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Original Article

The identification of an optimal body size parameter to adjust skeletal muscle area on chest CT in COVID-19 patients

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Abstract

Objectives: The most efficient way to adjust skeletal muscle area (SMA) derived from chest CT to body size remains unclear. We hypothesized that vertebral body area (VBA) measurement would allow such efficient adjustment. **Methods**: We conducted a retrospective observational study of chest CT imaging in a cohort of critically ill COVID-19 patients. We measured paravertebral SMA at T5 level and T5 vertebral body anteroposterior length, width, and area. We used linear regression and multivariable modelling to assess the association of VBA with SMA. **Results**: In 48 COVID-19 patients in ICU, T5 VBA could be easily derived from simple width and anteroposterior length linear measurements. T5 VBA (measured manually or estimated from width and length) performed similarly to height (R^2 of 0.22) as an adjustment variable for SMA, with R^2 of 0.23 and 0.22, respectively. Gender had the strongest correlation with SMA (R^2 = 0.28). Adding height or age to a model using gender and VBA did not improve correlation. **Conclusions**: Gender and estimated VBA from simple linear measurements at T5 level on CT images can be utilized for adjustment of SMA without the need for height. Validation of these findings in larger cohorts of critically ill patients is now needed.

Keywords: Chest computed tomography, Sarcopenia, Skeletal muscle area

Introduction

Sarcopenia (low skeletal muscle mass) has been linked to poor outcomes in patients with COVID-19 pneumonia[1,2]. In patients hospitalized with COVID-19 pneumonia, sarcopenia is associated with longer hospital stay, intensive care unit (ICU) admission and in-hospital mortality[3]. Among those admitted to ICU, sarcopenia is associated with longer ICU stay, failure of extubation and mortality[4,5]. The relationship between sarcopenia and COVID-19 pneumonia is not unique. Prior to the COVID-19 pandemic, several studies showed an association between sarcopenia and community-

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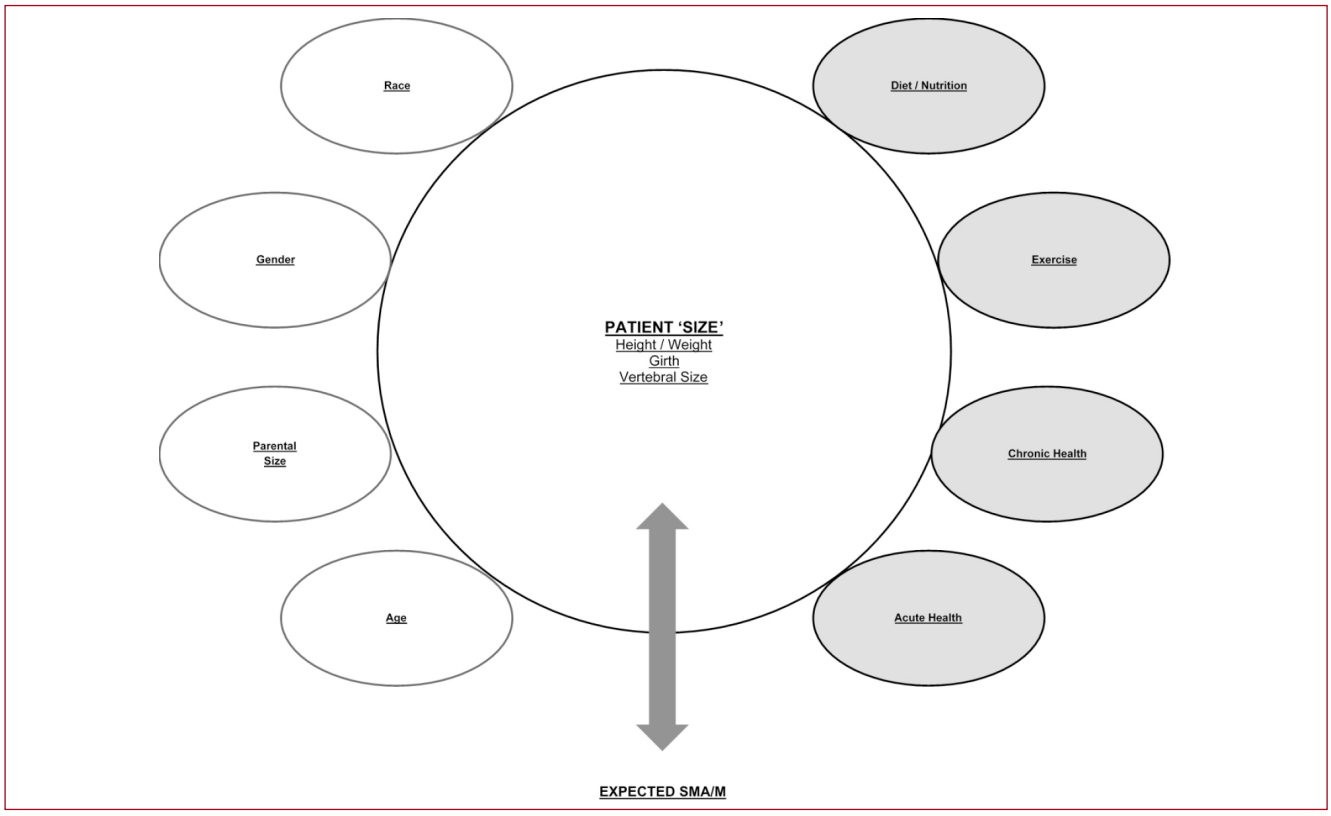

