J Musculoskelet Neuronal Interact 2023; 23(2):196-204

Journal of Musculoskeletal and Neuronal Interactions JMNI

Original Article

Pectoralis muscle area measured at T4 level is closely associated with adverse COVID-19 outcomes in hospitalized patients

Zeynep Nilufer Tekin[1], Bilinc Dogruoz Karatekin[2], Mahmut Bilal Dogan[1], Zeynep Bilgi[3]

[1]Istanbul Medeniyet University, Goztepe Prof Dr Suleyman Yalcin City Hospital, Radiology, Istanbul, Turkey;
[2]Istanbul Medeniyet University, Goztepe Prof Dr Suleyman Yalcin City Hospital, Physical Medicine and Rehabilitation, Istanbul, Turkey;
[3]Istanbul Medeniyet University, Faculty of Medicine, Thoracic Surgery, Istanbul, Turkey

Abstract

Objectives: Skeletal muscle area (SMA) at T4 level on chest computed tomography (CT) is a newly available method that can be used as a surrogate sarcopenia marker. The objective of this study is to evaluate association of SMA with adverse COVID-19 outcomes in hospitalized patients. **Methods**: Hospitalized COVID-19 patients were prospectively recorded in a database containing age, gender, date of admission, date of outcome (discharge, mortality, presence of intensive care unit (ICU) stay, additional coding information (comorbidities, superimposed conditions). Admission CT-scans were retrospectively evaluated for segmentation (bilateral pectoralis major/minor, erector spinae, levator scapulae, rhomboideus minor and major and transversospinalis muscles) and SMA calculation using 3-D slicer software. **Results**: 167 cases were evaluated (68 male, 72 female, 140 survived, 27 dead). Muscle area was lower in patients with ICU stay (p=0.023, p=0.018, p=0.008) and mortality outcome (p=0.004, p=0.007, p=0.002) for pectoralis, back and SMA. In multivariate Cox-regression analysis, hazard ratio (HR) value for the pectoralis muscle area value below 2800 mm^2 was found to be 3.138(95% CI: 1.171-8.413) for mortality and 2.361(95% CI: 1.012-5.505) for ICU. **Conclusions**: Pectoralis muscle area measured at T4 level with 3-D slicer was closely associated with adverse outcomes (mortality, ICU stay) in hospitalized COVID-19 patients. Since early treatment methods for COVID-19 are being evaluated, this method may be a useful adjunct to clinical decision making in regard to prioritization.

Keywords: Computed Tomography, COVID-19, Pectoralis Muscle Area, Sarcopenia, T4 Vertebra

Introduction

Sustained community transmission of COVID-19 and the resulting pandemic gave rise to many new clinical challenges. While the speedy discovery and application of effective vaccines changed the clinical landscape enormously, clinical behavior of COVID-19 is still not fully elucidated[1,2]. In addition to vaccines, several treatment methods have been proposed (monoclonal antibodies, antiviral agents) but risk stratification after being symptomatic for prioritization for those treatment methods is still debated[3,4].

Sarcopenia is defined as the presence of low skeletal muscle mass and either low muscle strength (e.g. handgrip) or low muscle performance (e.g. walking speed or muscle power)[5]. Sarcopenia is also closely associated with frailty[5] which is an adverse prognostic factor for many types of diseases[6,7]. Most patients with sarcopenia and frailty generally do not fare well during or after medical episodes involving invasive mechanical ventilation, sepsis, or prolonged hospital stay[8,9].

While most frailty assessments are complex with many data points[5], some requiring specialized equipment[5], diagnosis of low skeletal muscle area (SMA) with 3-D slicer image procession with user-friendly, open-source software

The authors have no conflict of interest.

Corresponding author: Bilinc Dogruoz Karatekin, M.D., PhD., Egitim mahallesi Göztepe Şehir Hastanesi, Fizik Tedavi Ünitesi. 34730 Kadıköy, İstanbul, Turkey
E-mail: bilincdogruoz@hotmail.com
ORCID: 0000-0002-0568-9498

