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Prevalence of Sarcopenia in Older Patients with Colorectal Cancer

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Abstract

Objective: Sarcopenia is the age-related loss of muscle mass, strength, and function. It is a common finding in older patients and is associated with decreased life expectancy and potentially higher susceptibility to chemotherapy toxicity. This study describes the prevalence of sarcopenia in older adults with early stage colorectal cancer.

Materials and Methods: Patients 70 years old who underwent surgical resection for stage I-III colorectal cancer between 2008 and 2013 were identified from the medical record. Sarcopenia was assessed by measuring the total muscle area on computerized tomography (CT) images obtained prior to surgery. Total muscle area was measured at the level of L3 and normalized using each patient's height to produce a Skeletal Muscle Index (SMI). Sarcopenia was defined using sex- and body mass index (BMI)-specific threshold values of SMI.

Results: Eighty-seven patients were included, median age 77 years (70–96). Twenty-five men (60% of 42) and 25 women (56% of 45) had sarcopenia. Sarcopenic patients had significantly lower BMI ($p=0.03$) compared to non-sarcopenic patients. There was a positive correlation between BMI and SMI for both men ($r=0.44$) and women ($r=0.16$).

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Conclusion: Sarcopenia is highly prevalent among older patients with early stage colorectal cancer. BMI alone is a poor indicator of lean body mass and improved methods of screening for sarcopenia are necessary. CT scans are a viable option for identifying sarcopenic patients in whom timely interventions may improve survival, quality of life, and functional outcomes.

Keywords

sarcopenia; colorectal cancer; cachexia; older patients

Introduction

Sarcopenia is the age-related loss of muscle mass. The prevalence of sarcopenia in community dwelling adults ranges from 13–24% in those under age 70 to more than 50% in persons over the age of 70 [1]. In the elderly, sarcopenia may lead to frailty and is predictive of impairments in instrumental and basic activities of daily living (IADL, ADL), falls, and death [2,3]. As both cancer and sarcopenia are associated with advancing age, it is important to assess whether an elderly patient with cancer is sarcopenic as this is related to reduced survival, poor response to chemotherapy, and increased chemotherapy toxicity [4].

The study presented here pertains to older patients with a colorectal cancer diagnosis. Of the estimated 143,460 new patients with colorectal cancer in 2012, about half were age 70 or older [5]. Patients with early stage (stage I-III) colorectal cancer are offered surgical resection with or without adjuvant chemotherapy, depending on the depth of invasion and involvement of lymph nodes. In patients with non-metastatic colorectal cancer, sarcopenia has been linked to postoperative infection and delayed recovery [6]. Despite the prevalence and negative outcomes of sarcopenia, there is little data on its frequency in older patients with early stage colorectal cancer.

The purpose of this study is to define the prevalence of sarcopenia in older adults with early stage colorectal cancer. The specific focus is patients age 70 and older because they are at especially high risk for poor outcomes due to diminished physiologic reserves. The study uses computed tomography (CT) – a procedure used in routine management of colorectal cancer – to measure lean body mass in patients age 70 and older.

Materials and Methods

Design

This study is a cross-sectional analysis of CT data collected routinely in the diagnosis and treatment of patients with colorectal cancer. This study was approved by the Institutional Review Board of the University of North Carolina at Chapel Hill.

Population Cohort and Data Acquisition

Study participants.—Eligible patients were treated at the North Carolina Cancer Hospital between 2008–2013 and met the following criteria: (1) 70 years of age at the time of stage I-III colorectal cancer diagnosis, (2) underwent surgical resection of their cancer (patients undergoing transanal excision for stage I cancers were excluded from the study), (3) had a

CT scan of the abdomen that had been reviewed and stored electronically at UNC Hospitals and performed 42 days before surgical treatment, and (4) at least one visit to a medical or surgical oncologist at UNC Hospitals.

Data Collection.—For each patient, a retrospective chart review was conducted of their UNC Hospitals electronic medical record to collect patient characteristics (height, weight, body mass index [BMI], race) measured pre-operatively, CT images, and date of surgery.

