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RESEARCH ARTICLE

# Reliable and robust method for abdominal muscle mass quantification using CT/MRI: An explorative study in healthy subjects

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# Abstract

# Background

Quantification of abdominal muscle mass by cross-sectional imaging has been increasingly used to diagnose sarcopenia; however, the technical method for quantification has not been standardized yet. We aimed to determine an optimal method to measure the abdominal muscle area.

# Methods

Among 50 consecutive subjects who underwent abdominal CT and MRI for possible liver donation, total abdominal muscle area (TAMA) and total psoas muscle area (TPA) at the L3 inferior endplate level were measured by two blinded readers. Inter-scan agreement between CT and MRI and inter-reader agreement between the two readers were evaluated using intraclass correlation coefficient (ICC) and within-subject coefficient of variation (WSCV). To evaluate the effect of measurement level, one reader measured TAMA and TPA at six levels from the L2 to L4 vertebral bodies.

# Results

TAMA was a more reliable biomarker than TPA in terms of inter-scan agreement (ICC: 0.928 vs. 0.788 for reader 1 and 0.853 vs. 0.821 for reader 2, respectively; WSCV: 8.3% vs. 23.4% for reader 1 and 10.4% vs. 22.3% for reader 2, respectively) and inter-reader agreement (ICC: 0.986 vs. 0.886 for CT and 0.865 vs. 0.669 for MRI, respectively; WSCV: 8.2% vs. 16.0% for CT and 11.6% vs. 29.7% for MRI, respectively). In terms of the measurement level, TAMA did not differ from the L2<sub>inf</sub> to L4<sub>inf</sub> levels, whereas TPA increased with a decrease in measurement level.

## Conclusions

TAMA is a better biomarker than TPA in terms of inter-scan and inter-reader agreement and robustness to the measurement level. CT was a more reliable imaging modality than MRI. Our results support the use of TAMA measured by CT as a standard biomarker for abdominal muscle area measurement.

# Introduction

Sarcopenia is characterized by an age-related decline of muscle mass with low muscle strength and/or physical performance, and it has recently been assigned the International Classification of Diseases (ICD-10CM) code [M62.84] [1–3]. The assessment of muscle and fat tissues is essential in the management of patients with obesity, aging, and wasting diseases [4, 5]. Recent accumulating evidence strongly suggests that sarcopenia is predictive of certain clinical outcomes including postoperative complications, hospital stay, and final survival/mortality in various diseases [6–11]. Therefore, sarcopenia is regarded as a diagnostic and prognostic biomarker.

Cross-sectional imaging techniques, such as magnetic resonance imaging (MRI) and computed tomography (CT), are the most reliable methods and thus, regarded as gold standard methods for quantifying the muscle mass and visceral fat area (VFA) or volume. CT has been the most widely used cross-sectional imaging modality, because it is readily available in most hospitals worldwide owing to its reasonable cost and high scan speed. Currently, the use of MRI for the abdomen has been increasing because of radiation exposure concerns as well as the potential to achieve improved tissue contrast [12, 13].

However, the quantification of abdominal muscle mass by CT and MRI as a diagnostic biomarker for sarcopenia assessment has not been fully validated. The two main requirements for validating the abdominal muscle area as a quantitative biomarker for sarcopenia are as follows: (1) clinical validation, which involves the evidentiary process of linking the abdominal muscle area with clinical endpoints such as survival or mortality, and (2) standardization, which is the process of implementing and developing technical standards [14]. In terms of clinical validation, increasing evidence has demonstrated a strong association of the abdominal muscle area measured by cross-sectional imaging with survival of patients with various diseases such as cancer, cardiovascular disease, or trauma [15–17].

However, the technical method for quantifying abdominal muscle mass by CT/MRI has not been standardized because of the following issues: (1) The area that should be segmented on abdominal CT/MRI has not been standardized, because segmentation areas vary among total abdominal muscle area (TAMA), total psoas muscle area (TPA), and other muscle areas; (2) it is unclear whether CT and MRI are interchangeable for quantifying abdominal muscle mass because of insufficient evidence on inter-scan agreement between CT and MRI; and (3) the measurement level of abdominal muscle mass has not been standardized; it varies from L2 to L4 in prior studies [18–20].

So far, only a few studies have examined these issues [20]. Therefore, we aimed to determine an optimal method for measuring the abdominal muscle area.

# Materials and methods

This retrospective study adhered to the guidelines established by the Declaration of Helsinki, and it was approved by the Institutional Review Board of Asan Medical Center, Seoul, Korea (No. 2018–0382). The requirement for informed consent was waived.

#### Patients

We retrospectively searched our institution's computerized databases for a clinical cohort of liver transplantation and found 50 consecutive healthy subjects who underwent abdominal CT and MRI for possible liver donation from March 2016 to June 2016. All the liver donors underwent CT and MRI within a 2-week interval as a preoperative work-up for liver transplantation.

