Original article

Preoperative sarcopenia determinants in pancreatic cancer patients

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SUMMARY

Background & aims: Recent studies report that muscle depletion can impair short and long-term results after abdominal surgery. The aim of the present study is to quantify sarcopenia rate in patients undergoing pancreatic resection for cancer and to identify possible determinants of muscle waste.
Methods: Total abdominal muscle area (TAMA) and visceral fat area (VFA) were measured by preoperative CT scan imaging at the level of the third lumbar vertebra in 273 patients undergoing pancreas resection for cancer. Demographics, preoperative parameters, and cancer stage were prospectively collected in our Institutional electronic database. An adjusted regression model was used to identify independent predictors for low TAMA.
Results: 176 (64.5%) patients were sarcopenic, with only 52 of them showing weight loss > 10%. Patients with cancer stage II and III had lower TAMA compared to patients with stage I (p = 0.002). The magnitude of weight loss was inversely correlated with VFA (p = 0.001), while no correlation with TAMA was found. Multivariate analysis showed that cancer stage was an independent predictor of low TAMA. Patients aged over 75 had the highest probability of having both low TAMA (p = 0.031) and high VFA (p < 0.0001).
Conclusions: Most of patients undergoing oncologic pancreatic surgery are sarcopenic. Cancer stage was an independent determinant of sarcopenia while nutritional factors seem less important. An age of over 75 years was significantly correlated with both muscle compartment depletion and visceral fat increase.

1. Introduction

The muscle compartment represents a patient's homeostatic reserve and reflects the general state of health. Sarcopenia is age-associated progressive and generalized loss of muscle mass and strength. However, secondary sarcopenia often occurs in multiple pathological processes such as cancer, malnutrition, inflammatory and neurodegenerative processes, anorexia nervosa, conditions requiring treatment in critical care units, and terminal diseases [1,2]. Computed tomography (CT) allows precise identification of muscle mass depletion, which might be considered a reliable indicator of operative risk [3].

Sarcopenia is observed in most pancreatic cancer patients during the clinical course [4]. In about one third of these patients, death is due to cachexia-related complications, such as immobility, deterioration of the respiratory muscles leading to heart failure, and alterations of the immune system [5]. Pancreatic cancer patients with sarcopenia show poor physical performance, increased postoperative morbidity, reduced response to chemo-radiotherapy, and shorter life expectancy [6–9]. Moreover, sarcopenia has been associated to a higher rate of major complication and longer recovery times following colorectal or liver resection [10–12].

The aim of this study was to assess the rate of sarcopenia and identify its major determinants in patients undergoing surgery for pancreatic cancer.

2. Materials and methods

Between January 2011 and December 2014, we recruited 273 consecutive pancreatic cancer patients undergoing elective surgery. Inclusion criteria were the presence of malignant disease and the availability of a CT scan performed at our hospital in the 30-day period before scheduled surgery. A CT scan for anthropometric assessment was carried out solely for routine preoperative cancer staging.

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Two trained radiology residents (GC, AD) supervised by a senior radiologist (FDC) carried out analysis of CT images (Slice-O-Matic V4.3 software, Tomovision, Montreal, Canada) as described previously [13]. Two consecutive axial CT images extending upward from the level of third lumbar vertebra (L3) were assessed in each patient and then averaged. Using predefined Hounsfield unit (HU) thresholds, specific tissue demarcation was carried out using image analysis software.

Total abdominal muscle area (TAMA) including both paraspinal and abdominal wall muscles was quantified using HU thresholds of -29 to $+150$. Both visceral and subcutaneous fat areas were quantified using the following adipose tissue HU thresholds: -150 to -50 and -190 to -30, respectively [14] (Fig. 1).

Cross-sectional areas (cm^2) were computed automatically by summing tissue pixels and multiplying by pixel surface area. Muscle area was also normalized for height. Sarcopenic patients were defined using a priori determined sex-specific TAMA cut-off values: 52.4 cm^2/m^2 for men and 38.5 cm^2/m^2 for women [15].

Before surgery, demographics, routine laboratory parameters, American Society of Anesthesiologists (ASA) grade, weight loss (WL), body mass index (BMI), and possible comorbidities were prospectively collected for all patients and recorded in our Institutional electronic database. Pathology data, including cancer site and stage according to AJCC classification [16], were retrieved after surgery.

2.1. Statistical analysis

Descriptive data were reported as mean (standard deviation), or median (range), otherwise specified. Categorical variables were compared using the Chi-square test or Fisher's exact test when appropriate. Continuous variables were compared with the Student's t-test and one-way ANOVA test.

