Clinical Nutrition 38 (2019) 862–869

Contents lists available at ScienceDirect

Clinical Nutrition

journal homepage: http://www.elsevier.com/locate/clnu

Original article

# Comparing Western and Eastern criteria for sarcopenia and their association with survival in patients with pancreatic cancer

Chih-Horng Wu [a, b], Ming-Chu Chang [c], Vladimir K. Lyadov [d], Po-Chin Liang [a], Chyi-Mong Chen [a], Tiffany Ting-Fang Shih [a], Yu-Ting Chang [c, *]

[a] Department of Medical Imaging, National Taiwan University Hospital, College of Medicine, National Taiwan University, Taiwan
[b] Graduate Institute of Clinical Medicine, College of Medicine, National Taiwan University, Taiwan
[c] Department of Internal Medicine, National Taiwan University Hospital, College of Medicine, National Taiwan University, Taiwan
[d] Department of Surgical Oncology, Federal Medical and Rehabilitation Center, Russian Academy of Continuous Medical Education, Moscow, Russia

ARTICLE INFO

*Article history:*
Received 26 November 2017
Accepted 12 February 2018

*Keywords:*
Sarcopenia
Intra-abdominal fat
Body compositions
Pancreatic neoplasms
Tomography scanners
X-ray computed

SUMMARY

*Background & aims:* Sarcopenia and cachexia are associated with pancreatic cancer and serve as important adverse prognostic factors. Body composition can be analyzed by routine computed tomography (CT) for cancer staging and has been used to study many types of cancer. The CT measurements are robust, but the diagnostic criteria for sarcopenia vary among different studies. Age, sex and race are important factors that affect muscle and fat masses. This study aimed to analyze the effect of different sarcopenia diagnostic criteria on the prognosis of patients with pancreatic cancer.

*Methods:* Patients with newly diagnosed pancreatic cancer at National Taiwan University Hospital between October 2013 and October 2016 were retrospectively reviewed in this study. Body composition was assessed using cross-sectional CT images to calculate the total skeletal muscle (TSM) index. The concordance and interobserver variability of the TSM measurements were evaluated using both the Western criteria and the Eastern criteria. Kaplan–Meier analyses and the Cox proportional hazard ratio with two different diagnostic criteria for sarcopenia were used to compare the effect on overall survival (OS).

*Results:* A total of 146 patients with pancreatic cancer were enrolled. The TSM index measured by the Western institute was highly correlated with that measured by the Eastern institute ($r = 0.953$, $p < 0.001$). The prevalence of sarcopenia in the patient group at baseline was 66.4% (97/146) by the Western criteria and 11.0% (16/146) by the Eastern criteria, and only low agreement was found between the Western and Eastern criteria (Kappa value = 0.028, $p = 0.149$). Patients who were sarcopenic by the Western criteria showed no significant difference in OS versus those who were not sarcopenic ($p = 0.807$). However, patients who were sarcopenic by the Eastern criteria showed a significant difference in OS versus those who were not sarcopenic in a univariate analysis ($p = 0.008$) and multivariate analysis after adjustment for AJCC stage ($p = 0.014$).

*Conclusions:* Our study demonstrates that different diagnostic criteria may result in different diagnoses and that sarcopenia is an important poor prognostic factor for pancreatic cancer when appropriate diagnostic criteria are selected.



## 1. Introduction

Sarcopenia is associated with many chronic diseases and characterized by the loss of muscle mass and strength [1]. It is defined by pathological changes in different metabolic pathways and is often associated with increased morbidity and mortality irrespective of the underlying disease [2–4]. Patients with pancreatic cancer commonly exhibit sarcopenia and cachexia [5]. Previous studies have demonstrated that sarcopenia is associated with the surgical outcome after pancreaticoduodenectomy [6] or with outcomes in patients with an unresectable tumor who receive chemotherapy [7,8]. Cross-sectional imaging modalities, such as computed tomography (CT) or magnetic resonance imaging, are

* Corresponding author. Department of Internal Medicine, National Taiwan University Hospital, College of Medicine, National Taiwan University, No. 7 Chung Shan South Road, Taipei 100, Taiwan. Fax: +886 2 23633658.
*E-mail address:* yutingchang@ntu.edu.tw (Y.-T. Chang).

https://doi.org/10.1016/j.clnu.2018.02.016
0261-5614/

routinely performed in cancer staging and can serve as a gold standard in the evaluation of body composition [9]. The CT scanner differentiates body tissues by Hounsfield units (HU) based on tissue-specific attenuation values [10]. The total skeletal muscle (TSM) area of a single CT slice at the third lumbar vertebra (L3) is strongly correlated with total body skeletal muscle area [11]. Due to the significant difference in body composition between males and females, sex-specific skeletal muscle index cut-off values are adjusted by body height (BH) at the level of the L3 vertebra. Prado et al. used 52.4 $cm^2/m^2$ for males and 38.5 $cm^2/m^2$ for females as cut-off values to define sarcopenia that was associated with mortality and survival for solid tumors of the respiratory and gastrointestinal tracts in a large population-based study [12].

However, the cut-off values for sarcopenia in cancer research differ among various studies, and body composition is greatly affected by different regions and ethnicities. A recent nationwide survey conducted in Japan revealed a different cut-off value for sarcopenia (36.2 $cm^2/m^2$ in males and 29.6 $cm^2/m^2$ in females) that independently predicted the outcomes of hepatocellular carcinoma [13]. A gap exists in the diagnostic criteria for sarcopenia between these two large-scale studies. The cut-off values found in the Western cohort of patients with respiratory and gastrointestinal cancers might not be feasible for the pancreatic cancer patients in Taiwan. To the best of our knowledge, no previous study has compared the Western and Eastern diagnostic criteria for sarcopenia in patients with pancreatic cancer and correlated with the clinical outcomes. After separating study population into female and male, optimal cut-off values for sarcopenia can be obtained by maximally selected rank statistics to differentiated survival [14]. The aims of this study are to estimate the concordances and agreements of body composition analysis for two different criteria from two institutes (one in East and the other in West), to evaluate the different diagnostic criteria in relation to the survival of patients with pancreatic cancer in Taiwan and to explain the reason of difference.