CT and MR images were anonymized and transferred from our picture archiving and communication system (PetaVision; Hyundai Information Technology, Seoul, Korea) to the central imaging review system (AiCRO<sup>TM</sup>; Asan Image Metrics, Seoul, Korea). A staff (S.E.W.) of an imaging core lab in our institution (Asan Image Metrics, <u>www.aim-aicro.com</u>) independently performed the imaging process following our request.

#### **Image acquisition**

**Computed tomography.** The CT examinations were performed using a Somatom Definition AS+ scanner (Siemens Healthineers, Erlangen, Germany). The CT examinations were obtained with standard exposure parameters (200 effective mAs and 120 kVp; the actual radiation dose was adjusted according to the patient's body size and shape by automatically modulating the tube current, a detector configuration of 1.5 mm × 16 mm, a table feed of 24 mm per rotation, and a gantry rotation time of 0.5 s. Contrast-enhanced CT scans were performed in the supine position in the portal venous phase with a fixed delay of 70 s after contrast agent injection. By using an autoinjector, 120 mL of nonionic contrast material was intravenously administered at the rate of 3 mL/s. The images were reconstructed with a section thickness and interval of 5 mm.

**Magnetic resonance imaging.** Abdominal MRI was performed using a 1.5T scanner (Magnetom Avanto; Siemens Healthineers, Erlangen, Germany) with dedicated six-channel torso array coils. The maximum gradient strengths were 45 mT/m for the amplitude and 200 mT/m/s for the slew rate. The parameters for the transverse breath-hold T1-weighted gradient-echo images without fat-suppression were as follows: repetition time, 4.2 ms; echo time, 2.5 ms; flip angle, 7.0°; slice thickness, 3 mm; field of view, 341 × 420 mm; and matrix size,  $208 \times 256$ . These images were used for body morphometric analysis. The other imaging sequences of the abdominal MRI included transverse T2-weighted fast spin-echo imaging, MR cholangiography, in-phase and opposed-phase chemical shift imaging, and contrast-enhanced multiphasic MRI.

**Body morphometric analysis.** Our imaging processing team members (Y.S., S.E.W., and Y.S.S.) developed AsanJ-Morphometry<sup>TM</sup>, a software dedicated to the measurement of abdominal muscle and fat area, on the basis of ImageJ (NIH, Bethesda, MD, USA). The software is publicly available for non-profit research in a website (available at http://datasharing. aim-aicro.com/en/morphometry).

TAMA (cm<sup>2</sup>) including all the muscles on the selected axial images, i.e., psoas, paraspinal, transversus abdominis, rectus abdominis, quadratus lumborum, and internal and external obliques, was demarcated using predetermined thresholds for the Hounsfield unit (HU) on CT (>–30 HU and  $\leq$ 150 HU) and the signal intensity (SI) on precontrast T1-weighted MRI (>350 SI and  $\leq$ 750 SI). The VFA (cm<sup>2</sup>) and subcutaneous fat area (SFA) (cm<sup>2</sup>) were also demarcated using the fat tissue thresholds in CT ( $\leq$ –30) and MRI (>100 SI and  $\leq$ 350 SI) (Fig 1).

To evaluate the inter-reader and inter-scan agreements, we selected CT and MR images at the L3 inferior endplate level. Reader 1 (J.P., image analyst with 11 years experience) and reader 2 (J.R.G., abdominal radiologist with 5 years experience) independently measured TAMA, VFA, SFA with blinding to clinical information. The time spent on measuring TAMA, TPA, and VFA using the AsanJ-Morphometry<sup>TM</sup> software was recorded only by a reader (J.

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**Fig 1. Semi-automatic segmentation for body morphometric analysis.** (A) ImageJ after running the program and uploading a CT or an MR image. (B) Adjustment of the threshold of total abdominal muscle area (TAMA), total psoas muscle area (TPA), and visceral fat area (VFA). (C) Measurement of the semi-automatic regions of interest (ROI). (D) Segmentation and color mapping.

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P.). The definition of the time spent was set to include opening the software, importing the prepared CT/MR images, finding the L3 inferior endplate level, and segmenting the abdominal muscle.

#### Level of body morphometric measurement

To evaluate the effect of measurement level on the results of body morphometric analysis, an abdominal radiologist (J.H., 9 years experience) measured TAMA, TPA, and VFA at six levels starting from the L2 to L4 vertebral bodies (Fig 2). For each vertebral body level, we performed measurements at the mid-body level (hereafter referred to as  $L2_{mid}$ ,  $L3_{mid}$ , and  $L4_{mid}$ ) and inferior endplate level (hereafter referred to as  $L2_{infb}$  L3<sub>infb</sub> and L4<sub>inf</sub>).



Fig 2. Representative images of TAMA, TPA, and VFA at different measurement levels. The vertebral bodies were measured at different vertebral levels. The axial CT images were segmented into TAMA (purple), TPA (blue), and VFA (green).