Edited by: G. Lyritis
Accepted 3 August 2022

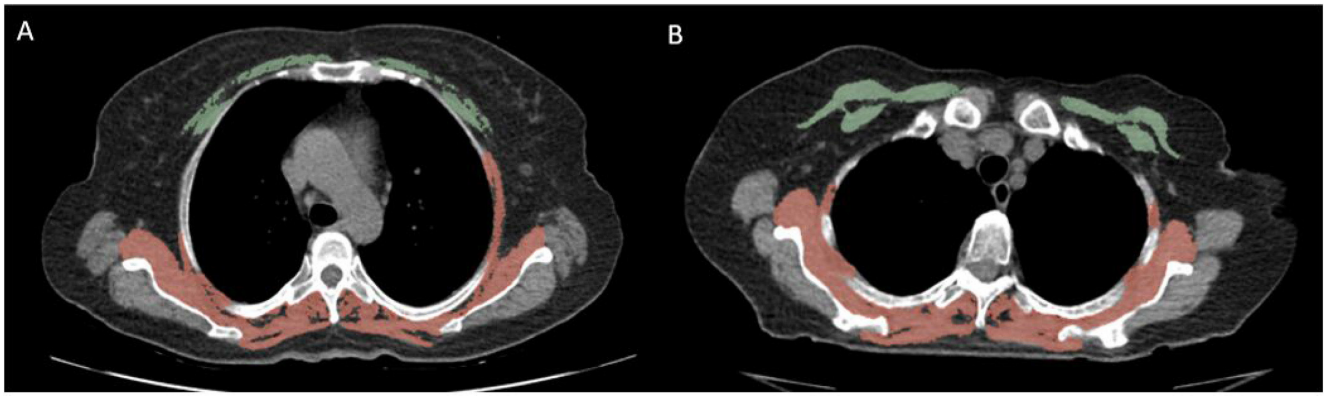

Figure 1. Examples of muscle (pectoral, back and skeletal muscles) segmentation performed with 3-D Slicer with lower (A) and higher muscle area (B).

may be more feasible for speedy integration to clinical prognostication[10]. 3-D slicing technology is a method used in many studies on different subjects in abdomen and chest CT, as well as skeletal muscle measurements specifically in the diagnosis of sarcopenia[11-13]. SMA has been assessed at L3 and has been shown to correlate with SMA measured at the level of T4 vertebra level[10].

In recent studies, pectoralis musculature was reported to have a prognostic role in patients with COVID-19[14,15].

Since chest CT is standard of care for hospitalized COVID-19 cases, we aimed to evaluate the prognostic efficacy of SMA at T4 level on clinical outcomes (ICU stay, length of hospital stay, mortality) for this patient group.

Materials and Methods

Patient Characteristics

Patients admitted to the hospital between 1 October 2021 and 30 November 2021 with a primary diagnosis of COVID-19 were prospectively recorded in a database. Age, gender, comorbidities, ICU stay, length of hospital stay, and ultimate outcome were recorded.

Radiological Assessment

Chest CT was performed for every patient with a primary admission diagnosis of COVID-19, within 1-2 days of hospitalization per clinician discretion.

Multi-slice routine Chest CT examination was performed using 64-detector CT scanner (GE Optima CT660 GE Healthcare, Milwaukee, WI) with/without IV contrast medium. The CT image data was collected with a GE system equipped with a 512×512 matrix detector. The helical scanning region was performed in supine position without the gantry angle, from 1 cm above lung apices to completion of adrenal glands. Images were obtained using acquisition 24x1.2 mm, slice collimation 1.2 mm with, slice width 2,5 mm, pitch 0.98, 120 Kv and 75 mAs. Increment of 3 mm was shown to result in a variance of 1%, which was deemed as an acceptable variance for SMA measurements[10,16]. Same measurements were also shown to be relatively unchanged by introduction of contrast agents[10,17,18].

For CT-image analysis, two researchers (ZNT and MBD) performed image selection at T4 vertebra level using previously described method[10]. 20 cases were randomly selected for inter-observer agreement evaluation. Left and right pectoralis minor and major muscles (pectoral muscle area) and the combined bilateral muscles of the erector spinae, levator scapulae, rhomboideus minor and major, and transversospinalis groups (back muscle area) were manually segmented by researchers and pixels between - 29 and + 150 HU were chosen via automated thresholding, the image data was then processed using 3-D Slicer per developer's specifications (Figure 1).

Statistical Analysis

The data were analyzed by using SPSS software (IBM SPSS Statistics for Windows, version 23.0, Armonk, NY: IBM corporation). Mean, standard deviation, and median values were calculated. The distribution of variables was determined by using Kolmogorov – Smirnov test. Student's t test was used for comparisons between groups of normally distributed variables. Pearson Chi Square test and Fisher's Exact test were used to compare qualitative data. ROC curve analysis was used to determine the cut-off points of muscle measurements according to mortality. Considering the length of stay (LOS) durations, evaluations were made for mortality and ICU using univariate and multivariate Cox regression analysis. Significance was evaluated at the $p<0.05$ level.

Interobserver agreement was determined by using intraclass correlation coefficient (ICC), values between 0.75

Table 1. Patient characteristics.