Figure 1. Intrinsic (no shading) and extrinsic (shaded) factors influencing patient size and therefore expected skeletal muscle area (eSMA) and mass (eSMM).

acquired pneumonia outcomes including ICU admission and mortality[6-8]. Furthermore, several studies have shown an association between sarcopenia and poor outcomes in patients admitted to ICU with various conditions including critical illness, trauma, and sepsis[9]. Its assessment, therefore, has clinical prognostic value and may influence decisions on therapeutic interventions such as early mobilization and nutritional support[11].

Most studies assessing sarcopenia using medical imaging have focused on abdominal CT and measurement of skeletal muscle area (SMA) at L3 with adjustment for patient size[11]. Ideally, such adjustment would include all relevant patient factors (Figure 1). However, most of this information is typically unavailable. A simplified approach is to adjust measurements to the patient's height (cm) squared, resulting in the skeletal muscle index (SMI)=SMA/height^2 [11]. However, this approach is problematic. For example, correlation R-squared values are in the range 0.3 to 0.4[12]. Thus, only 30 to 40% of the variation in SMA is explained by height alone. Moreover, in COVID-19 patients admitted to ICU, information on height is often missing or inaccurate and abdominal CT scans are uncommon. In contrast, in COVID-19 patients in ICU, chest CT scans are common.

To provide SMA measurement from chest CT, previous studies have utilised the paraspinal muscle area at other vertebral levels such as T5 or T12, or pectoralis muscle area, which have demonstrated correlation with muscle area measurements at L3 level[13,14]. However, they still require adjustment to body size. In this regard, the use of cross-sectional area measurements alone or adjustment to surrogate parameters for body size (e.g. vertebral size) has been employed[3,15,16]. Moreover, a range of measurements at various vertebral levels and with different body size adjustments have also been utilised in studies assessing sarcopenia for patients with COVID-19 (Table 1)[3-5,17-30]. This creates further difficulties in comparison across cohorts, limits generalizability, and suggests the need for a simple, reproducible, standardized, pragmatic, and efficient way to adjust for body size.

We aimed to assess parameters available from routine chest CT to adjust SMA for body size in the assessment of sarcopenia in critically ill COVID-19 patients. We hypothesized that vertebral body area would show an equivalent or stronger correlation with SMA compared with height. Moreover, given its universal availability from chest CT, we reasoned that it would be a logistically superior and more efficient adjustment standard for SMA using chest CT scans.

Table 1. Studies using muscle area measurements from chest CT for evaluating sarcopenia in COVID-19 patients. All studies were retrospective.