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## Statistical analysis

Data are expressed as mean  $\pm$  standard deviation (SD). The mean values of body morphometric analysis were compared by Student's *t*-test or analysis of variance (ANOVA) and post-hoc multiple comparison tests.

The measurement agreements between CT and MRI (inter-scan agreement) and between readers 1 and 2 (inter-reader agreement) were assessed on the basis of the intraclass correlation coefficient (ICC) of a single measurement calculated according to the two-way random-effects

model, for consistency. The 95% confidence intervals (CIs) associated with the ICCs were also determined. The ICC estimates the overall correlation between all possible values within the variable taken by the same reader. The ICCs were interpreted as poor (0.00–0.49), fair (0.50–0.74), and good (0.75–1.00) [21].

To evaluate the inter-reader and inter-scan agreements, we used statistical tools recommended by the methodological guidelines of the Radiological Society of North America-Quantitative Imaging Biomarkers Alliance (RSNA-QIBA) (https://www.rsna.org/QIBA) and Park et al. [14–16]. By using these methods, the within-subject coefficient of variation (WSCV) and repeatability coefficient (RC) were calculated. Bland-Altman plots were also constructed. To evaluate the difference between measurement levels, one-way ANOVA was performed with post-hoc Tukey-Kramer pairwise comparison tests. For statistical analysis, we used a web-calculator (available at http://datasharing.aim-aicro.com/reliability) and MedCalc version 13.1.2 (MedCalc Software, Ostend, Belgium).

#### Results

#### Patients

The average age (mean  $\pm$  SD) of the 50 subjects was 29.9  $\pm$  8.3 years (range, 17–57 years; median, 37; interquartile range, 11.5). The subjects included 29 men (mean age, 29.03 years; range, 18–57 years) and 21 women (mean age, 31.05 years; range, 17–47 years).

#### Body morphometric analysis

The measured TAMA, TPA, and VFA values are summarized in Table 1. There was no significant difference between reader 1 and reader 2 with regard to the measurement of TAMA (*t*-test, P = 0.925 for CT, P = 0.121 for MRI), TPA (P = 0.738 for CT, P = 0.223 for MRI), and VFA (P = 0.919 for CT, P = 0.01). Similarly, no significant difference was observed between CT and MRI with regard to the measurement of TAMA (*t*-test, P = 0.333 for reader 1, P = 0.636 for reader 2), TPA (P = 0.520 for reader 1, P = 0.097 for reader 2), and VFA (P = 0.154 for reader 1, P = 0.176 for reader 2).

By using the ImageJ-based software (AsanJ-Morphometry<sup>TM</sup>), the mean time spent by reader 1 on measuring TAMA, TPA, and VFA was  $3.63 \pm 0.57$  min for CT and  $5.65 \pm 1.55$  min for MRI (P < 0.001, *t*-test). The time spent for MRI was longer, which may be attributed to a greater difficulty in identifying the L3 inferior endplate level on MR images and the necessity of adjusting the semi-automatically drawn muscle boundaries.

Fable 1. Mean TAMA, TPA	., and VFA values derived b	y body morp	hometric analysis
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	TAMA (cm <sup>2</sup> )		TPA (cm <sup>2</sup> )		VFA (cm <sup>2</sup> )				
	СТ	MRI	P <sup>a</sup>	СТ	MRI	P <sup>a</sup>	СТ	MRI	P <sup>a</sup>
Reader 1	$137.0 \pm 37.9 \\ (137.6, 59.1)$	$144.6 \pm 40.6 \\ (139.0, 59.9)$	0.333	$18.6 \pm 8.7 \\ (17.5, 12.3)$	$17.4 \pm 9.5$ (14.6, 11.6)	0.520	67.6 ± 44.0 (57.8, 60.4)	62.0 ± 42.3 (51.1, 54.3)	0.516
Reader 2	$136.3 \pm 38.0$ (139.8, 59.8)	$132.8 \pm 34.6 \\ (127.2, 52.7)$	0.636	$18.0 \pm 8.7 \\ (16.8, 12.7)$	$14.7 \pm 6.5 \\ (14.1, 11.0)$	0.097	68.5 ± 45.2 (60.5, 64.0)	56.5 ± 42.3 (44.6, 48.6)	0.176
P <sup>b</sup>	0.925	0.121		0.738	0.223		0.919	0.525	

Data are presented as mean ± standard deviation. Data in parentheses represent the median value and interquartile range.

