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Original article

Value of sarcopenia assessed by computed tomography for the prediction of postoperative morbidity following oncological colorectal resection: A comparison with the malnutrition screening tool

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SUMMARY

Background: Computed tomography (CT) can be used for accurate estimation of whole-body muscle mass and muscle density and for detection of sarcopenia. The goal of this study was to evaluate the additional value of CT measured sarcopenia and muscle attenuation alongside the Malnutrition Universal Screening Tool (MUST) for the prediction of post-operative morbidity after oncological colorectal resection, whilst correcting for known risk factors.

Methods: A prospective cohort study of 80 patients undergoing elective colorectal surgery in the Netherlands. Patients were screened for nutritional risk upon admission using the MUST. Additionally, preoperative CT scans were used to determine skeletal muscle mass for the detection of sarcopenia and muscle attenuation. Univariate and multivariable analyses were performed to evaluate associations between the MUST, muscle attenuation and sarcopenia on the one hand and post-operative complications measured by the Clavien-Dindo score on the other hand.

Results: American Society of Anesthesiology-classification (ASA) $\geq$3, age $\geq$70, MUST $\geq$2 and lower than median muscle attenuation were significantly associated with a higher risk for postoperative complications (Clavien-Dindo score $\geq$2) ($p \leq 0.05$), whereas sarcopenia was not ($p = 0.59$). Multivariate analyses showed that only MUST $\geq$2 remained significantly associated with postoperative complications when corrected for age ($p = 0.03$, OR 5.8, 95%CI 1.1–29.6), but not when corrected for age $\geq$70 and ASA $\geq$3. Muscle attenuation and sarcopenia were not significantly associated with postoperative complications.

Conclusion: Our results suggest that using CT measured sarcopenia may have only little additional value over the MUST for the prediction of increased short-term post-operative morbidity after oncological colorectal surgery. It also underlines the importance of currently implemented easy-to-use nutritional screening tools (MUST) and raises the question of the evaluation of muscle quality versus quantity in body composition imaging. However, further research is needed to investigate the role of sarcopenia for predicting outcome after colorectal surgery, and investigate the role of muscle attenuation measurements for the prediction of muscle function.

Category of submission: observational study.

1. Introduction and rationale

In the Netherlands, colorectal cancer (CRC) constitutes the second most common type of malignant disease. According to statistics from the population-based Netherlands Cancer Registry almost

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15,600 new cases of CRC were diagnosed in the Netherlands in 2015 (almost 8900 men and almost 6700 women). A general epidemiological trend in CRC shows an increase in incidence over time, increased incidence with age and decreasing mortality [1].

Nutritional status has been shown to be an independent risk factor for post-operative complications amongst all patients undergoing colorectal resection [2–5]. Typical measures used to screen for and assess malnutrition include dietary intake and changes in body mass index (BMI). Nutritional screening tools that use these parameters have been shown to be useful for the identification of individuals at nutritional risk [6–8]. The European Society for Clinical Nutrition and Metabolism (ESPEN) recommends the use of the Malnutrition Universal Screening Tool (MUST) for clinical use [6]. Nutritional screening tools have been shown to be independent risk predictors for post-operative complications [2–5]. Recently, the use of computed tomography (CT) has been suggested to be a reliable tool for accurate estimation of whole-body muscle mass and the detection of sarcopenia [9–15], although not all evidence unequivocally supports this [16–18]. This technique uses CT images at the level of the third lumbar vertebra (L3) to determine cross-sectional area of skeletal muscle at L3, which when corrected for the patient's height is a measure of lean body mass [9,19]. Besides estimation of body mass, e.g. for the detection of sarcopenia, CT image analysis has been used for the estimation of muscle density, also known as muscle attenuation. Muscle attenuation measures the mean value of Hounsfield units in skeletal muscle mass at the L3 level, and may possibly be used for the estimation of muscle function, rather than muscle mass [20].

This direct quantification of lean body mass and muscle attenuation offers a potentially objective measure of patients' body composition and potential loss of functional muscle mass. The goal of this study was to assess whether CT sarcopenia screening has additional value besides the MUST for the prediction of post-operative complications after oncological colorectal resection.

