to treat cancer. While there is certainly no shortage of anecdotal reports suggesting that certain cancer patients were “cured” by a particular diet and a specific supplemental protocol, the research I have seen on using diet and supplements as stand-alone, predictable, highly efficacious treatments for cancer has demonstrated uniformly poor outcomes from both a quality of life and mortality standpoint.

With the above in mind, why do I want to write about nutrition and cancer now? What can I offer that has not been stated all too many times before? Very simply, it is my opinion that all the passionate, black and white, panacea or poison arguments and counter arguments that have been tossed about over the last 30-40 years on the subject of nutrition and cancer

have blinded all too many in both the clinical nutrition and allopathic medicine communities to another research-supported, common sense, middle ground approach to the subject. Even though diet and supplements have not convincingly demonstrated value as stand-alone preventive or treatment modalities, could it be that diet and supplements demonstrate outstanding, research supported value when used as a complementary adjunct to conventional medical cancer treatments? What you will be reading in this newsletter series is a review of two impressive, recently published papers that make it clear that many cancer patients who are not responding well to chemotherapeutic agents in terms of efficacy and/or quality of life will often see improvements with both when nutritional needs are addressed with diet, supplements, or both. In addition, as I review the various sections of these papers, I will be making recommendations, based on the research presented, how Moss Nutrition products can be used to assist your cancer patients as they face therapeutic and quality of life challenges.

#### ***THE IMPACT OF MALNUTRITION, WEIGHT LOSS, AND LOSS OF MUSCLE MASS ON SURVIVAL AND QUALITY OF LIFE IN CANCER PATIENTS***

As suggested by its title, “Effects of weight loss and sarcopenia on response to chemotherapy, quality of life, and survival” by Ryan et al (Ryan A et al. *Nutrition*, Vol. 67-68, November/December 2019) discusses why chemotherapy sometimes demonstrates suboptimal results from both a quality of life and mortality standpoint and what to do about it. First, the why. Ryan et al are emphatic that

the central issue is the grossly underappreciated state of malnutrition, weight loss, and accompanying loss of muscle mass (sarcopenia) that is of disturbingly high prevalence in cancer patients. In introducing this issue, the authors state the following:

**“It has frequently been shown that patients with cancer are one of the largest hospital patient groups with a prevalence for malnutrition. Weight loss is a frequent manifestation of malnutrition and is an important criterion in several malnutrition screening tools commonly used in clinical settings.”**

How common is weight loss among cancer patients?

**“Several large scale studies over the past 35 y have reported that involuntary weight loss affects 50% to 80% of patients with cancer with the degree of weight loss dependent on tumor site, and type and stage of disease.”**

Is there a relationship between weight loss and outcome? The authors state:

**“The prognostic effects of weight loss on overall survival (OS) has long been recognized, with recent data suggesting ongoing weight loss of >2.4% predicting survival, independent of disease site, stage, or performance score.”**

Furthermore, weight loss is significantly correlated with negative reactions to chemotherapeutic agents and loss of quality of life:

**“In addition to the adverse effects on survival, weight loss has been associated with severe chemotherapy-related toxicity and leads to a significant deterioration in patients’ performance status, psychological well-being, and overall quality of life (QoL).”**

Compounding the problem of weight loss is the grossly underappreciated, almost universal malnutrition that is seen with cancer patients:

**“Nutritional deterioration unfortunately has become an accepted part of the pathogenesis of cancer and its treatment.”**

Why is malnutrition so important and so challenging with cancer patients? One reason

is that it is not solely due to poor eating habits. Rather it is due both to poor eating habits and the unique, cancer-driven metabolism of cancer patients that creates a negative energy balance:

**“The form of malnutrition that occurs in malignancy is particularly challenging to address as it is not driven by simple starvation but occurs secondary to a negative energy balance caused by the detrimental combination of reduced oral intake and metabolic derangements unique to cancer.”**

More specifically why does malnutrition occur in cancer patients? Ryan et al point out:

**“Cancer-associated malnutrition can occur as a result of poor oral intake, mechanical or physiologic changes in the gut, side effects of treatment, or metabolic abnormalities caused by the tumor. Both the quantity and the quality of dietary intake can be significantly altered due to any one of a number of factors including dysphagia, nausea, changes in taste and smell, pain, early satiety, or fatigue.”**