<sup>a</sup>Derived by comparing CT and MRI using *t*-test

<sup>b</sup>Derived by comparing reader 1 and reader 2 using *t*-test

Abbreviations: TAMA = total abdominal muscle area; TPA = total psoas muscle area; VFA = visceral fat area

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		Inter-scan agreement			
		ICC	WSCV (%)	RC	
TAMA	Reader 1	0.928	8.3	32.484	
	Reader 2	0.853	10.4	38.811	
TPA	Reader 1	0.788	23.4	11.694	
	Reader 2	0.821	22.3	10.341	
VFA	Reader 1	0.950	15.9	28.576	
	Reader 2	0.899	25.9	44.850	
		Inter-reader agreement			
TAMA	СТ	0.986	8.2	31.010	
	MRI	0.865	11.6	44.448	
TPA	СТ	0.886	16.0	8.1217	
	MRI	0.669	29.7	13.499	
VFA	СТ	0.989	6.9	13.011	
	MRI	0.954	16.6	27.169	

Table 2. Inter-scan and inter-reader agreements for TAMA, TPA, and VFA.

TAMA = total abdominal muscle area; TPA = total psoas muscle area; VFA = visceral fat area; ICC = intraclass correlation coefficient; WSCV = within-subject coefficient of variation; RC = repeatability coefficient

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#### Inter-scan and inter-reader agreements

The ICC, WSCV, and RC for inter-scan and inter-reader agreements are shown in <u>Table 2</u>. Bland-Altman plots for all pairs of comparison are illustrated in the Supporting Information <u>\$1, \$2, and \$3</u> Figs.

The comparison of the inter-scan and inter-reader agreements for TAMA, TPA, and VFA yielded ICC values that were generally higher than 0.75. However, the ICC of TAMA was higher than that of TPA with regard to both inter-scan agreement (0.928 vs. 0.788 for reader 1 and 0.853 vs. 0.821 for reader 2, respectively) and inter-reader agreement (0.986 vs. 0.886 for CT and 0.865 vs. 0.669 for MRI, respectively). Based on the WSCV, the reliability of TAMA was better than that of TPA with regard to both inter-scan agreement (8.3% vs. 23.4% for reader 1 and 10.4% vs. 22.3% for reader 2, respectively) and inter-reader agreement (8.2% vs. 16.0% for CT and 11.6% vs. 29.7% for MRI, respectively). These findings suggest that the measurement of TAMA might be a more reliable method for abdominal muscle mass quantification than the measurement of TPA.

A comparison of the inter-reader agreement between CT and MRI revealed that the ICC for CT was higher than that for MRI in the measurement of TAMA (0.986 vs. 0.865), TPA (0.886 vs. 0.669), and VFA (0.989 vs. 0.954). The WSCV for CT was also lower (i.e., better reliability) than that for MRI in the measurement of TAMA (8.2% vs. 11.6%), TPA (16.0% vs. 29.7%), and VFA (6.9% vs. 16.6%). We evaluated all regions of interest (ROI) on CT and MR images in a side-by-side manner and found that the anatomical boundary of the muscles was degraded and less clear in some parts because of artifacts such as bowel gas susceptibility artifacts, motion artifacts, or chemical shift artifacts (14/50, 28%) (Fig 3).

#### Effect of measurement level on body morphometric analysis

One-way ANOVA revealed a significant difference between measurement levels in TAMA (P = 0.003) and TPA (P < 0.001) but not in VFA (P = 0.525). The post-hoc test results for TAMA showed a significant difference only between L2<sub>mid</sub> and L3<sub>inf</sub> (P < 0.05) and between L2<sub>mid</sub> and L4<sub>mid</sub> (P < 0.05). The TAMA from L2<sub>inf</sub> to L4<sub>inf</sub> did not differ significantly (range,



Fig 3. Quality of CT and MR images for TAMA measurement. (A) In the CT image, the abdominal muscle boundary is clear. (B) In the MR image, the presence of susceptibility and motion artifacts due to bowel gas degraded the image quality of the adjacent left rectus muscle and left psoas muscle.

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122.5–139.6 cm<sup>2</sup>) (Fig 4A). The mean TAMA values of  $L3_{mid}$  and  $L3_{inf}$ , which are the most commonly used measurement levels, were 132.3 ± 36.1 cm<sup>2</sup> and 139.6 ± 36.6 cm<sup>2</sup>, with no significant difference shown by post-hoc test (P > 0.05). In contrast, TPA increased with a decrease in measurement level from  $L2_{mid}$  to  $L4_{inf}$  significant differences were noted between levels (Fig 4B). VFA did not differ among the measurement levels (Fig 4C). According to the results, the measurement of TAMA and VFA was robust to measurement level from  $L2_{inf}$  to  $L4_{inf}$ . The raw data is provided in the Supporting Information S1 File.

## Discussion

This study aimed to standardize a method for the quantification of abdominal mass using CT/ MRI by demonstrating that TAMA is more reliable and robust than TPA in terms of interscan agreement and inter-reader agreement as well as the effect of measurement level. The results also indicated that the measurement of TAMA can be easily integrated into routine clinical care by using a software, which is highly reliable in quantifying body composition from clinically acquired CT/MRI scans.