## 2. Materials and methods

### 2.1. Patients and study design

This retrospective study followed the Health Insurance Portability and Accountability Act guidelines, and the protocol was approved by the institutional review board of National Taiwan University Hospital. Informed consent was waived for all patients because all images were obtained during a routine pancreatic cancer staging protocol. The inclusion criteria were adults (20–99 years of age) with newly diagnosed pancreatic cancer at our institute. CT was performed to evaluate local extension (T stage), regional lymph node status (N stage) and possible metastasis (M stage) according to the American Joint Committee on Cancer (AJCC) guidelines, 7th edition [15]. Clinical data, including age, gender, presence of diabetes or smoking, body weight (BW), BH, body mass index (BMI), albumin (Alb) level, and received curative resection or not were obtained from electric medical records. Age was categorized as equal to or below 70 years old (y/o) or above 70 y/o. For patients equal to or below 70 y/o, BMI was categorized as underweight (<18.5 $kg/m^2$) versus non-underweight (≧18.5 $kg/m^2$) and for patients above 70 y/o, BMI was categorized as underweight (<22 $kg/m^2$) versus non-underweight (≧22 $kg/m^2$) according to the European Society of Clinical Nutrition and Metabolism consensus statement [16]. The Alb level was categorized as equal to or below 40 g/L or above 40 g/L. The digital imaging and communications in medicine (DICOM) files for the CT scans were collected from our picture archiving and communication system (PACS). The time interval for acquiring clinical, laboratory and CT data was within one week. A total of 162 patients were consecutively enrolled in this study from October 2013 to October 2016. We included patients with an Eastern Cooperative Oncology Group (ECOG) performance status (PS) of 0–1, and PS 2–4 patients were excluded because comorbidities could exist. Finally, a total of 146 patients were included. All patients underwent standard treatments after staging and clinical evaluation. Demographic characteristics are presented in Table 1.

### 2.2. Imaging processing

The DICOM files of abdominal CT at the L3 level were collected from our PACS. The CT scanner differentiates body tissues by HU from non-enhanced images based on tissue-specific attenuation values, including TSM (−29, +150), visceral adipose tissue (VAT, −150, −50) and subcutaneous adipose tissue (SAT, −190, −30). The images were processed on a compatible computer using the open source software ImageJ available from the National Institutes of Health, and a radiologist (C.H.W) with 10 years of experience in abdominal imaging performed the processing according to previous literature [17]. Finally, the areas and mean signal intensities of the TSM, VAT and SAT were derived from the CT (Fig. 1) images. An independent research team at the Federal Medical and Rehabilitation Center, Russian Academy of Continuous Medical Education, Moscow, who was blinded to our results also performed the TSM, VAT and SAT measurements. Under the Western criteria, sarcopenia is

**Table 1**
Demographic data show that the presence of sarcopenia diagnosed by the Western criteria and the Eastern criteria.

| Clinical, laboratory and imaging parameters | Total (N = 146) | Sarcopenia by Western criteria (N = 97) | Non-sarcopenia by Western criteria (N = 49) | p value | Sarcopenia by Eastern criteria (N = 16) | Non-sarcopenia by Eastern criteria (N = 130) | p value |
|---|---|---|---|---|---|---|---|
| F/M | 63/83 | 32/65 | 31/18 | <0.001* | 74/9 | 56/7 | 0.959 |
| Age (years) | 65.5 | 65.7 | 65.2 | 0.837 | 71.2 | 64.8 | 0.136 |
| BW (kg) | 59.2 | 57.9 | 61.7 | 0.043* | 49.4 | 60.4 | 0.049* |
| BH (cm) | 162.0 | 163.8 | 158.6 | <0.001* | 162.0 | 162.0 | 0.994 |
| BMI ($kg/m^2$) | 22.5 | 21.5 | 24.4 | <0.001* | 18.9 | 22.9 | <0.001* |
| Alb (g/L) | 40.8 | 40.0 | 42.2 | 0.042* | 36.9 | 41.3 | 0.010* |
| Diabetes (Yes/No) | 50/96 | 30/67 | 20/29 | 0.234 | 7/9 | 43/87 | 0.396 |
| Smoking (Yes/No) | 27/119 | 18/79 | 9/40 | 1.000 | 1/15 | 26/104 | 0.181 |
| AJCC stage (1 and 2/3/4) | 28/29/89 | 17/18/62 | 11/11/27 | 0.584 | 2/2/12 | 26/27/77 | 0.475 |
| TSM area ($cm^2$) | 109.1 | 110.8 | 124.0 | 0.013* | 83.4 | 112.2 | <0.001* |
| VAT area ($cm^2$) | 112.7 | 99.0 | 114.4 | 0.215 | 57.3 | 119.5 | 0.001* |
| SAT area ($cm^2$) | 104.2 | 95.7 | 125.7 | 0.001* | 53.4 | 110.5 | <0.001* |
| Visceral obesity (Yes/No) | 13/133 | 86/11 | 47/2 | 0.146 | 12/4 | 121/9 | 0.017* |

F: female, M: male, BW: body weight, BH: body height, BMI: body mass index, Alb: albumin, TSM: total skeletal muscle, VAT: visceral adipose tissue, SAT: subcutaneous adipose tissue, *: $p < 0.05$.

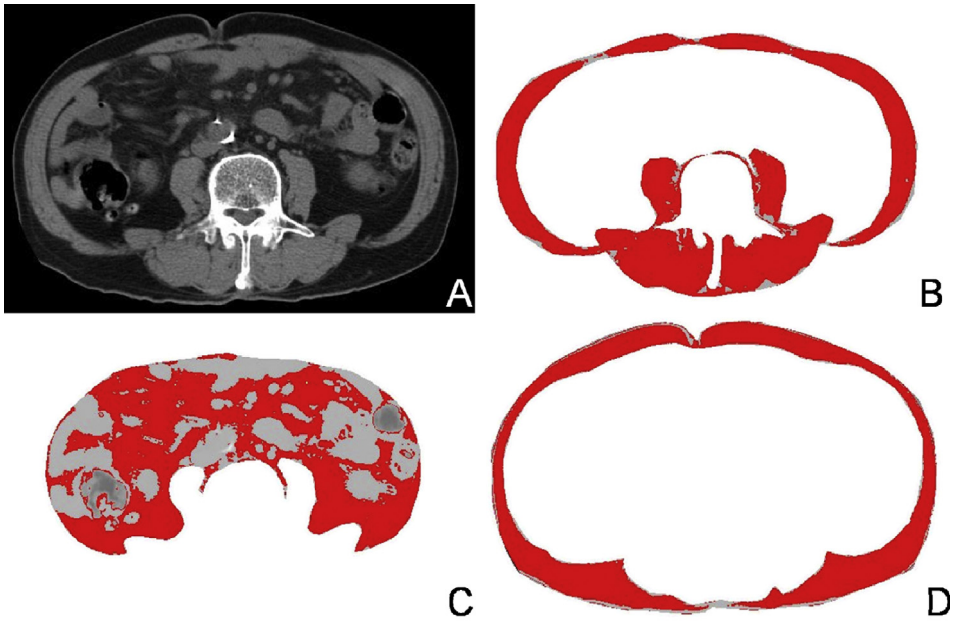


**Fig. 1.** A 73-year-old male had stage 3 pancreatic cancer. The non-enhanced CT image (A) at the L3 level was analyzed to determine the TSM (B), VAT (C), and SAT (D) using ImageJ. The TSM, VAT and SAT areas were 122.79, 118.41 and 91.52 $cm^2$ by our measurements and 125.50, 121.00, and 82.88 $cm^2$ as measured by the Russian institute, respectively. These values are consistent with each other. However, the TSM index measured by our team was 40.56 $cm^2/m^2$, which is regarded as non-sarcopenic by our criteria, and the TSM index measured by the Russian institute was 41.45 $cm^2/m^2$, which is regarded as sarcopenic by the Western criteria. Disagreement can be found between the two criteria. TSM: total skeletal muscle, VAT: visceral adipose tissue, SAT: subcutaneous adipose tissue.