Body Mass Index (BMI).—BMI was calculated using the following formula: $BMI = \text{weight (kg)} / \text{height}^2 (\text{m}^2)$. BMI categories typically applied to adults were used to classify the patients as follows: <20.0 kg/m², underweight; 20.0 to 24.9 kg/m², normal weight; 25.0 to 29.9 kg/m², overweight; and ≥30.0 kg/m², obese.

Sarcopenia.—Sarcopenia was assessed by measuring the cross sectional area of the abdominal wall (rectus abdominis, transversus abdominis, internal and external obliques), psoas, and paraspinal (erector spinae, quadratus lumborum) muscles on CT images obtained for diagnostic and staging purposes in patients with colorectal cancer. Total muscle area was measured at the level of L3 using a three-dimensional computerized image analysis software, Aquarius iNtuition 4.4 (TeraRecon, San Mateo, CA). Measurements were performed in a semi-automated fashion with manual outlining of muscle borders and volumetric analysis of the outlined area by setting a density threshold between −30 and +110 Hounsfield Units (HU) (Figure 1). Automatic calculation of total muscle area was performed by excluding vasculature, bony structure, and areas of intramuscular fatty infiltration based on HU. The measured muscle area was then normalized for height (in meters) to calculate a Skeletal Muscle Index (SMI) (cm²/m²). The CT images were processed and analyzed by a single radiologist, to minimize measurement error.

Sarcopenia was defined using sex- and BMI-specific threshold values of SMI (men with BMI <25, 43 cm²/m²; men with BMI ≥25, 53 cm²/m²; women regardless of BMI, 41 cm²/m²). These cut points were identified in the largest analysis of skeletal muscle to date in a predominately colorectal cancer population using optimal stratification for cut points in relation to increased mortality [7].

Statistics

Differences between groups were analyzed using independent t-tests, Fisher's exact test, and Pearson's chi-square tests. Correlations between continuous variables were assessed using Pearson correlation coefficients. Results were considered statistically significant at the $p < 0.05$ level.

Results

Sample

Of patients diagnosed with non-metastatic colorectal cancer (N=1,029), 218 were 70 years or older at time of diagnosis. Of the patients age 70 or older (N=218), 214 had adenocarcinoma or mixed endocrine carcinoma and 197 met the surgery criteria (17 patients undergoing transanal excision for stage 1 disease were excluded). One hundred had an

abdominal CT scan within 42 days prior to surgery; however, only 87 were technically adequate for SMI assessment..

The sample was distributed roughly evenly between males (n=42) and females (n=45), and mean age was 78 (SD 5.6) and 80 years (SD 6.5), respectively. Sixty-nine patients (79%) were Caucasian. In the overall sample, frequency of Stage I, II, and III colorectal cancer was 25%, 41%, and 34%, respectively.

Prevalence of Sarcopenia

In our sample, n=25 (60%) men and n=25 (56%) women had sarcopenia. Sarcopenia was not significantly associated with gender ($p=0.83$) or race ($p=0.29$). Among males, 72% of sarcopenic patients and 75% of non-sarcopenic patients were overweight or obese. Among females, 42% sarcopenic patients and 54% of non-sarcopenic patients were overweight or obese. Sarcopenic women had significantly lower BMI compared to non-sarcopenic women, median 23 vs 27 respectively, $p=0.01$. In the overall sample, there was a positive correlation between BMI and SMI for men ($r = 0.45$) and women ($r = 0.17$), and a small negative correlation between SMI and age (data not presented) for men ($r = -0.12$) and women ($r = -0.05$).