We investigated why TAMA is more reliable than TPA in terms of the inter-scan and interreader agreements and found that readers may have difficulty in manually drawing the posterior margin of the psoas muscle on both CT and MR images, because the psoas muscle is closely attached posteriorly to the quadratus lumborum and erector spinae muscle. In contrast, TAMA is generally calculated by a semi-automatic software on the basis of predetermined thresholds of the HU in CT or SI in MRI.

In terms of measurement level, TAMA was different between the  $L2_{mid}$  and  $L2_{inf}-L4_{inf}$  levels and similar between the  $L2_{inf}$  and  $L4_{inf}$  levels. Therefore, TAMA can be measured anywhere between the  $L2_{inf}$  and  $L4_{inf}$  levels. However, TPA was generally larger at a lower measurement level; consequently, TPA was different between the L2, L3, and L4 levels. Therefore, when using TPA as an index, it is important to select one level and measure at the same level consistently. As TAMA is less affected by the measurement level, it is considered as a more robust index of abdominal muscle mass than TPA.



**Fig 4. Effect of measurement level on TAMA, TPA, and VFA.** (A) TAMA at L2<sub>mid</sub> was different from that between L2<sub>inf</sub> and L4<sub>inf</sub>, and it was similar at other levels. (B) TPA was different at every level. (C) VFA was not significantly different between levels.

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Contrary to our initial expectation, CT was more robust and reliable for abdominal muscle mass quantification than MRI based on the ICC and WSCV values. This may be attributed to a clearer anatomical boundary of the muscles on CT images than on MR images. Bowel gas and motion artifacts caused the degradation of image quality of the adjacent abdominal muscle;

thus, the readers faced difficulty in drawing the boundaries of the muscle. Based on the results, the measurement of TAMA by CT might be the most robust method for sarcopenia evaluation compared to the measurement of TAMA by MRI and that of the TPA by CT/MRI.

Recently, studies on sarcopenia have been rapidly increasing because of various potential clinical applications such as the mortality assessment of patients requiring liver transplant [22], selective and non-abdominal aortic aneurysm repair [23, 24], and pancreatic adenocarcinoma treatment [25] and elderly patients requiring emergency surgery [26, 27].

In particular, patients with cancer are vulnerable to muscle wasting and they easily fall into a cachectic state; thus, sarcopenia assessment plays an important role. As most of the patients with cancer are followed up by CT/MRI, there are increasing efforts to evaluate the muscle mass using CT/MRI scans [27–29]. In many studies, TPA was used mainly because it is easier and faster to measure than TAMA [25, 30]. Nevertheless, the results in our study showed that TAMA is more robust than TPA; TPA was higher at a lower level, and the posterior margin was not well distinguished, which is a disadvantage in terms of reliability. Indeed, our findings are consistent with those of several prior studies [6, 31]. In addition, TAMA has been shown to be a valid surrogate marker of the whole body muscle mass because it reflects all muscles of the abdomen [29, 32]. The results of our study would support the results of these prior studies by adding the value of reliability of TAMA.

Only one study has compared imaging modalities for sarcopenia assessment, which demonstrated that TAMA measured at the L3 level was comparable between CT and MRI for patients with liver cirrhosis [33]. In contrast, our study showed that CT was more robust than MRI. Differences in the imaging protocol or measurement software may cause these inconsistencies; thus, further studies are required.

Currently, measurement methods and measurement levels have not been standardized. On the basis of our results, we propose that TAMA rather than TPA should be used to reliably quantify the abdominal muscle mass. If possible, CT should be the primary cross-sectional imaging modality. However, if only MRI is available, then measurement by MRI would be acceptable. Regarding the measurement level, L3 level has been widely used, because the muscle mass measured on L3 level reflects the whole body muscle mass well [34]. Most of the studies used L3<sub>mid</sub> level, where transverse processes are fully visualized [35, 36], while some used L3<sub>inf</sub> level nearest the inferior aspect of vertebral body [37, 38]. In our study, there was no significant difference in the measurement level, further large-scale studies and international consensus meeting would be necessary.

Body morphometric analysis based on cross-sectional images can be easily integrated into routine clinical care by using a simple image processing software to perform reliable measurement of the abdominal muscle and fat with clinically obtained scans. As increasing evidence supports cross-sectional imaging-based surveillance as an objective method for identifying sarcopenia in patients with various diseases, clinically acquired CT/MRI scans of patients with various diseases may be used concurrently to diagnose sarcopenia, identify patients at risk of poor survival, and contribute towards general health improvement [15].

There are several limitations to this study. First, this study was conducted in a retrospective manner with a relatively small number of subjects. A large-scale, prospective validation study is needed. Second, the subjects enrolled in this study were healthy prospective liver donors, which might limit the generalizability of the study results. Nevertheless, it was the best approach to accumulate data for the measurement of abdominal muscle area while minimizing the confounding effects of pathological conditions. This method should be further evaluated using patients with various diseases. Third, among various MRI sequences, we measured abdominal muscle and fat quantity only in the T1-weighted image without fat-saturation. The

value of abdominal muscle mass quantification in the other MRI sequences would be our future research topic.