defined as less than 52.4 $cm^2/m^2$ for males and less than 38.5 $cm^2/m^2$ for females, according to the protocol in Prado's article [12]. However, for the Eastern diagnostic criteria for sarcopenia, we used less than 36.2 $cm^2/m^2$ for males and less than 29.6 $cm^2/m^2$ for females, according to the criteria used in Fujiwara's study [13], because the body shape of our patients is more similar to that of the Japanese population than to that of Western populations. Two different sets of diagnostic criteria for sarcopenia, one developed for Western populations and one developed for Eastern populations, were used to assess the effect on overall survival (OS) in patients with pancreatic cancer. Additionally, visceral obesity, which refers to the excessive accumulation of visceral fat in the abdominal cavity, was calculated as the ratio of the VAT area to the SAT area, where a ratio greater than 0.4 was considered visceral obesity (VO), which affects the outcomes of cardiovascular disease [18], colorectal cancer [19] and pancreatic cancer [20].

### 2.3. Statistical analysis

Data analysis was performed using the following tools: Excel 2013 (Microsoft, Redmond, WA, USA), SPSS Statistics 20 (IBM, Armonk, NY, USA) and Small Stata 12.0 for Windows (College Station, TX, USA). The Chi-square test was used to compare categorical variables, and Student's t test was used to compare continuous variables in patients with or without sarcopenia by the Western or Eastern criteria. The correlations of the TSM, VAT and SAT areas measured by the Western and Eastern institutes were compared via Pearson's correlation coefficient (r). We also computed Lin's concordance coefficient correlation ($\rho$). Lin's coefficient combines measures of precision and accuracy to determine whether the observed data deviate significantly from the line of perfect concordance. The agreement of continuous data between two measurements was estimated using the 95% limits of the agreement method developed by Bland and Altman. The agreement of categorical data between the Western and Eastern criteria was estimated with a cross-table, and the Kappa value was calculated. The Kaplan–Meier (KM) method was used to estimate the OS differences using the log-rank test. The Cox proportional hazards model, in which stepwise selection was used for variable selection with entry ($p < 0.1$) and removal ($p > 0.15$) limits, was employed to identify factors that were independently associated with OS. Variable risk is expressed as a relative risk with a corresponding 95% confidence interval (CI). Differences with values of $p < 0.05$ were considered statistically significant. In order to find out optimal sex-specific cut-off values in our study population, we performed subgroup analysis of the KM curve according to different gender. Then, we determined optimal sex-specific cut-off values to predict mortality, with the aid of maximally selected rank statistics, as described by Lausen [14,21].

## 3. Results

### 3.1. Clinical and laboratory assessment

Dynamic CT was successfully performed and processed in all 146 patients. The subjects included 63 females and 83 males with a mean age of 65.5 (36.7–92.2) y/o, BW of 59.2 (36.6–89.0) kg, BH of 162.0 (144.3–180.0) cm, BMI of 22.5 (14.9–31.5) $kg/m^2$ and Alb level of 40.8 (18.0–53.0) g/L. In total, 33 patients were underweight and 113 patients were non-underweight after adjusting age. Seventy-nine patients were ≦70 y/o, and 57 patients were >70 y/o. Fifty patients (34.2%) had diabetes, and 27 patients (18.5%) had a history of smoking. Twenty-eight patients were classified as AJCC stage 1 and 2, 29 patients were classified as stage 3, and 89 patients were classified as stage 4. Twenty-eight patients received curative resection and 118 patients didn't. The mean TSM, VAT, and SAT areas were 109.1 $cm^2$, 112.7 $cm^2$ and 104.2 $cm^2$, respectively. Ninety-seven patients (97/146, 66.4%) had sarcopenia, and 49 patients (49/146, 33.6%) did not have sarcopenia according to the Western criteria. Gender, BH, BW, BMI, Alb level, and TSM and SAT areas were significantly associated with sarcopenia diagnosed by the Western criteria ($p < 0.05$). Sixteen patients (16/146, 11.0%) had

sarcopenia, and 130 (130/146, 89%) did not have sarcopenia according to the Eastern criteria. BW, BMI, Alb level, and TSM, VAT and SAT area were significantly associated with sarcopenia diagnosed by the Eastern criteria ($p < 0.05$). Visceral obesity was not associated with sarcopenia diagnosed by the Western ($p = 0.146$) but was significantly associated with the Eastern criteria ($p = 0.017$) (Table 1) and the presence of diabetes ($p = 0.035$).

### 3.2. Body composition analysis by different institutes

Significant strong correlations of the TSM ($r = 0.974$, $p < 0.001$, Fig. 2A), VAT ($r = 0.978$, $p < 0.001$, Fig. 2B), and SAT areas ($r = 0.979$, $p < 0.001$, Fig. 2C) and the TSM index ($r = 0.953$, $p < 0.001$) were found between the measurements of the Russian Institute in Moscow and our measurements (Fig. 2D, Table 2). The concordance correlation coefficients were $\rho = 0.950$ for the TSM area, $\rho = 0.970$ for the VAT area, $\rho = 0.979$ for the SAT area and $\rho = 0.913$ for the TSM index. On the Bland–Altman plot, the percentages of points within the 95% limits of agreement were as follows: 94.5% (138/146) for the TSM area, 95.2% (139/146) for the VAT area, 97.3% (142/146) for the SAT area and 93.8% (137/146) for the TSM index (Fig. 3, Table 2). Regarding the diagnosis of sarcopenia, 97 patients (66.4%) had sarcopenia according to the Western criteria, and 16 patients (11%) had sarcopenia according to the Eastern criteria. Only low agreement was noted (Kappa value: 0.028, $p = 0.149$) between the Western and Eastern criteria.

**Table 2**
Statistical analysis of the correlation, concordance and points within the 95% limits of agreement between our measurements and those of the Russian institute. High correlation, concordance and numbers of points within the 95% limits of agreement can be found in all comparisons.

| Comparison between measurements by two institutes | Person's correlation coefficient (r) | p value | Concordance correlation coefficient (ρ) | Points within the 95% limits of agreement |
|---|---|---|---|---|
| TSM area | 0.974 | <0.001* | 0.950 | 94.5% (138/146) |
| VAT area | 0.978 | <0.001* | 0.970 | 95.2% (139/146) |
| SAT area | 0.979 | <0.001* | 0.979 | 97.3% (142/146) |
| TSM index | 0.952 | <0.001* | 0.913 | 93.8% (137/146) |

TSM: total skeletal muscle, VAT: visceral adipose tissue, SAT: subcutaneous adipose tissue. TSM index = TSM area/body height $(m)^2$, *: $p < 0.05$.