Univariate and multivariate linear regression analyses were carried out to assess the association of independent variables with TAMA. Variables significant at $p < 0.10$ were retained in the final model. To identify possible age cut-offs associated with both sarcopenia and visceral obesity patients were compared using intuitive thresholds that could be used in clinical practice (70, 75, and 80 years old).

Statistical analyses were performed using SPSS® version 20 (IBM Corp, Armonk, NY). All statistical tests were 2-sided, a "p" value < 0.05 was considered to indicate statistical significance.

3. Results

Table 1 shows patient preoperative characteristics, morphometric body composition parameters, and oncologic data in the

Table 1
Demographics, preoperative, and operative variables.

Variables	n = 273
Age	66.6 (10.9)
Gender	
Men	152 (55.7%)
Women	121 (44.3%)
BMI (kg/m^2)	23.7 (3.7)
<18.5	18 (6.6%)
18.5–24.9	165 (60.4%)
25.0–29.9	75 (27.5%)
≥30	15 (5.5%)
ASA score	
I – II	187 (68.5%)
≥III	86 (31.5%)
Missing data	2 (1%)
Diabetes	65 (23.8%)
Hemoglobin serum levels (g/dL)	12.0 (1.6)
Patients with levels < 11.5 g/dl	102 (37.4%)
Weight loss ≥ 10%	52 (24.5%)
Preoperative chemotherapy	59 (21.6%)
TAMA (cm^2/m^2)	43.6 (8.8)
VFA (cm^2)	107.9 (75)
SFA (cm^2)	148 (77.8)
TFA (cm^2)	256 (132.9)
Sarcopenic patients	176 (64.5%)
Albumin serum level (g/L)	37.4 (5.4)
Patients with levels < 35 g/L	73 (30.3%)
Cancer stage:	
IA–IB	33 (12.2%)
IIA–IIB	202 (74.8%)
III	35 (13.0%)

Data are number of patients (%), or mean (standard deviation).
BMI indicates Body Mass Index, ASA indicates American Society of Anesthesiologists.
TAMA indicates Total Abdominal Muscle Area, TFA indicates Total Fat Area.
SFA indicates Subcutaneous Fat Area, VFA indicates Visceral Fat Area.

overall series. According to predefined sex-specific cut-offs, 176 (64.5%) patients were seen to be sarcopenic. The sarcopenia rate was 72.4% in men and 54.1% in women.

Table 2 shows TAMA, visceral fat area (VFA), and WL in the three cancer stage groups. Although the rate of patients with WL > 10% was not significantly different in the three groups, patients with cancer stages II and III had lower TAMA compared to stage I patients (p = 0.022). Sarcopenia rate was 51.5%, 64.9%, and 74.3% in cancer stages I, II, and III, respectively (p = 0.06). Cancer stage did not affect VFA.

Figure 2a and b show TAMA and VFA mean values in the three subgroups with increasing WL. The WL percentage was inversely correlated with VFA (p = 0.01), while no correlation with TAMA was found. Preoperative serum albumin (SA) level did not reflect muscle
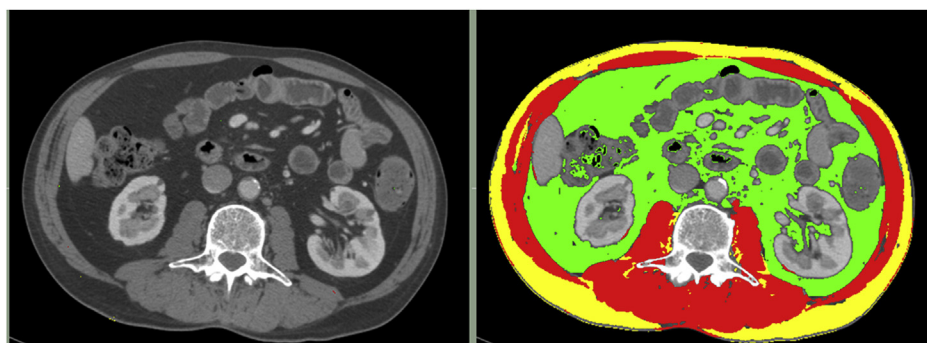

Fig. 1. CT scan at the third lumbar vertebra level in a patient included in the study. In the processed image, subcutaneous fat area (SFA) is highlighted in yellow, total abdominal muscle area (TAMA) in red, and visceral fat area (VFA) in green. (For interpretation of the references to color in this figure legend, the reader is referred to the web version of this article.)