In conclusion, as a cross-sectional imaging-based biomarker of sarcopenia, TAMA was more reliable than TPA in terms of inter-scan and inter-reader agreements and robustness in measurement. Furthermore, CT was a more reliable imaging modality than MRI. To use these sarcopenia biomarkers in clinical practice, the standard measurement methods should be determined from the international consensus of academic communities on the basis of largescale evidence obtained from both healthy subjects of variable age ranges (young adults to elderly subjects) and patients with various diseases.

## Supporting information

**S1 Fig. Bland-Altman plots for TAMA.** (A) CT vs. MRI for reader 1 (Inter-scan agreement). (B) CT vs. MRI for reader 2 (Inter-scan agreement). (C) Reader 1 vs. Reader 2 for CT (Inter-reader agreement). (D) Reader 1 vs. Reader 2 for MRI (Inter-reader agreement). (TIF)

**S2 Fig. Bland-Altman plots for TPA.** (A) CT vs. MRI for reader 1 (Inter-scan agreement). (B) CT vs. MRI for reader 2 (Inter-scan agreement). (C) Reader 1 vs. Reader 2 for CT (Inter-reader agreement). (D) Reader 1 vs. Reader 2 for MRI (Inter-reader agreement). (TIF)

**S3 Fig. Bland-Altman plots for VFA.** (A) CT vs. MRI for reader 1 (Inter-scan agreement). (B) CT vs. MRI for reader 2 (Inter-scan agreement). (C) Reader 1 vs. Reader 2 for CT (Inter-reader agreement). (D) Reader 1 vs. Reader 2 for MRI (Inter-reader agreement). (TIF)

**S1** File. The raw data of the body morphometry measurement values. (XLSX)

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#### References

- 1. Cao L, Morley JE. Sarcopenia is recognized as an independent condition by an international classification of disease, tenth revision, clinical modification (ICD-10-CM) code. J Am Med Dir Assoc. 2016; 17 (8):675–7. Epub 2016/07/30. https://doi.org/10.1016/j.jamda.2016.06.001 PMID: 27470918.
- Chen LK, Liu LK, Woo J, Assantachai P, Auyeung TW, Bahyah KS, et al. Sarcopenia in Asia: consensus report of the Asian Working Group for Sarcopenia. J Am Med Dir Assoc. 2014; 15(2):95–101. Epub 2014/01/28. https://doi.org/10.1016/j.jamda.2013.11.025 PMID: 24461239.
- 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(4):412–23. Epub 2010/04/16. <u>https://doi.org/10.1093/ageing/afq034</u> PMID: 20392703; PMCID: PMC2886201.
- 4. Jaap K, Hunsinger M, Dove J, McGinty K, Stefanowicz E, Fera J, et al. Morphometric predictors of morbidity after pancreatectomy. Am Surg. 2016; 82(12):1221–6. Epub 2017/02/25. PMID: 28234188.
- Joglekar S, Mezhir JJ. Response to letter to editor by Safer et al. J Surg Oncol. 2015; 112(1):117. Epub 2015/07/16. https://doi.org/10.1002/jso.23968 PMID: 26175340.
- Lee CS, Cron DC, Terjimanian MN, Canvasser LD, Mazurek AA, Vonfoerster E, et al. Dorsal muscle group area and surgical outcomes in liver transplantation. Clin Transplant. 2014; 28(10):1092–8. Epub 2014/07/22. https://doi.org/10.1111/ctr.12422 PMID: 25040933; PMCID: PMC4205192.
- DiMartini A, Cruz RJ Jr., Dew MA, Myaskovsky L, Goodpaster B, Fox K, et al. Muscle mass predicts outcomes following liver transplantation. Liver Transpl. 2013; 19(11):1172–80. Epub 2013/08/21. <u>https://doi.org/10.1002/lt.23724 PMID: 23960026; PMCID: PMC4382961.</u>