### 3.3. Univariate and multivariate analyses of predictors of survival

The median survival was 9.34 months (range, 0.36–42.77 months) in our population. The median survival was 17.03 months (range, 4.70–38.50 months) for AJCC stage 1 and 2, 10.95 months (range, 0.86–42.77 months) for stage 3 and 6.67 months (range, 0.36–28.08 months) for stage 4 patients with pancreatic cancer in this study. The median survival was 10.13 months (0.43–42.77 months) for the non-sarcopenic group and 5.23 months (0.36–12.07 months) for the sarcopenic group as diagnosed by the Eastern criteria. In the univariate analysis, a diagnosis of sarcopenia by the Eastern criteria ($p = 0.008$, Fig. 4A) and an advanced AJCC stage

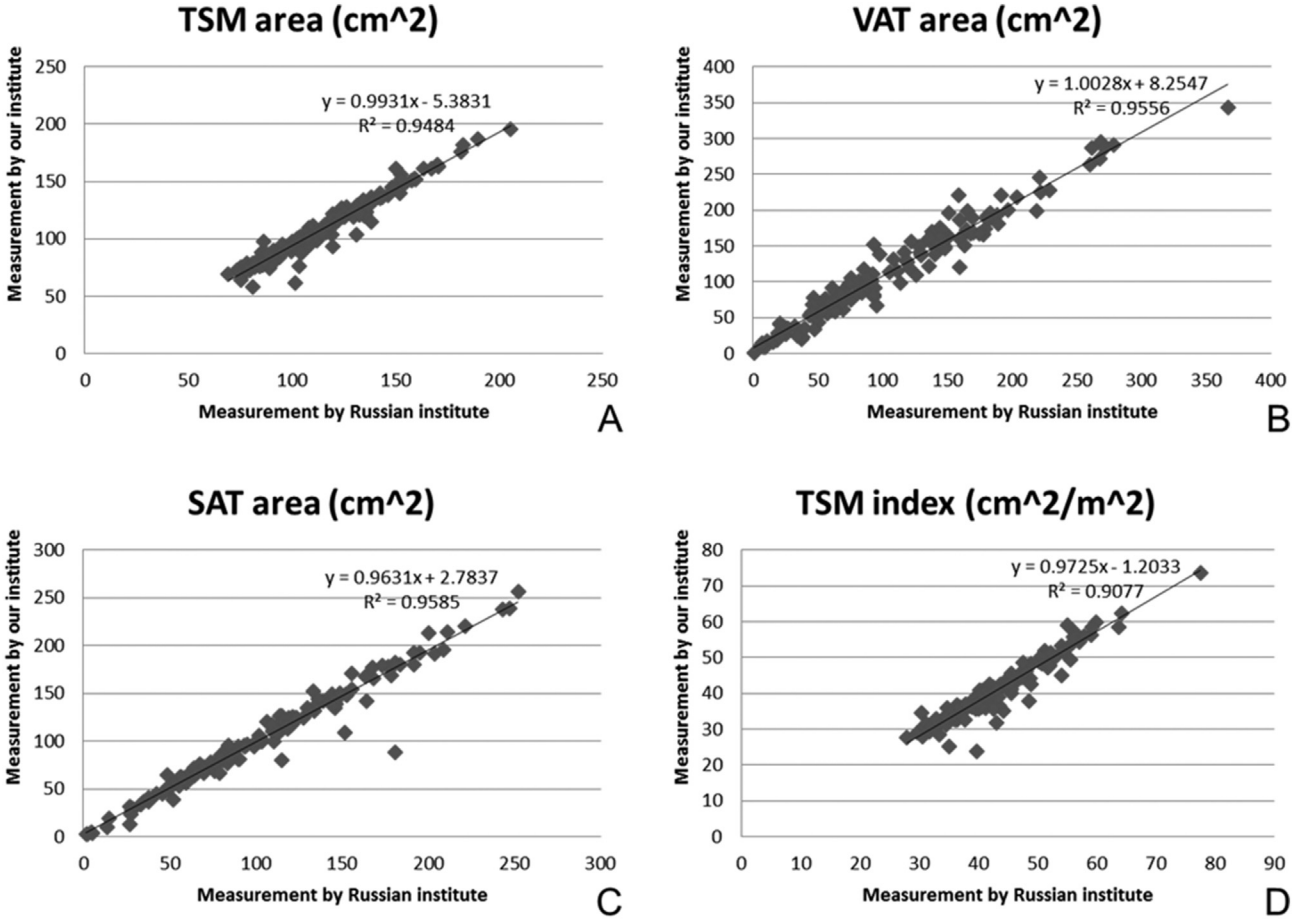


**Fig. 2.** The scatter-plots show strong correlation between measurements of the TSM (A), VAT (B), and SAT (C) areas and the TSM index (D) by our institute and the Russian institute. TSM: total skeletal muscle, VAT: visceral adipose tissue, SAT: subcutaneous adipose tissue. TSM index = TSM area/body height $(m)^2$.