Author	Year	Country	Patients, *n*	Age Years (Mean) [Median]	Gender (female), *n* (%)	ICU admission, *n* (%)	Muscle group	Anatomical level	Area reference index
Ufuk[17]	2020	Turkey	130	(48)	54 (42%)	Unknown 15 (12) intubated	PMA	Above aortic arch	None
Kottlors[18]	2020	Germany	58	(59)	21 (36%)	26 (45)	Paraspinal muscles area	T12	Body circumference at T12
Schiaffino[3]	2021	Italy	552	[65]	188 (34%)	92 (17)	Paraspinal muscles area	T5 and T12	T12 vertebral A-P length.
Hocaoglu[19]	2021	Turkey	217	[61]	109 (50%)	Unknown	Pectoralis major volume	Single slice, above aortic arch	None
Besutti[20]	2021	Italy	318	[66]	38	Unknown 68 (21%) intubated	Right PMA	Above aortic arch	None
Poros[4]	2021	Germany	67	(66)	14 (19%)	67 (100)	SMA PMA	T5 for SMA. Above aortic arch for PMA	None
Kim[21]	2021	South Korea	121	(62)	77 (64%)	10 (8.3)	SMI	T12	Height^2
Moctezuma-Velázquez[22]	2021	Mexico	519	(51)	187 (36%)	207 (40)	SMI	T12	Height^2
Antonarelli[5]	2022	Italy	112	(61)	30 (27%)	112 (100) intubated	PMA	T4	None
Ying-hao[23]	2022	China	116	[69]	76 (66%)	Excluded severe illness, mechanical ventilation patients on admission	PMA	Above aortic arch	Body surface area
Yi[24]	2022	China	234	[45]	101 (43%)	Unknown 31 (13) with severe illness	SMA	T12	Vertical spine length (T1 to T9)-squared
Kardas[25]	2022	Germany	46	[65]	19 (41%)	37 (80)	PMA	T4	Height^2
Molwitz[26]	2022	Germany	46	(64)	19 (41%)	Unknown 39 (85) intubated	Paraspinal muscles area SMI	T12 for paraspinal muscles L3 for SMI	Height^2
Tekin[27]	2022	Turkey	167	(63)	87 (52%)	28 (17)	PMA Paraspinal muscles area	T4	None
Ufuk[28]	2023	Turkey	238	(48)	117 (49%)	24 (21) intubated	Right PMA	T5	None
Surov[29]	2023	International	547	(55)	547 (48%)	220 (19)	PMA	T4	Height^2
Grigioni[30]	2023	France	244	(62)	110 (45%)	86 (35)	SMI	T12	Height^2

PMA: pectoralis muscle area; refers to pectoralis major and minor bilaterally unless side specified. SMA: skeletal muscle area. SMI: skeletal muscle index; refers to SMA adjusted for height^2.

Methods

This was a single centre retrospective study, which was performed at the Austin Hospital, a tertiary hospital in Melbourne, Australia.

Patients

Consecutive patients admitted to ICU with COVID-19 acute respiratory distress syndrome from 19 September to 27 December 2021 who underwent a chest CT

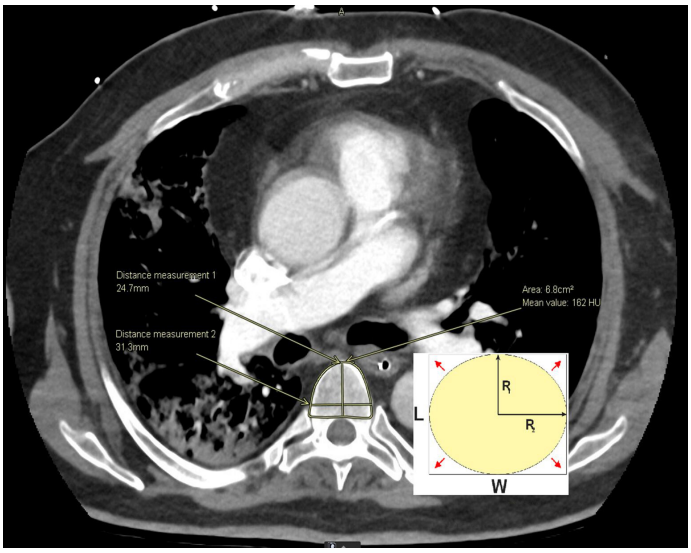

Figure 2. Measurement of T5 vertebral body area (VBA) by manual trace outline and estimated VBA from anteroposterior length (L) and width (W), giving radii R_1 and R_2 respectively.

