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Original article

Contrast-enhancement influences skeletal muscle density, but not skeletal muscle mass, measurements on computed tomography

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SUMMARY

Background & aims: Low skeletal muscle mass and density have recently been discovered as prognostic and predictive parameters to guide interventions in various populations, including cancer patients. The gold standard for body composition analysis in cancer patients is computed tomography (CT). To date, the effect of contrast-enhancement on muscle composition measurements has not been established. The aim of this study was to determine the effect of contrast-enhancement on skeletal muscle mass and density measurements on four-phase CT studies.

Design: In this observational study, two observers measured cross-sectional skeletal muscle area corrected for patients' height (skeletal muscle index [SMI]) and density (SMD) at the level of the third lumbar vertebra on 50 randomly selected CT examinations with unenhanced, arterial, and portal-venous phases. The levels of agreement between enhancement phases for SMI and SMD were calculated using intra-class correlation coefficients (ICCs).

Results: Mean SMI was 42.5 (±9.9) cm^2/m^2 on the unenhanced phase, compared with 42.8 (±9.9) and 43.6 (±9.9) cm^2/m^2 for the arterial and portal-venous phase, respectively (both $p < 0.01$). Mean SMD was lower for the unenhanced phase (30.9 ± 8.0 Hounsfield units [HU]) compared with the arterial (38.0 ± 9.9 HU) and portal-venous (38.7 ± 9.2 HU) phase (both $p < 0.001$). No significant difference was found between SMD in the portal-venous and arterial phase ($p = 0.161$). The ICCs were excellent (≥0.992) for all SMIs and for SMD between the contrast-enhanced phases (0.949). The ICCs for the unenhanced phase compared with the arterial (0.676) and portal-venous (0.665) phase were considered fair to good.

Conclusions: Statistically significant differences in SMI were observed between different enhancement phases. However, further work is needed to assess the clinical relevance of these small differences. Contrast-enhancement strongly influenced SMD values. Studies using this measure should therefore use the portal-venous phase of contrast-enhanced CT examinations.

1. Introduction

The involuntary loss of skeletal muscle mass, quality and function is considered to be a result of aging (i.e. sarcopenia), or as part of muscle wasting syndromes (i.e. cancer cachexia, chronic diseases, bed rest) [1–3]. Low skeletal muscle mass has recently been identified as a prognostic factor for treatment outcome and survival in various populations, such as in cancer and liver transplant

Abbreviations: HU, Hounsfield units; ICC, intraclass correlation coefficient; SDC, smallest detectable change; SEM, standard error of the measurement.

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patients [4,5]. Furthermore, it is associated with an increased risk of postoperative complications, chemotherapy toxicity and increased hospital expenditure [4,6–8]. Low skeletal muscle density, a measure for intramuscular adipose content, has recently been described as a risk factor for mortality in patients with lymphoma, melanoma, metastatic renal cell carcinoma, pancreatic carcinoma, and metastatic gastric cancer [9–13]. Body composition measures may guide future interventions to manage skeletal muscle wasting and to increase patients' resistance towards stressors, such as surgery and chemotherapy [14].

The gold standard and most used modality to assess body composition is computed tomography (CT) due to its wide availability, especially in cancer patients [15–17]. Excellent inter-observer and intra-observer agreement, as well as excellent comparability of various commonly used software programs for skeletal muscle mass measurement have previously been described [18]. However, the effect of contrast-enhancement on skeletal muscle mass and density measurements remains unclear. It is well-known that contrast-enhancement may influence tissue attenuation [19] and may consequently influence skeletal muscle mass and density measurements. Nevertheless, various enhancement phases have been used in studies that investigated the association between CT-assessed skeletal muscle mass and density and outcome measures [9–12,20]. Therefore, the aim of this study was to compare skeletal muscle mass and density measurements on CT between different contrast-enhancement phases.

2. Materials and methods

2.1. Patients

A total of 50 patients with cancer or evaluated for liver transplantation in Erasmus MC University Medical Center between 2009 and 2015 with available multiphase (unenhanced, arterial, portal-venous) abdominal CT examinations were randomly selected retrospectively. Patients with CTs on which part of the cross-sectional skeletal muscle area was not depicted (e.g. due to obesity) or with artefacts (e.g. due to prostheses) were excluded. Date of birth, sex, body weight, and body height were collected from the electronic patient files within a month of the CT- examination. Body mass index (BMI) was calculated and patients were categorized as underweight (BMI <18.5), normal weight (BMI 18.5–24.9), overweight (BMI 25.0–29.9) or obese (BMI ≥30.0) according to the World Health Organization (WHO) definitions [21]. Approval from the local medical ethical committee was obtained and the study has been performed according to the 1964 Declaration of Helsinki and its later amendments.