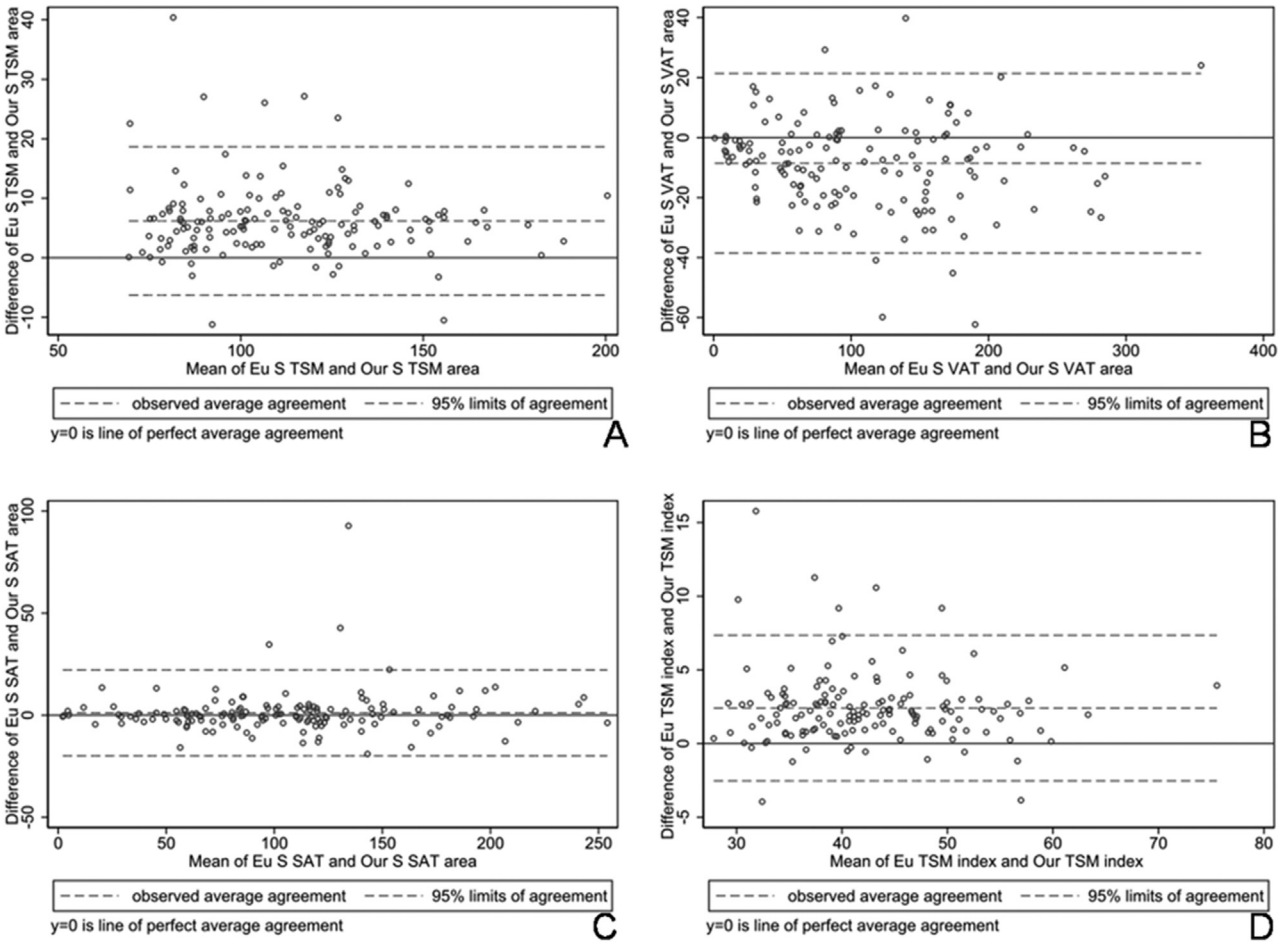


**Fig. 3.** The Bland–Altman 95% limits of agreement for the TSM (A), VAT (B), and SAT (C) areas and the TSM index (D).

**Table 3**
Clinical, laboratory factors and presence of sarcopenia as diagnosed by different criteria associated with overall survival in the univariate analysis.

| Univariate analysis | HR | 95% CI | p value |
|---|---|---|---|
| F/M | 0.961 | 0.631–1.465 | 0.855 |
| Age ≦70 or >70 y/o | 0.933 | 0.611–1.425 | 0.749 |
| Underweight (age-adjusted) | 1.136 | 0.603–2.138 | 0.693 |
| Alb ≦40 or >40 g/L | 0.737 | 0.481–1.128 | 0.160 |
| Diabetes | 1.096 | 0.713–1.685 | 0.675 |
| Smoking | 0.665 | 0.391–1.131 | 0.132 |
| AJCC stage 1, 2 and 3 versus 4 | 2.513 | 1.610–3.923 | <0.001* |
| Received curative resection | 0.364 | 0.204–0.648 | 0.001* |
| Sarcopenia by Western criteria | 0.807 | 0.614–1.462 | 0.807 |
| Sarcopenia by Eastern criteria | 2.428 | 1.266–4.656 | 0.008* |
| Visceral obesity | 1.637 | 0.662–4.044 | 0.286 |

F: female, M: male.

($p < 0.001$, Fig. 4C) were unfavorable prognostic factors. In contrast, a diagnosis of sarcopenia by the Western criteria was not a prognostic factor ($p = 0.807$, Fig. 4B). Patients received curative resection was a favorable prognostic factor ($p = 0.001$). The presence of visceral obesity also had no significant effect on OS ($p = 0.286$, Fig. 4D). Other clinical or laboratory-associated factors, including gender, age, age-adjusted underweight, low Alb level, diabetes and smoking, had no significant effects on OS (Table 3). In the multivariate analysis, advanced AJCC stage (hazard ratio [HR] = 1.807 and 95% CI: 1.051–3.105, $p = 0.032$) and a diagnosis of sarcopenia by the Eastern criteria (HR = 2.310 and 95% CI: 1.200–4.444, $p = 0.012$) were determinants of OS in patients with pancreatic cancer (Table 4).

### *3.4. Subgroup analysis by gender and maximally selected rank statistics to find out optimal cut-off values*

In female, the median survival was 9.34 months for the non-sarcopenic group and 4.31 months for the sarcopenic group as diagnosed by Eastern criteria; 9.34 months for the non-sarcopenic group and 7.50 months for the sarcopenic group as diagnosed by Western criteria. Sarcopenia was a significant prognostic factor ($p < 0.001$, Fig. 5A) by Eastern criteria but wasn't a prognostic factor ($p = 0.930$, Fig. 5B) by Western criteria in female. In male, the median survival was 11.21 months for the non-sarcopenic group and 8.38 months for the sarcopenic group as diagnosed by Eastern criteria; 12.13 months for the non-sarcopenic group and 10.13 months for the sarcopenic group as diagnosed by Western criteria. Sarcopenia was not a prognostic factor ($p = 0.320$ and $p = 0.873$, Fig. 5C and D) by Eastern and Western criteria in male. The optimal cut-off for defining sarcopenia in female was 32.53 $cm^2/m^2$ which was a significant prognostic factor by long-rank test. No optimal cut-off value can be found in male as a prognostic factor.

## 4. Discussion

In this study, sarcopenia defined by Eastern criteria, but not by Western criteria, was observed to be associated with worse OS in patients with pancreatic cancer in Taiwan. In addition, high correlation, concordances and agreements of body composition analysis, including the TSM, VAT, and SAT areas measured by CT scans, were

