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Feasibility of using head and neck CT imaging to assess skeletal muscle mass in head and neck cancer patients

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ABSTRACT

Objectives: Patients with head and neck cancer (HNC) have a higher risk of malnutrition and sarcopenia, which is associated with adverse clinical outcome. As abdominal CT-imaging is often used to detect sarcopenia, such scans are rarely available in HNC patients, possibly explaining why no studies investigate the effect of sarcopenia in this population. We correlated skeletal muscle mass assessed on head and neck CT-scans with abdominal CT-imaging.

Methods: Head and neck, and abdominal CT-scans of trauma (n = 51) and HNC-patients (n = 52) were retrospectively analyzed. On the head and neck CT-scans, the paravertebral and sternocleidomastoid muscles were delineated. On the abdominal CT-scans, all muscles were delineated. Cross-sectional area (CSA) of the muscles at the level of the C3 vertebra was compared to CSA at the L3 level using linear regression. A multivariate linear regression model was established.

Results: HNC-patients had significantly lower muscle CSA than trauma patients (37.9 vs. 45.1 cm^2, $p < 0.001$, corrected for sex and age). C3 muscle CSA strongly predicted L3 muscle CSA ($r = 0.785$, $p < 0.001$). This correlation was stronger in a multivariate model including sex, age and weight ($r = 0.891$, $p < 0.001$).

Discussion: Assessment of skeletal muscle mass on head and neck CT-scans is feasible and may be an alternative to abdominal CT-imaging. This method allows assessment of sarcopenia using routinely performed scans without additional imaging or additional patient burden. Identifying sarcopenic patients may help in treatment selection, or to select HNC patients for physiotherapeutic or nutritional interventions to improve their outcome.

Introduction

Malnutrition is highly common in cancer patients. Patients with head and neck cancer (HNC) in particular have a significantly higher risk of severe malnutrition, compared to patients with other malignancies [1]. Cancer patients often have a decreased lean body mass, including muscle mass, while fat mass may be preserved or even increased [2]. The state of muscle mass depletion, termed sarcopenia, adversely impacts the prognosis of cancer patients. Sarcopenia is officially defined as low muscle mass, combined with either low muscle strength or low physical performance [3]. However, in cancer patients the loss of skeletal muscle mass alone already affects outcome.

Sarcopenic cancer patients have a higher rate of postoperative complications, longer hospital stay and decreased survival when treated with surgery [4–7]. Moreover, increased toxicity and a shorter time to tumor progression were observed in sarcopenic cancer patients treated with chemotherapy [2,8]. Standard treat-

Abbreviations: C3, third cervical vertebra; CSA, cross-sectional area; HNC, head and neck cancer; HU, Hounsfield units; L3, third lumbar vertebra; PVM, paravertebral muscles; SCM, sternocleidomastoid muscle.

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ment of advanced stage HNC often consists of high-dose radiotherapy, with or without chemotherapy, associated with high rates of toxicity [9–11]. A higher prevalence of sarcopenia may partially explain the high rate of toxicity, but unfortunately there is currently no literature available on the effect of sarcopenia in HNC patients.

One reason for the lack of evidence might be the absence of a widely available diagnostic tool to determine the presence of sarcopenia in HNC. Most studies determined skeletal muscle mass using CT-imaging at the level of the L3 vertebra in scans that had been made for routine diagnostic purposes [12,13]. The cross-sectional area (CSA) of the skeletal muscles is measured at the level of L3, which correlates well with total-body skeletal muscle mass [12]. Alternatively, dual energy X-ray absorptiometry (DEXA-) scanning has also been shown to reliably assess skeletal muscle mass [14–16]. Unfortunately, both CT-scans that include L3 and DEXA-scans are not routinely performed in HNC patients.

HNC staging diagnostics includes CT- or MRI-imaging of the head and the neck area. The aim of this study was to investigate whether skeletal muscle mass may be assessed on a routine head and neck CT-scan. We studied a group of 52 patients who received a whole body FDG-PET CT-scan because of advanced HNC and 51 patients without HNC who underwent a total body CT in a trauma setting, considered otherwise healthy controls. We compared muscle CSA at the level of C3 to L3. If C3-level CT-scans could be used to reliably determine skeletal muscle mass, this may be a cost-effective and widely available tool to determine sarcopenia in HNC patients.