study were included. Patient characteristics including demographics, symptoms, comorbidities, laboratory results and parameters specific to ICU including risk scores and mechanical ventilation details were retrieved from the digital medical records. Clinical outcomes from ICU admission and hospital stay were included from discharge summaries and comprehensive digital medical records.

Image acquisition and analysis

Chest CT imaging protocols were performed depending on the clinical setting. For disease severity assessment, chest CTs were performed with or without intravenous iodinated contrast depending on renal function. For assessment of pulmonary embolism, a CT pulmonary angiogram (CTPA) protocol was performed. All imaging was performed on one of two scanners (SOMATOM Force, Siemens Healthineers; or Aquilion One, Canon Medical Systems).

Image analysis was performed by two radiologists. The first radiologist measured paravertebral SMA at T5 level according to previously described methodology[3].

At the same level, the radiologist measured T5 vertebral body anteroposterior length, width, and area. Measurements were performed on axial slices. The vertical height of the thoracic spine from T1 to T9 was also measured on sagittal reformats according to the study by Yi et al[24]. The CT Severity Score (CT-SS) was used to quantify the severity of pulmonary involvement by a specialised chest radiologist[31].

For patients with available height, T5 vertebral body anteroposterior length and width were estimated by a second radiologist to assess inter-reader agreement.

Measurements for SMA adjustment

We hypothesised that, for the purpose adjusting SMA, vertebral body area (VBA) would correlate similarly to height with the observed SMA. Further, as trace area measurement is time consuming and skill dependent in the absence of automated artificial intelligence-based methods[32-34], we reasoned that approximation of VBA as an ellipsoid from the vertebral width and anteroposterior length would act as a suitable surrogate. These metrics are readily calculated using standard radiology viewing software (Figure 2).

T5 VBA was measured by manual outline trace and estimated VBA (eVBA) calculated as either a simple ellipse (Area = $Pi*R_1*R_2$) and as a "squared-ellipse" (Area = $(Pi*R_1*R_2) + 0.3*(W*L - Pi*R_1*R_2)$; where R_1 and R_2 are half the anteroposterior length (L) and width (W) respectively. An inflation factor of 0.3 was chosen as an approximation, i.e., assuming estimated VBA is 30% above a simple ellipse toward the bounding rectangle (Figure 2 - Inset).

Statistical analysis

Patient covariates are summarised as number (%), mean (standard deviation, SD) or median [inter-quartile range, IQR]. Missing data are indicated when greater than 5%.

Linear regression was used to assess the association of each subject variable with SMA, with the associated r-squared and p-values reported. Concordance between (1) radiologist CT calliper measurements for vertebral length and width; and (2) between measured and estimated VBA were assessed using Lin's concordance

Table 2. Cohort patient and CT scan characteristics.