However, beyond that, the cancer itself can play a powerful role in altering metabolism and promoting malnutrition:

**“Additionally, the presence of cancer in the body causes a variety of metabolic and endocrine changes (such as inflammation, anabolic resistance, proteolysis, lipolysis, and futile cycling) induced by the tumor and activated immune cells. Complex interactions between inflammation (proinflammatory cytokines), neurohormonal changes, and potential proteolytic and lipolytic factors produced by the host and the tumor, fuel weight loss and loss of lean mass.”**

**The impact of weight loss in cancer patients is largely a function of disturbances in body composition**

To truly understand why weight loss is so detrimental to survival and quality of life in cancer patients, it is important to understand exactly what is lost with “weight loss.” As you might expect, given all my writings and lectures on loss of muscle mass either as sarcopenia or cachexia, the key reason why weight loss has such a negative impact on

cancer patients is the fact that the weight loss, to a major extent, involves loss of muscle. Ryan et al point out:

**“Involuntary weight loss is a hallmark feature of cancer-associated malnutrition and can lead to cancer cachexia; a multifactorial syndrome characterized by ongoing loss of skeletal muscle mass (with or without loss of fat mass) that cannot be fully reversed by conventional nutritional support.”**

Before continuing, I would like to address the idea mentioned above about the role of nutritional support with patients suffering from cancer cachexia. Conventional medical thinking has long suggested that nutritional support is virtually worthless in terms of aiding cancer cachexia patients. As noted by Ryan et al above, this long held belief is incorrect. In fact, even though it is not a panacea, nutritional support can play a role in partial reversal. I have demonstrated this previously in my newsletters and lectures on **SarcoSelect**<sup>®</sup>. As I have pointed out, the basis for the formula for **SarcoSelect**<sup>®</sup> comes from the paper by Deutz et al (Deutz NE et al. Muscle protein synthesis in cancer patients can be stimulated with a specially formulated medical food, *Clin Nutr*, Vol. 30, No. 6, pp. 759-68, 2011) that demonstrated a unique macro/micronutrient formulation can stimulate muscle growth in advanced cancer patients.

Ryan et al continue their discussion on the nature of cancer cachexia and how incredibly prevalent it is in cancer patients:

**“Cachexia is characterized by a negative protein and energy balance driven by a variable combination of reduced food intake and abnormal metabolism. Studies dating back over the past 35 y have reported that moderate to severe weight loss is present in 30% to 70% of cancer patients.”**

If cancer cachexia is so prevalent, why is it not more acknowledged by many in the medical community and all too many in the clinical nutrition community? One reason is that many cancer patients are obese, making loss of

muscle mass less amenable to routine diagnosis by visual assessment alone:

**“Despite the fact that the majority of patients with involuntary weight loss at the time of diagnosis, in the era of obesity, patients may not appear malnourished and many in fact are well nourished according to international standards. Recent studies have reported that between 40% and 60% of patients with cancer are overweight or obese...even in the setting of metastatic disease.”**

Before continuing, I would like to comment on the first sentence in the above quote. As I have mentioned many times in past newsletters and lectures, a large body of published literature makes it clear that ailing patients, whether or not they have cancer, have unique nutritional requirements, mainly due to their equally unique metabolic imbalances discussed above. Given that international standards of nutrition are based on the nutritional needs of the general “normal” population, international standards of nutrition are totally inappropriate for determining the nutritional needs of the cachectic cancer patient.

The authors continue their discussion on obesity in cancer patients by pointing out that usual measurements of obesity are not effective in determining loss of muscle mass:

**“...the simple measure of BMI or percentage of weight loss does not capture abnormal body composition, including muscle mass. The most clinically relevant phenotypic feature of cancer cachexia is muscle loss and identifying those with low muscle mass can become a huge challenge in patients with overweight or obesity.”**

What is the specific impact of loss of muscle mass in cancer patients? Ryan et al state:

**“Low muscle mass is now known to be related to asthenia, fatigue, impaired physical function, increased chemotherapy toxicity, impaired quality of life, and reduced survival.”**

In addition, cancer treatment can accelerate the muscle loss that normally occurs with the presence of cancer:

**“Recent studies have shown that cancer, and its treatment, exacerbate muscle loss and that patients continually lose muscle mass while on treatment. Although healthy adults >40 y of age have been shown to lose muscle at a rate of 1% to 1.4% per year, patients with cancer have been shown to have a 24-fold higher rate of muscle loss than that observed in healthy aging adults.”**

Thus, as I hope you can see, many of the negative outcomes typically associated with malnutrition and weight loss in cancer patients are also a direct function of loss of muscle mass.