Materials and methods

Ethical considerations

All data, including the CT-scans, were used in an anonymized fashion. Moreover, our study concerned retrospective data of patients suffering from HNC, which is an illness with high morbidity and mortality. Because of these reasons, obtaining informed consent and ethical approval was not necessary according to the laws and 'Best Practice' guidelines in the Netherlands.

Study population

Total body CT-scans performed between 2009 and 2013 in the University Medical Center Utrecht, Utrecht, the Netherlands, were randomly selected from two retrospectively assigned groups of patients. Group 1 underwent a whole-body CT in a trauma setting and were considered otherwise healthy controls. Group 2 were randomly chosen HNC patients undergoing a total-body (PET-) CT-scan in radiation posture as a part of radiotherapy planning. Age, sex, weight and BMI were recorded if available. For the HNC patients, clinical AJCC TNM staging (7th Edition) was recorded as well.

Measurements

Muscle CSA was measured using the Volumetool Research software package [17]. This software package was designed in our center as an image evaluation, registration, and delineation system for radiotherapy treatment planning. The third cervical (C3) vertebra was chosen as the reference point in the head and neck CTs. This level was chosen as it is well identifiable on a CT-scan and only captures the neck itself. Depending on patient positioning, higher images often included the mandible and tongue muscles while lower levels also captured the trapezius muscle. Image selection was performed using a standard procedure: by scrolling through the C3 or L3 vertebra in a caudad to cephalad direction, the first CT-slide to completely show the entire vertebral arc and the transverse and spinous processes was selected, as shown in Fig. 1. Image analysis was performed as described in a previous report [16]. Briefly, skeletal muscle was identified using standard Hounsfield unit (HU) ranges, being -29 to $+150$ HU [18,19]. Delineation of the muscles was performed manually by a single researcher who first delineated all head and neck (C3) scans and then delineated all abdominal (L3) scans.

After delineation, the cross-sectional area of the delineated area was automatically retrieved as the total sum of delineated pixels. Separately, the cross-sectional area of pixels that had a radiodensity between -29 and $+150$ HU was retrieved (further referred to as "HU muscle area"). Both approaches were performed to assess whether visual delineation alone would result in overestimation, compared to automatic analysis by radiodensity. CSA of the paravertebral muscles (PVM) at the C3 level and the sternocleidomastoid (SCM) muscles were measured separately, as the SCM muscles can be invaded by lymph node metastases that may impair CSA measurement. The main outcomes were the CSA of the PVM and the combined CSA of the PVM and SCM muscles at the C3 level and the sum of all skeletal muscles at the L3 level (Fig. 1).

Statistical analysis

The characteristics and CSA of the two patient groups were compared using independent-samples *t*-tests for normally distributed variables, independent-samples median tests for skewed variables, and Fisher exact tests for categorical variables. Normality was investigated using the Kolmogorov-Smirnov test. Age, weight, muscle CSA of the PVM, the PVM and the SCM muscles combined, and muscle CSA at L3 were all normally distributed. BMI was not normally distributed.

For the purpose of establishing the model of the relation between C3 and L3, missing data were handled using multiple imputation. Ten multiple imputed datasets were generated. The independent covariates age, sex, weight, BMI, left- and right-sided SCM, and PVM, as well as the dependent variable L3 were used for imputation of the missing values. Pearson correlation coefficients were calculated between the measurements of CSA of the PVM at C3, as well as the sum of the PVM and the SCM muscles at C3, and L3. Linear regression analysis was used to examine the association between the two measurements of CSA at C3 and L3. Multivariate model selection was carried out using backward selection and a p-value of 0.05. Similarity of the association for the trauma and HNC patient groups was investigated by introducing the variable "group" as an interaction term in the statistical model. Using the prediction rule obtained in the linear regression analyses, the values for C3 were transformed and a Bland-Altman plot was constructed to analyze agreement between C3 and L3 muscle area measurement [20].

We evaluated several ways of handling missing data in a clinical setting and compared these methods to the original multivariate model. Two strategies were investigated: (1) assessment of only the PVM and (2) assessment of the PVM and only a single SCM muscle. Statistical significance was set at p-value < 0.05. All analyses were performed in SPSS Statistics version 22.0 (IBM).

Results

Patient demographics

Patient characteristics are shown in Table 1. The results of imputation and the proportion of missing data are shown Table S1. We included 51 trauma patients and 52 HNC patients.