Patient Covariate	Summary Measure N = 48
Age (years), median [IQR]	56 [52, 64]
Male gender, n (%)	29 (60)
Height (cm), median [IQR]	167 [155, 175]
Weight (kg), median [IQR]	89 [78, 103]
BMI (kg/m^2), median [IQR]	33 [28, 37]
APACHE[1] II Score, median [IQR]	14 [11, 16.5]
APACHE III ROD[1], mean (SD)	0.16 (0.11)
Plasma Lactate (mmol/L), median [IQR]	2.1 [1.8, 2.6]
Diabetes mellitus, n(%)	15 (31)
Frailty Index, n(%)	45 (94%)
Very fit	2 (4.4)
Well	11 (24)
Managing Well	28 (62)
Vulnerable	3 (6.7)
Mildly Frail	1 (2.2)
ICU Processes / Outcome	
Stay (Hours), median [IQR]	232 [130, 429]
Inotropes/vasopressors, n(%)	41 (85)
Invasive Ventilation, n(%)	39 (81)
Invasive Ventilation Hours , median [IQR]	204 [97, 355]
Non-invasive Ventilation, n(%)	27 (56)
Tracheostomy, n(%)	8 (17)
Renal Replacement Therapy, n(%)	4 (8.3)
Death, n(%)	2 (4.2)
Hospital Outcome	
Stay (Hours), median [IQR]	398 [283, 750]
Death, n(%)	3 (6.3)
Chest CT Observations	
COVID Severity Score, median [IQR]	33.5 [28.0, 38.0]
Skeletal Muscle Area (cm^2), median [IQR]	11.3 [9.5, 13.6]
Skeletal Muscle Density (HU)[2], median [IQR]	19.8 [5.3, 30.8]
Aortic Density (T5), median [IQR]	134.0 [81.5, 194.5]
Vertebral body (T5), median [IQR]	
Width (cm)	2.8 [2.5, 3.0]
Antero-posterior length (cm)	2.5 [2.3, 2.6]
CT Parenchymal features, n(%)	
CT Crazy Paving	18 (38)
Lymph Nodes (>10mm)	12 (25)
Effusion	36 (75)

1. IQR – interquartile range, APACHE – Acute physiology and chronic health evaluation, ROD – risk of death. 2. HU - Hounsfield Units.

correlation coefficient (rho_c) and 95% limits of agreement (LOA). As R-squared always increases with the inclusion of additional covariates, multivariable models were assessed using Akaike Information Criteria (AIC) and Bayesian Information Criteria (BIC), where lower values reflect better overall performance, with the model dataset kept constant. Delta AIC is reported as the AIC for a given model less the minimum AIC amongst the comparator model set; assuming ΔAIC < 2.0 reflects negligible difference, 2.0 ≤ ΔAIC < 4.0 minor difference, and ΔAIC ≥ 4.0 marked difference in model performance[35]. Given the small study size and the anticipated correlation between size-related covariates, models were effectively restricted to assessing the effects of including a second covariate only. P-values are included for perspective only, with no adjustment for multiple comparisons. No imputation was required for missing data, as the study cohort was restricted to individuals with complete data to enable model comparisons. All analyses were undertaken in StataMP/17.0 (StataCorp LLC, USA).

Results

A total of 121 patients admitted to ICU with COVID-19 were screened. Sixty-nine (57%) had chest CT scans and clinical parameters available. Of these, 48 (40%) had height recorded in the electronic medical record (EMR) and were included in this analysis. The median age was 56 [52, 64] years and 29 (60%) were male. The median duration between hospital admission and ICU admission was 1 day [0, 2] with 21 (44%) admitted directly to ICU and 12 (25%) at day 1. The median duration between CT and hospital admission was 7 days [2, 9.25] and for CT and ICU admission, it was 5 days [1, 8.25]. The median T5 SMI derived from SMA at T5 divided by height-squared was 4.18 cm^2/m^2 [3.7, 4.8]. Clinical and relevant CT scan parameters are shown in Table 2.

Associations with SMA

Univariate regression models against CT calculated SMA at T5 for height, age, gender, measured T5 vertebral body area, estimated T5 area (as a simple ellipse and 'squared'-ellipse) and T1 to T9 vertical height are presented in Table 3.

The lowest AIC for univariate models was seen for gender, which was, therefore, used as the base covariate for models assessing the influence of a second covariate. The ΔAIC values for the inclusion of height versus height-squared versus measured VBA versus estimated VBA ranged from 5.3 to 6.5, with a maximum ΔAIC 1.2, consistent with no meaningful information difference between these four models. The addition of age or height to the {gender + eVBA} model resulted in no model advantage.