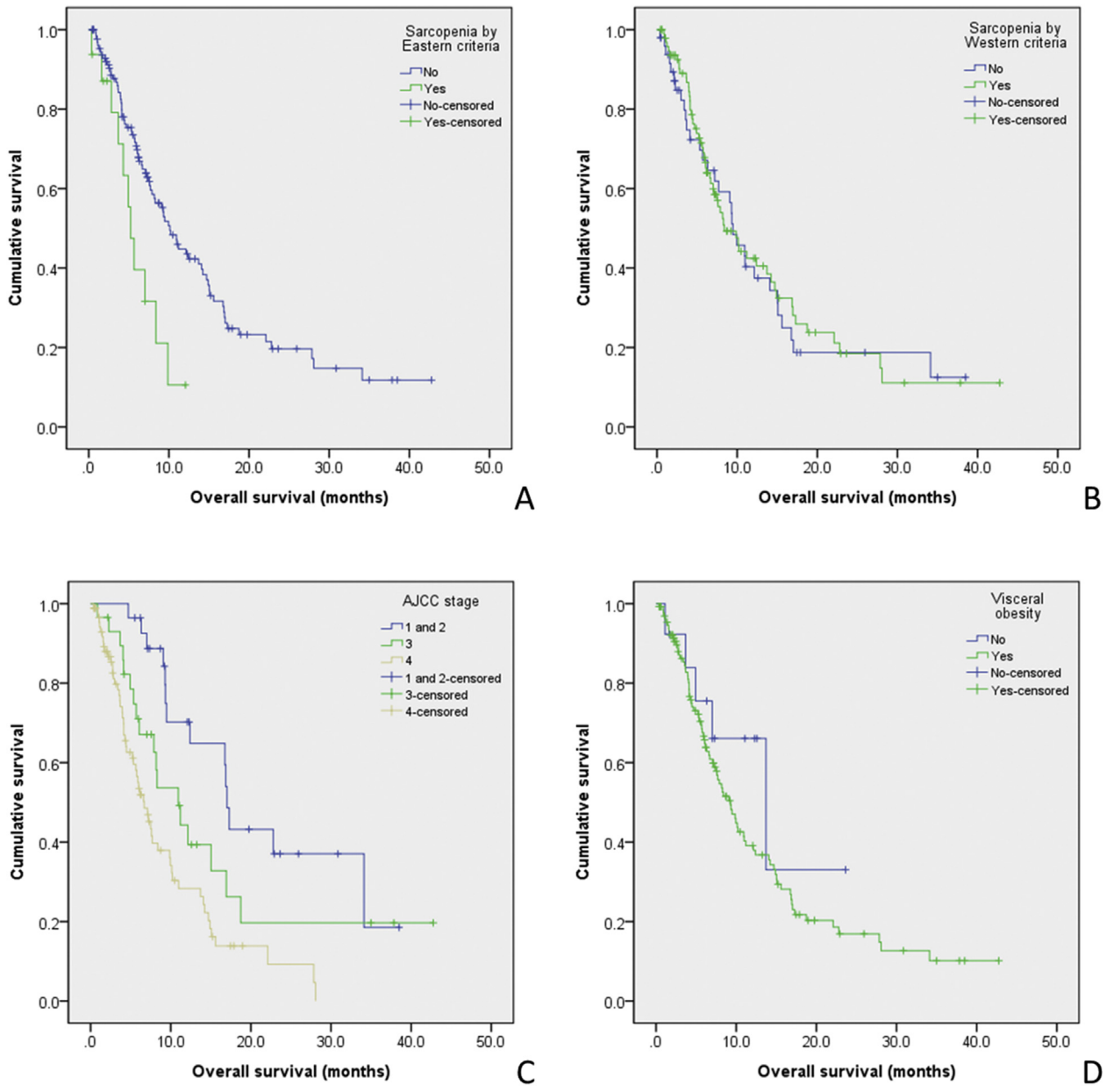


**Fig. 4.** Comparison of survival rates stratified by the presence of sarcopenia. Overall survival was significantly different when using the Eastern criteria (A, $p = 0.008$) than when using the Western criteria (B, $p = 0.807$). The AJCC stage is also an unfavorable prognostic factor (C, $p < 0.001$) but presence of visceral obesity is not a significant prognostic factor ($p = 0.286$).

**Table 4**
AJCC stage and presence of sarcopenia as diagnosed by the Eastern criteria associated with overall survival in the multivariate analysis.

| Multivariate analysis | HR | 95% CI | p value |
|---|---|---|---|
| AJCC stage 1, 2 and 3 versus 4 | 1.807 | 1.051–3.105 | 0.032* |
| Received curative resection | 0.545 | 0.270–1.100 | 0.090 |
| Sarcopenia by Eastern criteria | 2.310 | 1.200–4.444 | 0.012* |

observed between two different institutes. Sarcopenia is defined as the presence of both low muscle mass and low muscle function by the European Working Group on Sarcopenia in Older People [1]. Cross-sectional imaging serves as the gold standard for muscle mass evaluation [9]. According to the literature, among the multiple slices used to assess body composition, a single slice at the L3 level can represent the whole body skeletal muscle mass and VAT [17,22]. The CT scanner differentiates body tissues by HU based on tissue-specific attenuation values. Because of the significant difference in body composition between males and females, sex-specific skeletal muscle index cut-off values with adjustment of BH at the level of the L3 vertebra (52.4 $cm^2/m^2$ for males and 38.5 $cm^2/m^2$ for females) are used to define sarcopenia and are associated with mortality and survival in many types of cancer [12]. Therefore, adequate cut-off values should be independent of gender and BH. However, in this study, the diagnosis of sarcopenia by the Western criteria was significantly associated with gender and BH. In contrast, the diagnosis of sarcopenia by the Eastern criteria was only associated with BW, BMI and Alb level. These findings demonstrated that the Eastern criteria may be more appropriate for defining sarcopenia in Eastern countries, including Taiwan.