2.2. CT scanning protocol

All CT examinations were performed according to a standardized protocol. First, an unenhanced phase was obtained. Afterwards, intravenous (IV) contrast administration in an antecubital vein followed by saline flush of 20 ml was performed using a power injector. The contrast material used was Visipaque 320 mgI/ml (GE Healthcare, Cork, Ireland), adapted to a patient's body weight. Patients with body weight <80 kg received 120 ml contrast medium, whereas patients with body weight ≥80 kg received 150 ml contrast medium. Phases acquired were the arterial phase, determined using a bolus-tracking technique, followed by the portal-venous phase acquired 70 s after contrast administration. For the arterial phase, a region of interest (ROI) was placed in the upper abdominal aorta; when the threshold of +100 HU was reached, scanning started with a delay of 15 s. Estimated time after administration of the bolus was 30–35 s for the arterial phase. The portal-venous phase was obtained with a fixed delay of 70 s after administration of the contrast material. Axial reconstructions were created with a slice thickness of 3 mm in all phases. No adverse reactions were noted during contrast administration. All images were transferred to our local picture archiving and communication system (PACS).

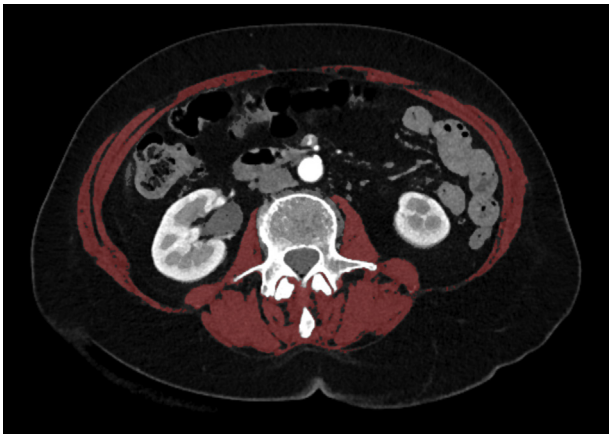

Fig. 1. Example of skeletal muscle mass and density measurement on a contrast-enhanced CT slice in the portal-venous phase at the level of the third lumbar vertebra (L3). The cross-sectional skeletal muscle area of this 71-year-old woman with a body mass index of 24.7 kg/m^2 was 95.6 cm^2, resulting in a skeletal muscle index of 33.1 cm^2/m^2. The mean skeletal muscle attenuation was 33 Hounsfield units. According to the cut-off values of Martin et al. [24], this patient is considered to have both sarcopenia and low skeletal muscle density.

An experienced abdominal radiologist (FEJAW) confirmed the different phases of contrast-enhancement per patient. Furthermore, the mean intraluminal attenuation (in HU) of the aorta was measured for every phase per patient.

2.3. Skeletal muscle mass and density measurements

The cross sectional muscle area (CSMA) was measured at the level of the third lumbar vertebra for the various contrast-enhancement phases (i.e. unenhanced, arterial, portal-venous).

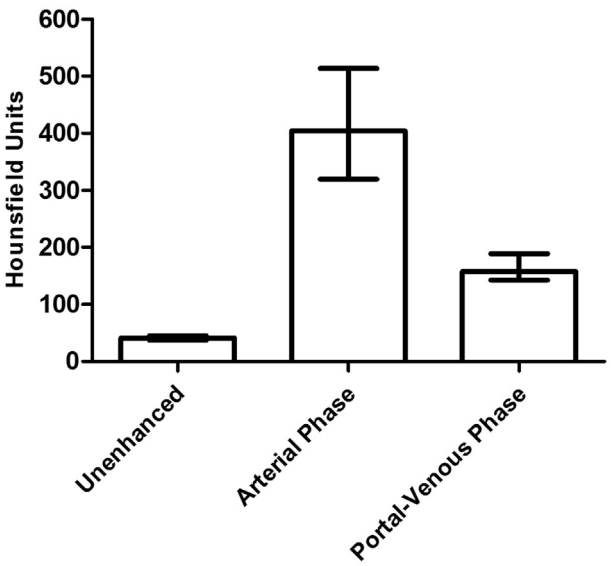

Fig. 2. Median intraluminal aorta attenuation per contrast-enhancement phase. The whiskers represent the interquartile range.

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