Estimation of vertebral body area

VBA at T5 was estimated from CT calliper estimates of A-P length and width, performed by 2 independent radiologists,

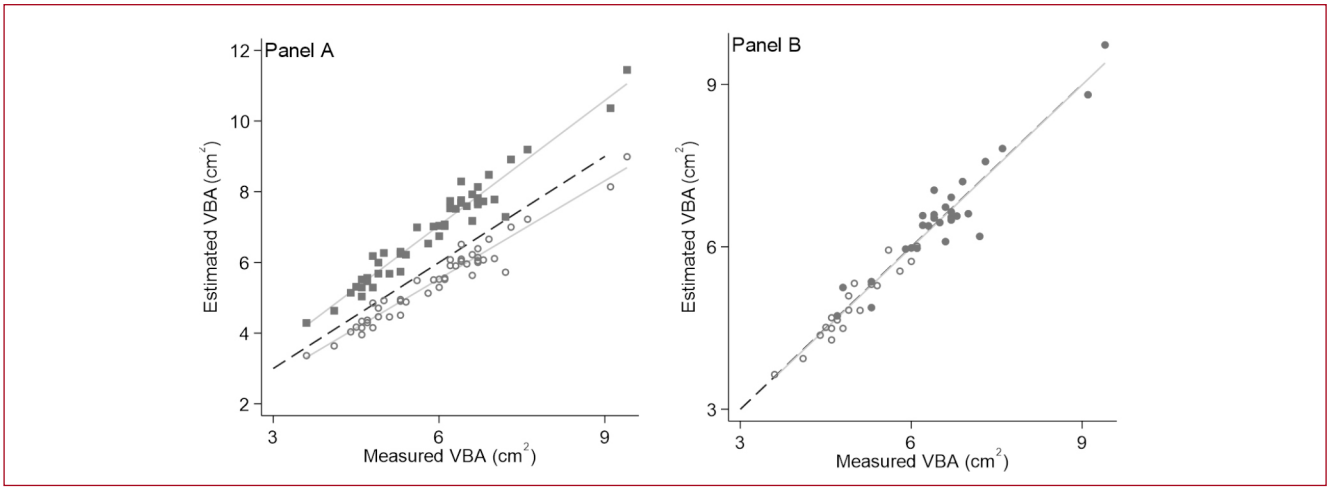

Figure 3. Estimated vs measured vertebral body area: Panel A - estimated as the bounding rectangle (solid squares) and as a simple ellipse (open circles), and Panel B - estimated as a 'squared'-ellipse (open circles = females, solid circles = males). The regression lines of best fit are shown (solid grey) together with the line of concordance (y=x: dashed black line). Correlation is identical for all models (R^2 = 0.94). Concordance is limited with the bounding rectangles or the simple ellipse in panel A (rho_c = 0.73 and 0.90, respectively) but substantial with the squared ellipse substantial in pane B (rho_c = 0.97).

with 95% limits of agreement (-2.0, 1.3) and (-3.7, 1.7) in mm respectively, giving concordance correlation coefficients (rho_c) of 0.95 and 0.85.

Using estimated VBA based upon calliper measured T5 length and width (either a simple ellipse, 'squared'-ellipse, or the bounding outer rectangle), showed a strong correlation with boundary-trace measured area (R^2 = 0.95). There was systematic under and over-estimation of VBA by simple ellipse and bounding rectangle, with limited concordance (Lin's rho_c = 0.73 and 0.90 respectively). Using a "squared-ellipse" formula, the estimated VBA achieved strong correlation (R^2 = 0.95) with substantial concordance (Lin's rho_c = 0.97) (Figure 3).

Discussion

Key findings

In a cohort of critically ill COVID-19 patients who underwent chest CT and had EMR information on height, we demonstrated that T5 VBA estimation can be easily derived from simple width and anteroposterior length linear measurements. We also found that T5 VBA (measured manually or estimated from width and length) performed similarly to height as an adjustment variable for SMA, with R^2= 0.23 and 0.22, respectively. Finally, we found that gender had the strongest correlation with SMA, and that, adding height or age to a predictive model using only gender and VBA did not improve correlation. Therefore, readily available data (i.e., gender) and measurements of VBA on CT images can be utilized for the adjustment of SMA without the need for height measurement, a clinical variable not routinely available in critically ill patients.