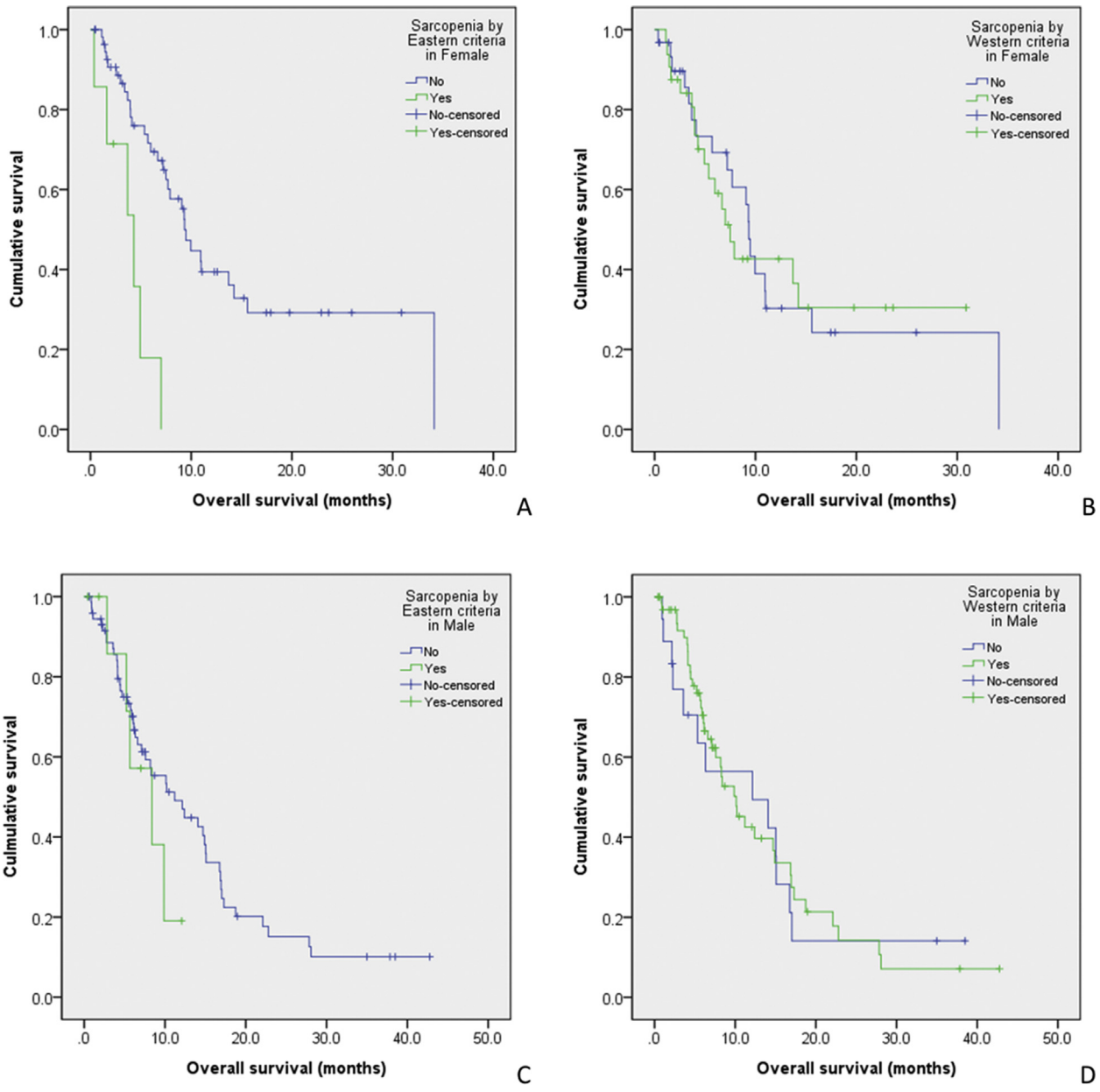


**Fig. 5.** Comparison of survival rates stratified by gender and presence of sarcopenia. Overall survival was significantly different when using Eastern criteria (A, $p < 0.001$) than when using Western criteria in female (B, $p = 0.930$). No significant difference was noted when using Eastern and Western criteria in male (C and D, $p = 0.320$ and $p = 0.873$).

To clarify the discordance of diagnoses, we compared our measurements with those of an independent research team in Moscow who were blinded to the measurement results. We analyzed the non-enhanced CT images at the L3 level with the same threshold settings as the Russian institute. Strong correlations (>0.9) and concordances (>0.9) and a high number of points within the 95% limits of agreement were observed between the measurements made by our team and by the Russian institute. Therefore, CT scanning is a reliable and reproducible modality for body composition analysis and is suitable for international multicenter studies or trials. Moreover, the disagreement of the diagnosis of sarcopenia (Kappa value: 0.028) was due to the different criteria used in this study. Differences in body shape and composition exist between Western and Eastern populations. More pancreatic cancer patients (66.4%, 97/146) were classified as sarcopenic at diagnosis by the Western criteria compared with those classified by the Eastern criteria (11.0%, 16/146). Our study also demonstrated that patients with pancreatic cancer who were sarcopenic by the Western criteria showed no significant difference in OS compared with those who were not sarcopenic (Fig. 4B, $p = 0.807$). However, in the univariate analysis, patients who were sarcopenic by the Eastern criteria showed a significant difference in OS compared with those who were not sarcopenic (Fig. 4A, $p = 0.008$), and this difference in OS remained in the multivariate analysis after adjustment for the AJCC stage ($p = 0.012$). Other clinical factors, including underweight and low Alb levels, were not associated with OS. Therefore, sarcopenia may serve as an independent unfavorable prognostic factor for the OS of patients with pancreatic cancer after the appropriate diagnostic criteria are selected. The Eastern criteria, instead of the Western criteria, are more suitable for evaluating sarcopenia in Taiwanese populations and may be a predictive marker of the OS of pancreatic cancer in Taiwan.

VO was reported to be associated with poor clinical outcomes and/or post-operative complications in pancreatic cancer [23–25]. In this study, VO was associated with the presence of diabetes but was not associated with sarcopenia defined by either the Eastern or Western criteria. Additionally, VO was not associated with OS in our study. Further studies are needed on the clinical effects of VO and combinations of the other assessed body composition measurements on the clinical outcomes of pancreatic cancer when the appropriate diagnostic criteria are employed. Previous studies in Europe and America have followed the protocol in Prado's article. The prevalence of sarcopenia in patients with pancreatic cancer is around 60% [26,27]. However, the study in Korea had lower prevalence (around 20%) of sarcopenia in advanced pancreatic cancer received palliative chemotherapy [7]. The prevalence and the cut-off of this article (<42.2 $cm^2/m^2$ in male and <33.9 $cm^2/m^2$ in female) were more similar to our study. Besides, the optimal cut-off value by maximally selected rank statistics for sarcopenia in female is 32.53 $cm^2/m^2$ which is more close to Eastern criteria (29.6 $cm^2/m^2$) than Western criteria (38.5 $cm^2/m^2$). In contrast, no optimal cut-off value can be found in male. Therefore, the sarcopenia may have more effect on female than male in pancreatic cancer and Eastern criteria may be more suitable to predict prognosis in Taiwan population.

There are some limitations to our study. This is a retrospective study with a modest (N = 146) case number. Additional international multicenter studies are needed to confirm our findings. We did not include ECOG 2–4 patients because these patients have a relatively poor prognosis, and comorbidities, such as infection, may be present in this population. However, our measurements of the TSM, VAT, and SAT areas and the TSM index were reviewed by two institutes, and high correlation and reproducibility were demonstrated. We did not compare different grades of pancreatic cancer because the pathological results were not always available. Patients received curative resection is a favorable prognostic factor in univariate analysis but the effect is not significant in multivariate analysis after adjusting with AJCC stage. We did not compare different treatments, such as surgery, chemotherapy, radiotherapy and symptomatic treatment, because we aimed to determine whether sarcopenia is an independent prognostic factor before treatment rather than a prognostic factor associated with various treatments. Our results support our hypothesis, and further study is indicated to identify the optimal diagnostic criteria in different study populations. Further international multicenter study may be indicated to determine adequate cut-off between different regions and ethnicities. A large scale study may also indicate to analyze the effects of sarcopenia in different treatments.

In conclusion, our study demonstrates that CT scanning is a robust modality for body composition analysis in different institutes, different diagnostic criteria for sarcopenia may dramatically affect the diagnoses in given populations, and sarcopenia is an important prognostic factor for pancreatic cancer when the appropriate diagnostic criteria are selected.

## Conflict of interest

The authors declare that there is no conflict of interest.

## References


[1] Cruz-Jentoft AJ, Baeyens JP, Bauer JM, Boirie Y, Cederholm T, Landi F, et al. Sarcopenia: European consensus on definition and diagnosis: report of the European Working Group on sarcopenia in older people. Age Ageing 2010;39:412–23.