### **Does loss of muscle mass increase the risk of chemotherapy toxicity and decreased chemotherapy efficacy**

As we all know, chemotherapy carries with it many possible side effects and toxicities that sometimes limit optimal dosing, thus reducing chances for optimal chemotherapy outcomes. Could this chemotherapy toxicity that sometimes results in dose limitations be related to loss of muscle mass? Ryan et al comment:

**“Chemotherapy often can be associated with severe toxicity that can result in dose delays, dose reductions, and treatment termination, referred to as dose-limiting toxicities (DLTs).”**

Could this be related to sarcopenia (loss of muscle mass)?

**“To date, >40 studies have examined the relationship between sarcopenia and the prevalence of DLT in patients with cancer. The relationship between low lean mass and increased toxicity to chemotherapy has been shown to be true in both early- and late-stage disease regardless of cancer site and type of systemic chemotherapy (cytotoxic single agents, regimens, targeted agents, and immunotherapies).”**

What is the specific relationship between loss of muscle mass and chemotherapy toxicity? It has to do with the fact that low muscle mass can have an effect on metabolism of chemotherapy drugs:

**“Increased toxicity in patients with low lean mass may be attributed to alterations in**

**distribution, metabolism, and clearance of systemic chemotherapy drugs. Chemotherapy is traditionally dosed according to body surface area (BSA) but its use has been criticized in the dosage or medications with a narrow therapeutic index, such as chemotherapy. A 4- to 10-fold variation in drug clearance has been shown in individuals with similar BSA and there is growing concern that this approach is invalid.”**

Ryan et al then provide additional detail on the specifics of this relationship:

**“If body weight comprises two major components (lean and fat mass), then these are the two major sites of distribution of hydrophilic and lipophilic drugs. Therefore, variability in individual lean or fat mass may lead to changes in the volume of distribution of drugs and therefore adversely affect the tolerance of cytotoxic drugs. Tolerance is further compromised in individuals with sarcopenic obesity, where the combination of excessive fat mass and diminished lean mass may significantly affect the tolerance of hydrophilic drugs by resulting in a disproportionately small volume of drug distribution in relation to their body weight or body surface area. Variations in lean and fat mass, therefore, can lead to considerable variation in the milligram of chemotherapy drug per kilogram lean mass with higher doses per kilogram lean mass shown to be associated with more frequent and severe toxic side effects. Pharmacokinetic data have supported this hypothesis with patients with low lean mass experiencing higher plasma concentrations of antineoplastic drugs and experiencing more toxicity. For lipophilic drugs such as doxorubicin or trabectedin, individuals with low fat mass also may present with toxicity due to a reduced volume of distribution.”**

If that were not enough, the chronic inflammation that is almost always present in this population can exacerbate the problem by having an adverse effect on detoxification and distribution of chemotherapeutic drugs:

**“Systemic inflammation has been shown to decrease liver cytochrome activities and drug clearance and may modify drug exposure. Low concentrations of circulating plasma proteins (e.g., albumin) also may affect the distribution of**

highly protein-bound drugs such as vandetanib sorafenib, and epirubicin.”