- Montano-Loza AJ, Meza-Junco J, Baracos VE, Prado CM, Ma M, Meeberg G, et al. Severe muscle depletion predicts postoperative length of stay but is not associated with survival after liver transplantation. Liver Transpl. 2014; 20(6):640–8. Epub 2014/03/29. <u>https://doi.org/10.1002/lt.23863</u> PMID: 24678005.
- Hasselager R, Gogenur I. Core muscle size assessed by perioperative abdominal CT scan is related to mortality, postoperative complications, and hospitalization after major abdominal surgery: a systematic review. Langenbecks Arch Surg. 2014; 399(3):287–95. Epub 2014/02/19. https://doi.org/10.1007/ s00423-014-1174-x PMID: 24535479.
- Barret M, Berthaud C, Taieb J. Sarcopenia: a concept of growing importance in the management of colorectal cancer. Presse Med. 2014; 43(6 Pt 1):628–32. Epub 2014/05/27. https://doi.org/10.1016/j. lpm.2013.12.021 PMID: 24857256.
- Yip C, Goh V, Davies A, Gossage J, Mitchell-Hay R, Hynes O, et al. Assessment of sarcopenia and changes in body composition after neoadjuvant chemotherapy and associations with clinical outcomes in oesophageal cancer. Eur Radiol. 2014; 24(5):998–1005. Epub 2014/02/19. https://doi.org/10.1007/ s00330-014-3110-4 PMID: 24535076.
- 12. Fearon K, Strasser F, Anker SD, Bosaeus I, Bruera E, Fainsinger RL, et al. Definition and classification of cancer cachexia: an international consensus. Lancet Oncol. 2011; 12(5):489–95. Epub 2011/02/08. https://doi.org/10.1016/S1470-2045(10)70218-7 PMID: 21296615.
- Fosbol MØ, Zerahn B. Contemporary methods of body composition measurement. Clin Physiol Funct Imaging. 2015; 35(2):81–97. Epub 2014/04/17. https://doi.org/10.1111/cpf.12152 PMID: 24735332.
- Amur S, LaVange L, Zineh I, Buckman-Garner S, Woodcock J. Biomarker Qualification: Toward a Multiple Stakeholder Framework for Biomarker Development, Regulatory Acceptance, and Utilization. Clin Pharmacol Ther. 2015; 98(1):34–46. Epub 2015/04/15. <u>https://doi.org/10.1002/cpt.136</u> PMID: 25868461.
- Caan BJ, Cespedes Feliciano EM, Prado CM, Alexeeff S, Kroenke CH, Bradshaw P, et al. Association of muscle and adiposity measured by computed tomography with survival in patients with nonmetastatic breast cancer. JAMA Oncol. 2018; 4(6):798–804. Epub 2018/04/06. https://doi.org/10.1001/jamaoncol. 2018.0137 PMID: 29621380.
- Dahya V, Xiao J, Prado CM, Burroughs P, McGee D, Silva AC, et al. Computed tomography-derived skeletal muscle index: a novel predictor of frailty and hospital length of stay after transcatheter aortic valve replacement. Am Heart J. 2016; 182:21–7. Epub 2016/12/05. https://doi.org/10.1016/j.ahj.2016. 08.016 PMID: 27914496.
- Malekpour M, Bridgham K, Jaap K, Erwin R, Widom K, Rapp M, et al. The effect of sarcopenia on outcomes in geriatric blunt trauma. Am Surg. 2017; 83(11):1203–8. Epub 2017/12/01. PMID: 29183520.
- Klopfenstein BJ, Kim MS, Krisky CM, Szumowski J, Rooney WD, Purnell JQ. Comparison of 3 T MRI and CT for the measurement of visceral and subcutaneous adipose tissue in humans. Br J Radiol. 2012; 85(1018):e826–30. Epub 2012/04/20. <u>https://doi.org/10.1259/bjr/57987644</u> PMID: 22514099; PMCID: PMC3474042.