[2] Argiles JM, Busquets S, Felipe A, Lopez-Soriano FJ. Muscle wasting in cancer and ageing: cachexia versus sarcopenia. Adv Gerontol 2006;18:39–54.

[3] Carrero JJ, Johansen KL, Lindholm B, Stenvinkel P, Cuppari L, Avesani CM. Screening for muscle wasting and dysfunction in patients with chronic kidney disease. Kidney Int 2016;90:53–66.

[4] Collamati A, Marzetti E, Calvani R, Tosato M, D'Angelo E, Sisto AN, et al. Sarcopenia in heart failure: mechanisms and therapeutic strategies. J Geriatr Cardiol 2016;13:615–24.

[5] Ninomiya G, Fujii T, Yamada S, Yabusaki N, Suzuki K, Iwata N, et al. Clinical impact of sarcopenia on prognosis in pancreatic ductal adenocarcinoma: a retrospective cohort study. Int J Surg 2017;39:45–51.

[6] Sur MD, Namm JP, Hemmerich JA, Buschmann MM, Roggin KK, Dale W. Radiographic sarcopenia and self-reported exhaustion independently predict NSQIP serious complications after pancreaticoduodenectomy in older adults. Ann Surg Oncol 2015;22:3897–904.

[7] Choi Y, Oh DY, Kim TY, Lee KH, Han SW, Im SA, et al. Skeletal muscle depletion predicts the prognosis of patients with advanced pancreatic cancer undergoing palliative chemotherapy, independent of body mass index. PLoS One 2015;10. e0139749.

[8] Rollins KE, Tewari N, Ackner A, Awwad A, Madhusudan S, Macdonald IA, et al. The impact of sarcopenia and myosteatosis on outcomes of unresectable pancreatic cancer or distal cholangiocarcinoma. Clin Nutr (Edinburgh, Scotland) 2016;35:1103–9.

[9] Yip C, Dinkel C, Mahajan A, Siddique M, Cook GJ, Goh V. Imaging body composition in cancer patients: visceral obesity, sarcopenia and sarcopenic obesity may impact on clinical outcome. Insights Imaging 2015;6:489–97.

[10] Kazemi-Bajestani SM, Mazurak VC, Baracos V. Computed tomography-defined muscle and fat wasting are associated with cancer clinical outcomes. Semin Cell Dev Biol 2016;54:2–10.

[11] Mourtzakis M, Prado CM, Lieffers JR, Reiman T, McCargar LJ, Baracos VE. A practical and precise approach to quantification of body composition in cancer patients using computed tomography images acquired during routine care. Appl Physiol Nutr Metab 2008;33:997–1006.

[12] Prado CM, Lieffers JR, McCargar LJ, Reiman T, Sawyer MB, Martin L, et al. Prevalence and clinical implications of sarcopenic obesity in patients with solid tumours of the respiratory and gastrointestinal tracts: a population-based study. Lancet Oncol 2008;9:629–35.

[13] Fujiwara N, Nakagawa H, Kudo Y, Tateishi R, Taguri M, Watadani T, et al. Sarcopenia, intramuscular fat deposition, and visceral adiposity independently predict the outcomes of hepatocellular carcinoma. J Hepatol 2015;63:131–40.

[14] Budczies J, Klauschen F, Sinn BV, Gyorffy B, Schmitt WD, Darb-Esfahani S, et al. Cutoff Finder: a comprehensive and straightforward Web application enabling rapid biomarker cutoff optimization. PLoS One 2012;7, e51862.

[15] Edge SB, Compton CC. The American Joint Committee on Cancer: the 7th edition of the AJCC cancer staging manual and the future of TNM. Ann Surg Oncol 2010;17:1471–4.

[16] Cederholm T, Bosaeus I, Barazzoni R, Bauer J, Van Gossum A, Klek S, et al. Diagnostic criteria for malnutrition – an ESPEN consensus statement. Clin Nutr (Edinburgh, Scotland) 2015;34:335–40.

[17] Gomez-Perez SL, Haus JM, Sheean P, Patel B, Mar W, Chaudhry V, et al. Measuring abdominal circumference and skeletal muscle from a single cross-sectional computed tomography image: a step-by-step guide for clinicians using National Institutes of Health ImageJ. J Parenter Enteral Nutr 2016;40:308–18.

[18] Matsuzawa Y, Nakamura T, Shimomura I, Kotani K. Visceral fat accumulation and cardiovascular disease. Obes Res 1995;3(Suppl 5):645S–7S.

[19] Tsujinaka S, Konishi F, Kawamura YJ, Saito M, Tajima N, Tanaka O, et al. Visceral obesity predicts surgical outcomes after laparoscopic colectomy for sigmoid colon cancer. Dis Colon Rectum 2008;51:1757–65. discussion 65–67.

[20] Mathur A, Hernandez J, Shaheen F, Shroff M, Dahal S, Morton C, et al. Preoperative computed tomography measurements of pancreatic steatosis and visceral fat: prognostic markers for dissemination and lethality of pancreatic adenocarcinoma. HPB (Oxford) 2011;13:404–10.

[21] Lausen B, Schumacher M. Maximally selected rank statistics. Biometrics 1992;48:73–85.

[22] Schweitzer L, Geisler C, Pourhassan M, Braun W, Gluer CC, Bosy-Westphal A, et al. Estimation of skeletal muscle mass and visceral adipose tissue volume by a single magnetic resonance imaging slice in healthy elderly adults. J Nutr 2016;146:2143–8.

[23] van Dijk DP, Bakens MJ, Coolsen MM, Rensen SS, van Dam RM, Bours MJ, et al. Low skeletal muscle radiation attenuation and visceral adiposity are associated with overall survival and surgical site infections in patients with pancreatic cancer. J Cachexia Sarcopenia Muscle 2017;8:317–26.

[24] Kirihara Y, Takahashi N, Hashimoto Y, Sclabas GM, Khan S, Moriya T, et al. Prediction of pancreatic anastomotic failure after pancreatoduodenectomy: the use of preoperative, quantitative computed tomography to measure remnant pancreatic volume and body composition. Ann Surg 2013;257:512–9.

[25] Tranchart H, Gaujoux S, Rebours V, Vullierme MP, Dokmak S, Levy P, et al. Preoperative CT scan helps to predict the occurrence of severe pancreatic fistula after pancreaticoduodenectomy. Ann Surg 2012;256:139–45.

[26] Baldwin A, Kundranda MN, Todd E, Whitehead RP, Winston R, Weber J, et al. Sarcopenia as a predictor of mortality in advanced pancreatic cancer. J Clin Oncol 2015;33:268.

[27] Carrara G, Pecorelli N, De Cobelli F, Cristel G, Damascelli A, Beretta L, et al. Preoperative sarcopenia determinants in pancreatic cancer patients. Clin Nutr (Edinburgh, Scotland) 2017;36:1649–53.