Discussion

In this study, we demonstrate that sarcopenia is prevalent among older persons with an early stage colorectal cancer diagnosis. To identify sarcopenic patients, we used information that is typically found in the medical record of patients with colorectal cancer: cancer stage, BMI, and CT imaging. CT scans are routinely ordered as standard of care for colorectal cancer, but are typically not used beyond the scope of assessing metastases, tumor location, size, and stage. We make further use of these CT images to assess muscle mass and identify sarcopenic patients who may be at increased risk for negative outcomes. The prevalence of sarcopenia in the general population of older adults is well-documented [1]. As cancer is largely a disease of aging, similar prevalence patterns are likely to be observed in older patients with cancer, with implications for cancer care and outcomes. As this line of research is pursued, it is important to specifically explore the prevalence and implications of sarcopenia in elderly populations with different types of cancer diagnoses. In this regard, our study makes a unique contribution to the literature with its focus on older persons with an early stage CRC diagnosis. Our findings of a prevalence of sarcopenia in 60% of men and 56% of women is higher than the prevalence of sarcopenia in elderly patients without cancer and with cancer of all ages [1]. For our study, we chose cut points derived from the largest analysis of skeletal muscle in patients with cancer to date and incorporate both sex-specific and BMI thresholds (N=1,476) [7]. In the absence of a consensus definition of sarcopenia in research and clinical practice, we believe our approach has advantages over cut points derived primarily from optimum stratification in study samples in relation to a negative outcome, most notably mortality.

Among medical practitioners, it is commonly believed that elderly, frail patients lack the necessary physiologic reserve to withstand rigorous treatments, such as chemotherapy and surgery. Indeed, sarcopenic patients with cancer have been shown to have worse post-

operative outcomes compared to patients without sarcopenia [8]. Given the risks associated with sarcopenia, it is important for providers to identify sarcopenia in patients with colorectal cancer when formulating treatment plans. In the clinical setting, sarcopenia frequently goes unrecognized because many sarcopenic patients do not appear to be emaciated. Indeed, 67% of the sarcopenic patients in our study were overweight or obese. This suggests a need for more sensitive testing to identify occult sarcopenia in patients whom may benefit from treatment of their underlying cachexia.

The early identification of sarcopenia in an elderly patient may present an opportunity for interventions that may help the patient maintain muscle mass during treatment. One option is to encourage the at-risk patient to maintain or increase their physical activity both before and after treatment. Patients undergoing surgery for colorectal cancer who received pre-operative physical therapy and protein supplementation were able to walk significantly farther at two months following surgery compared to patients who did not receive preoperative conditioning [9]. American Cancer Society guidelines recommend physical activity for patients with cancer and survivors of all ages, based on evidence gathered through decades of trials testing aerobic exercise and resistance training in this population.

To date, few studies have investigated the impact of physical activity interventions on the body composition of adults with a colorectal cancer diagnosis. Our review of the literature has identified 11 randomized controlled trials focused exclusively on patients with colorectal cancer, and several more that include CRC among a variety of additional cancer sites. Two studies focused on patients with CRC scheduled for surgery – which is a patient population similar to the sample analyzed in our study. The smaller of the two studies (N=31) showed promising findings with regard to the feasibility of physical activity interventions in colorectal patients, but no difference between exercise and control [10]. There is a need for further studies exploring interventions to maintain or improve lean body mass in order to improve functional status, quality of life, and care outcomes in elderly patients with colorectal cancer preparing for surgery.

As a preliminary study, our small sample size and retrospective design precluded an analysis of potential causal effects and confounding variables. Further, our inclusion of only patients undergoing primary surgical resection may have biased our sample towards those with favorable clinical characteristics compared to patients who were deemed unfit for surgery.

Sarcopenia is a common finding among elderly patients and can have negative implications for treatment options and care outcomes. There is currently no widely-accepted screening test to identify patients at risk for sarcopenic complications. However, among patients with CRC, CT scans are a quick and easy way to objectively assess muscle mass. In our experience, it takes only 5 minutes for a radiologist to obtain an SMI from an abdominal CT scan. Further research is needed to delineate a standardized diagnostic criterion for sarcopenia and to investigate interventions to maintain and improve lean body mass during and after cancer treatment.

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Figure 1. CT scan at L3.
The highlighted area was used to calculate skeletal muscle index.