Relationship to previous studies

Some studies on sarcopenia from chest CT in COVID-19 patients used SMA of paraspinal muscles or pectoralis muscles without adjustment to body size (Table 1). Several studies have used patient height^2 to adjust SMA and to derive SMI, and then applied gender-based cut-points. This approach effectively incorporates two adjustment covariates, i.e., height and gender, but limits the latter to a fixed level, generated from multiple published studies, which may reflect a completely different racial mix. Given these two covariates explain only 30-40% of the observed variability in SMA, misclassification of sarcopenia and disease-related outcomes is highly likely. Therefore, if this approach is adopted, maximal use of available information would logically be achieved by including both factors as continuous covariates in a regression analysis and defining sarcopenia by a percentile cut-point, rather than some arbitrary fixed number[11].

Lacking height and weight indices, Schiaffino et al correlated CT-derived paraspinal muscles mass at T5 and T12 levels with clinical outcomes in 552 hospitalised patients with COVID-19 (92 admitted to ICU) via direct adjustment with T12 vertebral body anteroposterior length measurement. They showed that low muscle mass, as a binary indicator above/below the median, was independently associated with ICU admission and in-hospital mortality. In

Table 3. Linear regression models for skeletal muscle area (SMA) at T5 as estimated by chest CT scan.

Model Factor	R-squared	P-value	AIC[1]	ΔAIC	BIC[1]
Univariate Factor Models					
Male	0.28	<0.001	221.73	0.0	225.47
Age	0.06	0.10	236.82	15.1	240.57
Height	0.22	<0.001	227.72	6.0	231.47
Height-squared	0.23	<0.001	227.03	5.3	230.77
T5 VBA[1] (measured)[2]	0.21	0.001	228.25	6.5	231.99
T5 VBA: Ellipse[3,6] 'Squared'-ellipse[4,6] Outer rectangle[5,6]	0.23	<0.001	227.82	6.1	231.57
T1-T9 Vertebral Height	0.30	<0.001	222.72	1.0	226.46
Multivariable Models					
Male	0.34	0.007	221.87	0.2	227.49
Height		0.190			
Male	0.34	0.009	221.65	0.0	227.26
Height-squared		0.165			
Male	0.33	0.011	222.74	1.1	228.35
T5 VBA (ellipse)		0.34			
Male	0.34	0.02	223.88	2.2	231.36
T5 VBA (ellipse)		0.30			
Age		0.38			
Male	0.35	0.05	223.27	1.6	230.75
T5 VBA (ellipse)		0.56			
Height-squared		0.25			

1. AIC = Akaike Information Criteria, BIC = Bayesian Information Criteria, VBA – vertebral body area
2. Measured VBA via manual trace outline
3. Estimated VBA, using the formula for a simple ellipse: = $Pi*R_1*R_2$
4. Estimated VBA, using the formula for a 'squared' ellipse: = $(Pi*R_1*R_2) + 0.3*(L*W - Pi*R_1*R_2)$
5. Estimated VBA, using the outer rectangle: = L*W
6. As all estimated VBA measures are simple linear transformations of (L*W), the model information is identical.

their study, SMA was adjusted to estimated height derived from T12 anteroposterior length rather than adjusting directly to vertebral measurements[3]. The height was not available, confirming the known problems associated with its unreliable collection. Thus, it was estimated based on a mathematical model derived from a study of 382 British patients who underwent CT for abdominal aortic aneurysms. In this study, Waduud et al published a validation of the estimation of patient height from 2-dimensional measurements of the vertebral body[36]. They showed highly significant p-values. However, correlation was poor with 95% limits of agreement for the estimation of height (-12.0, +13.2cm), i.e., true height might lie within a 25cm range of the estimated value. An external validation of this approach in an elderly Australian cohort showed suboptimal estimation of height[37]. Given true height explains only 30-40% of observed SMA, the utility of such an approach is therefore questionable.

