Lower muscle density is associated with major postoperative complications in older patients after surgery for colorectal cancer

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Abstract

Background: Reduced muscle density is associated with an increased risk of postoperative complications. We examined the prognostic value of muscle density as a predictor of postoperative complications in elderly patients undergoing surgery for colorectal cancer.
Methods: Patients ($\geq$70 years) who underwent surgery for colorectal cancer between 2006 and 2013 were selected from a prospective single centre database. The Hounsfield Unit Average (HUA or HU/mm^2) of the psoas muscles at the level of the third lumbar vertebra was calculated on the scan. High and low muscle density groups were identified based on the lowest gender specific HUAC quartile. Major postoperative complications (Clavien-Dindo (CD) $\geq$3) within 30 days after surgery were retrospectively documented. Logistic regression analysis was used to identify risk factors for postoperative complications.
Results: A total of 373 patients (median age = 78 years) were included in this study. The mean muscle density score was 24.5 $\pm$ 4.3 HU/mm^2 for males and 26.3 $\pm$ 5.0 HU/mm^2 for females. The cut-off point for the lowest gender specific quartile was $\leq$22.0 HU/mm^2 for males and $\leq$23.5 HU/mm^2 for females. After multivariable regression, there was a statistically significant association between muscle density and CD $\geq$ 3 (OR = 1.84 (95% CI 1.11–3.06), p = 0.019). Anastomotic leakage in patients with a primary anastomosis (n = 287) occurred more often in patients with low muscle density (11.7% vs 23.3%, p = 0.016). The associations remained significant after correction for confounders.
Conclusion: Low muscle density is associated with major postoperative complications in older patients who undergo surgery for colorectal cancer.
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Introduction

Colorectal cancer is a common form of cancer in the Western world.[1] On average, 60% of these patients are over 70 years old.[2] Since 1975, the incidence of colorectal cancer has been increasing and it is expected to increase even further with the aging of the general population.[3] Compared to their younger counterparts, older patients with colorectal cancer are at higher risk for complications after surgery.[5] The decision to perform surgery in older patients can be challenging due to poor performance status and the presence of comorbidities.[4] The length of postoperative hospital stay (LOS) and the risk of postoperative

morbidity increases with age. Surgery therefore can result in functional decline and even mortality.[6–8]

However, age might not be the best discriminative factor for deciding whether or not to operate. Recently, there has been a rising interest in the association between muscle density and postoperative outcome after surgery.[5] Loss of skeletal muscle density and loss of strength are associated with impaired functional status. An absolute muscle density of more than two standard deviations below the mean muscle density of healthy young adults is associated with inactivity, chronic disease and cancer.[6] Image-analyses software can be used to measure the cross-sectional muscle area accurately, and can be used to identify patients with low muscle density.

Colorectal cancer patients are at risk for physical frailty for two reasons. Firstly, age is a risk factor for low muscle density.[7] Fifty percent of colorectal cancer patients are over 70 years old.[8] Secondly, cancer is a risk factor for low muscle density. Low muscle density is associated with poor physical function and nosocomial infections in patients diagnosed with esophageal,[9] pancreatic[10] and colorectal cancer.[11,12] Previous studies have illustrated that low muscle density is associated with longer hospital stays after colorectal cancer surgery in patients of all ages.[12] The current study hypothesized the presence of an association between lower muscle density and major postoperative complications after surgery for colorectal cancer in elderly patients.

Methods

Patient selection

Patients were identified from a prospectively collected database of patients who underwent surgery for colorectal cancer between 2006 and 2013 in Gelre Hospital in Apeldoorn, The Netherlands. A total of 889 patients were registered in the database. All patients aged 70 years or older who underwent elective and acute surgery for colorectal cancer between 2006 and 2013 were included in this study. Patients were excluded if preoperative CT imaging of the abdomen was not available. Official approval of the Local Ethics Review Committee of Gelre Hospitals Apeldoorn was not required for this study.

Data collection

Baseline patient characteristics such as: gender, date of birth and date of surgery, were prospectively registered in a database. Medical files were used to retrospectively collect additional information about patient characteristics such as the degree of comorbidity (according to the Charlson Comorbidity Index (CCI) version ICD 10[13]) and the American Society of Anesthiologists (ASA score).[14] Tumor characteristics were described according to the American Joint Committee on Cancer Classification (AJCC) (TNM

staging manual[15]). Treatment characteristics included neoadjuvant treatment: urgency of surgery, laparoscopic or open technique, the segment that was resected and whether or not an anastomosis or a stoma was constructed. Postoperative course included: LOS (in days, starting at the day of surgery and ending at the day of discharge), intensive care unit (ICU) admission, readmission within 30 days after discharge, postoperative complications and postoperative mortality within 30 days after surgery. Major postoperative complications were categorized using the Clavien-Dindo score.[16] A Clavien-Dindo score ≥ 3 was considered as a major complication which resulted in an intervention, ICU admittance or death within 30 days after surgery.

Measurement of muscle density and definition of study groups

Abdominal CT scans are used for tumor staging in the preoperative work-up for colorectal cancer surgery. For the purpose of this study CT scans were used to perform a Hounsfield Unit Average Calculation (HUAC). Hounsfield Units (HU) express the muscle density and reflect the amount of fatty infiltration. The HUAC reflects the average muscle density after correction for surface area. The HU for muscle tissue has an average of 60.[17] Low HU is indicative of high amounts of fatty infiltration in the muscle. HU and the surface area (mm^2) of the left and right psoas muscle at the level of the third lumbar vertebra (L3) was measured with the computer software Secta Rix/Pax, 2014. At this level, the surface area of the psoas muscles is representative of muscle density on a full body level.[18] In addition, it gives information about the surface area of the following muscles: erector spinae muscles, quadratus lumborum muscles, transversus abdominis muscles, interior- and exterior oblique muscles and the rectus abdominis muscles.[19] The following formulas were used in order to calculate the HUAC: 1. Right Hounsfield Unit Calculation = (Right Hounsfield Unit * Right psoas Area)/(Total Psoas Area); 2. Left Hounsfield Unit Calculation = (Left Hounsfield Unit * Left Psoas Area)/(Total Psoas Area); 3. HUAC = (Right Hounsfield Unit Calculation + Left Hounsfield Unit Calculation)/2.[17,20,21] Measurements were performed by researcher CM. The researcher received instructions on how to identify the level of L3 from a professional radiologist. After analysis, the radiologist measured HUAC in a randomly selected sample of 10% of the total patient population to assure correct measurement. As carried out Joglekar (2014) study, low muscle density was defined as HUAC scores in the lowest gender specific quartile (<25th percentile) while high muscle density was defined as HUAC scores in the highest gender specific quartile (>25th percentile).[17]

Outcome and statistical analysis

The outcome of interest was major postoperative complications. Low muscle density and high muscle density groups