- Yoon DY, Moon JH, Kim HK, Choi CS, Chang SK, Yun EJ, et al. Comparison of low-dose CT and MR for measurement of intra-abdominal adipose tissue: a phantom and human study. Acad Radiol. 2008; 15(1):62–70. Epub 2007/12/15. https://doi.org/10.1016/j.acra.2007.07.013 PMID: 18078908.
- Yoshizumi T, Shirabe K, Nakagawara H, Ikegami T, Harimoto N, Toshima T, et al. Skeletal muscle area correlates with body surface area in healthy adults. Hepatol Res. 2014; 44(3):313–8. Epub 2013/04/24. https://doi.org/10.1111/hepr.12119 PMID: 23607375.
- Shrout PE, Fleiss JL. Intraclass correlations: uses in assessing rater reliability. Psychol Bull. 1979; 86 (2):420–8. Epub 1979/03/01. https://doi.org/10.1037/0033-2909.86.2.420 PMID: 18839484.
- Englesbe MJ, Patel SP, He K, Lynch RJ, Schaubel DE, Harbaugh C, et al. Sarcopenia and mortality after liver transplantation. J Am Coll Surg. 2010; 211(2):271–8. Epub 2010/07/31. https://doi.org/10. 1016/j.jamcollsurg.2010.03.039 PMID: 20670867; PMCID: PMC2914324.
- Ganapathi AM, Englum BR, Hanna JM, Schechter MA, Gaca JG, Hurwitz LM, et al. Frailty and risk in proximal aortic surgery. J Thorac Cardiovasc Surg. 2014; 147(1):186–91.e1. Epub 2013/11/05. <u>https:// doi.org/10.1016/j.jtcvs.2013.09.011</u> PMID: 24183336; PMCID: PMC4336171.
- Lee JS, He K, Harbaugh CM, Schaubel DE, Sonnenday CJ, Wang SC, et al. Frailty, core muscle size, and mortality in patients undergoing open abdominal aortic aneurysm repair. J Vasc Surg. 2011; 53 (4):912–7. Epub 2011/01/11. https://doi.org/10.1016/j.jvs.2010.10.111 PMID: 21215580.
- Peng P, Hyder O, Firoozmand A, Kneuertz P, Schulick RD, Huang D, et al. Impact of sarcopenia on outcomes following resection of pancreatic adenocarcinoma. J Gastrointest Surg. 2012; 16(8):1478–86. Epub 2012/06/14. <u>https://doi.org/10.1007/s11605-012-1923-5</u> PMID: <u>22692586</u>; PMCID: PMC3578313.
- Du Y, Karvellas CJ, Baracos V, Williams DC, Khadaroo RG. Sarcopenia is a predictor of outcomes in very elderly patients undergoing emergency surgery. Surgery. 2014; 156(3):521–7. Epub 2014/06/16. https://doi.org/10.1016/j.surg.2014.04.027 PMID: 24929435.
- Boutin RD, Yao L, Canter RJ, Lenchik L. Sarcopenia: Current Concepts and Imaging Implications. AJR Am J Roentgenol. 2015; 205(3):W255–66. Epub 2015/06/24. <u>https://doi.org/10.2214/AJR.15.14635</u> PMID: 26102307.
- Harimoto N, Shirabe K, Yamashita YI, Ikegami T, Yoshizumi T, Soejima Y, et al. Sarcopenia as a predictor of prognosis in patients following hepatectomy for hepatocellular carcinoma. Br J Surg. 2013; 100 (11):1523–30. Epub 2013/09/17. https://doi.org/10.1002/bjs.9258 PMID: 24037576.
- 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(5):997–1006. Epub 2008/10/17. https://doi.org/10.1139/H08-075 PMID: 18923576.
- 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(12):3897–904. Epub 2015/08/06. https://doi.org/ 10.1245/s10434-015-4763-1 PMID: 26242367.
- Rutten IJG, Ubachs J, Kruitwagen R, Beets-Tan RGH, Olde Damink SWM, Van Gorp T. Psoas muscle area is not representative of total skeletal muscle area in the assessment of sarcopenia in ovarian cancer. J Cachexia Sarcopenia Muscle. 2017; 8(4):630–8. Epub 2017/05/18. https://doi.org/10.1002/jcsm. 12180 PMID: 28513088; PMCID: PMC5566632.
- Lee SJ, Janssen I, Heymsfield SB, Ross R. Relation between whole-body and regional measures of human skeletal muscle. Am J Clin Nutr. 2004; 80(5):1215–21. Epub 2004/11/09. <u>https://doi.org/10. 1093/ajcn/80.5.1215 PMID: 15531668</u>.
- Tandon P, Mourtzakis M, Low G, Zenith L, Ney M, Carbonneau M, et al. Comparing the variability between measurements for sarcopenia using magnetic resonance imaging and computed tomography imaging. Am J Transplant. 2016; 16(9):2766–7. Epub 2016/04/20. https://doi.org/10.1111/ajt.13832 PMID: 27093434.
- Schweitzer L, Geisler C, Pourhassan M, Braun W, Glüer C-C, 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. The Journal of Nutrition. 2016; 146(10):2143–8. https://doi.org/10.3945/ jn.116.236844 PMID: 27581576
- 35. Tamandl D, Paireder M, Asari R, Baltzer PA, Schoppmann SF, Ba-Ssalamah A. Markers of sarcopenia quantified by computed tomography predict adverse long-term outcome in patients with resected oeso-phageal or gastro-oesophageal junction cancer. Eur Radiol. 2016; 26(5):1359–67. Epub 2015/09/04. https://doi.org/10.1007/s00330-015-3963-1 PMID: 26334504.
- **36.** van der Werf A, Langius JAE, de van der Schueren MAE, Nurmohamed SA, van der Pant KAMI, Blauwhoff-Buskermolen S, et al. Percentiles for skeletal muscle index, area and radiation attenuation

based on computed tomography imaging in a healthy Caucasian population. European Journal of Clinical Nutrition. 2018; 72(2):288–96. https://doi.org/10.1038/s41430-017-0034-5 PMID: 29242526

- Derstine BA, Holcombe SA, Ross BE, Wang NC, Su GL, Wang SC. Skeletal muscle cutoff values for sarcopenia diagnosis using T10 to L5 measurements in a healthy US population. Sci Rep. 2018; 8 (1):11369. Epub 2018/07/29. https://doi.org/10.1038/s41598-018-29825-5 PMID: 30054580; PMCID: PMC6063941.
- Derstine BA, Holcombe SA, Goulson RL, Ross BE, Wang NC, Sullivan JA, et al. Quantifying Sarcopenia Reference Values Using Lumbar and Thoracic Muscle Areas in a Healthy Population. J Nutr Health Aging. 2017; 21(10):180–5. Epub 2018/01/05. https://doi.org/10.1007/s12603-017-0983-3 PMID: 29300439.