In our study, we showed that paraspinal SMA correlated with vertebral body size similarly to true height; however, this question was not addressed by Schiaffino et al or other similar studies[3]. The anatomy of vertebral bodies in the cervical, thoracic, and lumbar spine depends on the spinal level. Thoracic vertebral bodies are close to a heart shape while lumbar vertebral bodies are larger and more ellipsoid. Therefore, applying measurements from lumbar levels to thoracic levels is problematic without performing validation studies. However, whilst we have shown that 'very close'

approximation of VBA can be achieved in the mid-thoracic level, accurate estimation of VBA is not actually required. As can be seen by the identical model performance for ellipse, 'squared'-ellipse, and bounding rectangle, the information required for SMA adjustment is contained within the 2 vertebral parameters length and width, all simple linear transformations of these do not influence that information. Therefore, the simplest approach would be to reference the bounding area (Area = L*W).

Study implications

Our study implies that T5 VBA estimation can be easily derived from simple width and anteroposterior length measurements, and that T5 VBA (measured manually or estimated) performed similarly to height as an adjustment variable for SMA. Moreover, it implies that greatest information with respect to SMA comes from gender. This is consistent with the knowledge that height and eVBA are correlated with gender, with Pearson correlation coefficients of 0.61 and 0.68 respectively. Therefore, some of the information conveyed from height and eVBA is included within gender. This explains why the increment in R-squared seen with the 2-covariate models is limited. Finally, it implies that gender and simple vertebral measurements can be utilized for adjustment of SMA without the need for height measurement. This simple approach opens the door to rapid and reliable assessment of adjusted SMA in large cohorts of patients.

Strengths and limitations

Our study has several strengths. First, we utilised real-world data of critically ill COVID-19 patients who underwent CT scans for various clinical indications using two different CT scanners. Second, our radiological measurements were obtained on a standard radiology viewer, which can be easily replicated. Third, we utilised simple vertebral measurements to derive estimated VBA in a cohort of patients with available height information yielding an important radiological surrogate for body size adjustment for SMA.

We acknowledge some limitations. First, our study sample is small which limits assessment of multiple covariates with SMA. For example, the observation that age is 'not significantly' associated with SMA is likely due to the small sample size and the expected collinearity between factors affecting patient size. These limitations, however, exist for all studies of sarcopenia, especially where N is small and need careful consideration in model development. In this regard, automated 'step-wise' model building techniques are best avoided[38]. Second, the retrospective nature of our study meant that we utilised real-world data from chest CT studies performed in slightly different clinical settings resulting in heterogeneity of acquired images. This may have introduced variations to how muscle and vertebral measurements were performed. Third, our study applies to those critically ill patients with COVID and information on height, a unique ICU population. Thus, their generalizability is limited, and further studies are needed to test the robustness of our preliminary observations.

In regard to radiological measurements, our study could not elaborate on limitations in VBA measurement techniques due to a small sample size. Widening of the vertebral body from compression fractures and osteophytes at the margins may influence length, width, and area measurements. However, the concordance between the two radiologists for such measurements was high. We also did not assess the impact of arm position on vertebral and muscle area measurements. Intubated patients tend to have their arms positioned by the sides of their body during a CT scan while non-intubated patients are usually asked to elevate their arms above their heads to reduce image artefact. This could have influenced area measurements particularly the paraspinal musculature. However, such real-life limitation is difficult to quantify given the lack clinical scenarios in which patients could be scanned in both "arms down" and "arms up" positions.

Conclusion

In conclusion, comparison of chest CT-derived SMA at T5 level across patients without body size adjustment cannot be recommended. Adjustment for gender is a base requirement. Further adjustment of SMA without available height can be efficiently performed using estimated vertebral body area from simple linear measurements at the T5 level. These preliminary findings from our small study may have important practical implications for the assessment, epidemiology, diagnosis, and monitoring of sarcopenia. However, validation from a large population is required to provide appropriate reference levels and test the robustness of these observations.

Ethics approval

Approval from the Austin Health ethics committee was obtained with waiver of informed consent (Project Number: 22/Austin/24).

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