2. Study design & methods

A prospective cohort study of patients undergoing elective surgical intervention was conducted. All patients aged 18 years and older undergoing elective oncological colorectal resection between October 2012 and July 2013 for the treatment of colon and rectal cancer in VieCuri teaching hospital in the south of the Netherlands were included (N = 80). Patients with American Society of Anesthesiology (ASA)-classification V, severe liver cirrhosis – Child grade C, end stage renal disease requiring dialysis, severe heart disease – New York Heart Association class IV and chronic obstructive pulmonary disease (COPD) requiring (home)oxygen therapy or an interval greater than 2 months between the time of the scan and the operation were excluded (N = 6).

Prior to this study, a nutritional screening and intervention algorithm had successfully been implemented at our hospital in accordance with ESPEN guidelines. All patients were screened using the MUST screening tool upon hospital admission. Patients with MUST scores of 2 or higher received a nutritional intervention in the form of additional high caloric food products before surgery, in accordance with ESPEN guidelines. As a nutritional screening and treatment algorithm was already in place, no change in the nutritional intervention regime was implemented in this study.

Patients with rectal carcinoma underwent neoadjuvant therapy for a period of 8 weeks, followed by a restaging CT and then surgery within 2 weeks in accordance with dutch guidelines. Colon carcinoma patients did not receive neoadjuvant treatment. For the purpose of this study, the restaging CT was used for sarcopenia measurements.

Besides nutritional status, known risk factors for post-operative complications were recorded: age (<70 and ≥ 70 years), ASA-classification (<3 and ≥ 3), stage of disease (1–4), planned type of procedure (laparoscopic or open: conversion from laparoscopic to open surgery was classified as open surgery) and peri-operative blood transfusion. Comorbid diseases were categorized according to the Charlson Comorbidity Index. In the Charlson Comorbidity index, a weighted score is assigned to each of 17 comorbidities and the sum of the index score is an indicator of disease burden and an estimator of mortality. For the analyses we classified the Charlson index as a binary variable; a score of 3 or more was considered an increased comorbidity risk [21].

The primary endpoint was the occurrence of post-operative complications within 30 days after surgery, which were prospectively registered. Post-operative complications were categorized by severity as proposed by Clavien-Dindo [22]. According to this classification, complications are defined as any deviation from the normal post-operative course. Complications were graded from I to V, based on the extent of intervention needed to correct the complication. In the case of several complications these were recorded separately, and the most severe complication was used in the statistical analyses. For the statistical analyses, we classified postoperative complications as a binary outcome: complications graded 2 or higher were categorized as the occurrence of serious post-operative complications, whereas grade 0 and 1 were graded as no serious complications.

Data from this cohort has previously been used for a different study [23].

3. CT measured sarcopenia

Pre-operative abdominal CT scans were available for all patients (N = 80). Exclusion was on the basis of poor quality of CT scans (N = 5), scans not showing the abdominal wall (N = 4), absence of the third lumber vertebra on the scan (N = 2), and/or an interval greater than 2 months between the time of the scan and the operation (N = 6).

Muscle mass was measured by analyses of electronically stored CT images, which had been routinely taken for diagnostic purposes. The third lumbar vertebra (L3) was used as a standard landmark to measure muscle cross-sectional area in cm^2. Skeletal muscle tissue was identified and quantified on CT images by means of Hounsfield unit (HU) thresholds (−29 to +150 HU). The total cross-sectional area of skeletal muscles at L3 was computed by use of Slice-O-matic software, version 5.0 (Tomovision, Montreal, QC, Canada) (Fig. 1). Total muscle area at L3 normalized for body height (L3 skeletal muscle index, cm^2/m^2) is linearly related to whole-body muscle mass. Based on the L3 skeletal muscle index, sarcopenia was defined using sex-specific cutpoints: 43 cm^2/m^2 for males with BMI <25.0 kg/m^2 and 53 cm^2/m^2 for males with BMI ≥25.0 kg/m^2; the cutpoint for sarcopenia in females was 41 cm^2/m^2, irrespective of BMI [24,25]. Besides muscle mass, muscle radiation attenuation (i.e. the mean HU of muscle tissue) was also determined as an indicator of muscle density. Study participants were divided in groups of high versus low muscle attenuation based on the median value as cutoff (low: <34.1 HU; high: ≥34.1 HU).

4. Statistical analyses

Frequencies are presented as absolute numbers and percentages. Univariate analyses were used to determine the association between each individual variable and the outcome variable using Chi-square analysis or Fisher's Exact test and or likelihood ratio test in case of low expected frequencies. P=<0.05 was considered significant.