### **The impact of malnutrition and weight loss on quality of life (QoL) in cancer patients**

As we all know, traditional determinants of treatment success with cancer patients have almost always focused exclusively on mortality. Fortunately, this is now changing with increased emphasis on quality of life:

**“It is now universally accepted that QoL is the central tenet in cancer care, especially in those patients with incurable disease.”**

What is the impact of malnutrition and weight loss on quality of life:

**“Weight loss and malnutrition has been shown to have profound negative effects on QoL in patients with cancer. A recent systematic review examining the effects of weight loss on QoL in patients with cancer reported a negative correlation between weight loss and QoL is 23 of 27 studies. The negative effects on QoL are not surprising as cancer-related malnutrition is a major cause of fatigue, reduced functional ability, and a source of emotional distress.”**

In addition, as you might expect, inflammation adds fuel to the fire in terms of adverse impacts on quality of life:

**“Systemic inflammation and loss of muscle is also thought to drive cancer-related fatigue, which is thought to affect  $\leq 80\%$  of patients both during and after treatment cessation. Severe and persistent fatigue, along with muscle wasting, has been shown to inhibit QoL by considerably reducing functional capacity to fully participate in daily living tasks. Also, evidence from a variety of preclinical and clinical studies suggest that systemic inflammation has a direct role in the development of cancer-associated symptom clusters including pain, fatigue, mood, anorexia, and physical function. Systemic inflammation has been shown to be associated with poorer QoL even in those with good performance scores.”**

Can nutritional therapies be helpful in this regard?

**“Importantly, interventions aimed at targeting nutritional status and attenuating weight loss have proven successful in improving aspects of QoL in patients with cancer.”**

### **Muscle mass and overall survival**

Does muscle mass in cancer patients have an impact on overall survival? Ryan et al state:

**“Most studies report a significant decrease in overall survival in patients with low muscle mass compared with their counterparts, regardless of the primary cancer site and stage.”**

Furthermore:

**“In addition to sarcopenia, low muscle attenuation (indicative of fatty infiltration of muscle tissue) is also associated with poorer survival in a variety of tumors including non-small cell lung cancer, colorectal cancer, endometrial, renal, and ovarian cancers. Importantly, in some cases, low muscle attenuation appears to be superior in predicting mortality than low lean mass alone.”**

Can loss of muscle during treatment be a concern? The authors point out:

**“Notwithstanding the effects of low muscle mass on survival, several studies emphasized that patients continually lose muscle while on treatment and this is associated with an increased risk for mortality in a number of cancers. Patients with advanced pancreatic cancer (n = 97) who experienced early loss of skeletal muscle ( $> 10\%$  within 3 mo of diagnosis) were at increased risk of poorer overall survival and progression-free survival than patients who did not experience muscle loss to the same degree.”**

### **Concluding remarks from Ryan et al**

Ryan et al finish their paper by emphasizing the need that I mentioned in the introduction to this newsletter – that we need to dismiss ancient and outmoded, all-or-none, thinking about how to assist cancer patients for all of their needs, which certainly include reducing loss of life but must also include quality of life considerations. With this type of thinking in mind, a multifactorial approach, which includes diet, nutritional supplements, and lifestyle

modification as well as drug therapy, will be optimal:

**“Early screening to identify individuals with muscle loss and decreased muscle quality would allow for earlier multimodal interventions to attenuate adverse body composition changes. These include resistance exercise training and optimal dietary intake and supplementation, combined with pharmacotherapy.”**

### ***SOME FINAL THOUGHTS FOR PART I***

As was mentioned in the introduction, I feel that the health care community, both allopathic and alternative, and the public in general have spent way too much time, energy, and passion on debating, at best, and arguing, at worst, whether or not diet and nutritional supplementation can prevent or cure cancer. Because of this, they have ignored the massive body of research that makes it clear that diet and nutritional supplementation can immensely benefit the cancer patient to adjunctively maintain an improved quality of life, particularly when undergoing the challenges of chemotherapy. With that thought in mind, please consider the use of **SarcoSelect®**, which comes in both whey and pea protein versions, with this category of patients. Because the formula is based on research that was performed on cancer patients for the purpose of improving muscle mass, I feel it will be ideal for the many cancer patients who are losing muscle mass and attendant quality of life due to malnutrition, the cancer itself, chemotherapy, or all of the above.

Are there other supplemental options that might be helpful for the malnourished cancer patient experiencing weight loss and/or loss of quality of life? In part II of this series I will review the paper “Use and effects of oral nutritional supplements in patients with cancer” by de van der Schueren (de van der Schueren MAE. *Nutrition*, Vol. 67-68, November/December 2019) that addresses this very question.

### **SarcoSelect® – with Whey Protein**

585 grams - 14 Servings



### **SarcoSelect® DF – with Organic Pea Protein**

532 grams - 14 Servings