	Survived (n=140)	Dead (n=27)	P value
Male/Female	68/72	12/15	0.69**
Age	60.8±16.7	73.4±11.4	0.001*
LOS	8.4±5.7 (7)	14.6±6.9 (14)	0.001**
ICU yes/no	2/138	26/1	0.001***
DM yes/no	25/115	2/25	0.18***
COPD yes/no	16/124	0/27	0.08***
Malignancy yes/no	1/139	0/27	1.000***
HT yes/no	3/137	0/27	1.000***
Bacterial pneumonia yes/no	26/114	5/22	0.99*

Student t test, ** Pearson Chi-Square, * Fisher's Exact test, LOS: length of stay, ICU: intensive care unit, DM: diabetes mellitus, COPD: chronic obstructive pulmonary disease, HT: essential hypertension.*

Table 2. The evaluation of inter-observer reliability for muscle areas.

		Intraclass Correlation	95% Confidence Interval	
			Lower Bound	Upper Bound
Pectoralis muscle area	Single Measures	.988	.970	.995
	Average Measures	.994	.985	.998
Back muscle area	Single Measures	.987	.966	.995
	Average Measures	.993	.983	.997
Total Skeletal muscle area	Single Measures	.987	.969	.995
	Average Measures	.994	.984	.997

Two-way mixed effects model where people effects are random and measures effects are fixed.

and 0.9 were determined as good and an ICC greater than 0.90 was determined as excellent.

Results

167 consecutive patients (80 male, 87 female) were identified during the study period. Mean age was 62.90±16.68 years. Age distribution was similar for both genders (64.9±16.2 vs 60.9±16.9 years, p=0.12), length of hospital stay was also comparable (8.8±5.9 vs 9.9±6.7 days, p=0.18). Presence of comorbidities (diabetes, chronic obstructive pulmonary disease, hypertension, previous malignancy), likelihood of ICU stay and superimposed bacterial pneumonia were also equivalent between male and female patients (Table 1).

Twenty cases were randomly selected for inter-observer reliability assessment. The evaluation of inter-observer reliability was rated as excellent with ICCs ranging from 0.985 to 0.998 for pectoralis muscle, 0.983 to 0.997 for back muscle and 0.984 to 0.997 for skeletal muscle (Table 2). Male patients on average had greater muscle area for pectoral and total muscle but not for back muscle area measurements (8569±5061 mm^2 vs 4059±1450 mm^2, 5841±1599 mm^2 vs 7935±2831 mm^2, 14411±50685 mm^2 vs 11995±3919 mm^2, p<0,0001). Male and female patients were distributed comparably between survivors and fatal cases. Fatal cases were on average older and had a longer hospital stay. The rest of the patient characteristics are summarized in Table 1.

Pectoral, back and total SMA were significantly lower in patients with a mortality outcome or ICU stay (Table 3).

ROC curve analysis was used to determine the cut-off point for pectoralis muscle, back muscle and total skeletal muscle values that were found to be significant according to mortality (Table 4) (Figure 2). The cut-off point for pectoralis muscle area measurements according to mortality was determined as 2800 mm^2 and below. For the 2800 mm^2 cut-off value of the pectoralis muscle area; sensitivity was 51.85%, specificity was 74.10%, positive predictive value was 28.0% and negative predictive value was 88.79%. The standard error of 68% of the area under the ROC curve

Table 3. Distribution of pectoralis, back and total skeletal muscle area (mm^2) in patient subgroups.

	Survived (n:140)	Exitus (n:27)	P value*
Pectoralis muscle area	3670±1383	2876±1287	0.006
Back muscle area	7180±2507	5649±2384	0.004
Total skeletal muscle area	14045±8525	8525±3449	0.002
	No ICU(n=139)	Yes ICU(n=28)	
Pectoralis muscle area	3652±1400	2994±1256	0.022
Back muscle area	7157±2551	5816±2231	0.011
Total skeletal muscle area	14027±3840	8810±3257	0.008
**Student t test.*			

Table 4. Diagnostic screening tests and ROC curve results for pectoralis, back and total skeletal muscle area (mm^2) measurements for mortality.

	Diagnostic Scan					ROC Curve		*p*
	Cut off	Sensitivity	Specificity	Positive Predictive Value	Negative Predictive Value	Area	95% CI	
Pectoralis m.	≤***2800***	51.85	74.10	28.00	88.79	**0.680**	0.560-0.800	***0.003****
Back m.	≤***5400***	51.85	69.29	24.56	88.18	**0.664**	0.548-0.778	***0.007****
Total m.	≤***8000***	48.14	73.57	26.00	88.03	**0.687**	0.564-0.804	***0.003****
CI: Confidence Interval.								

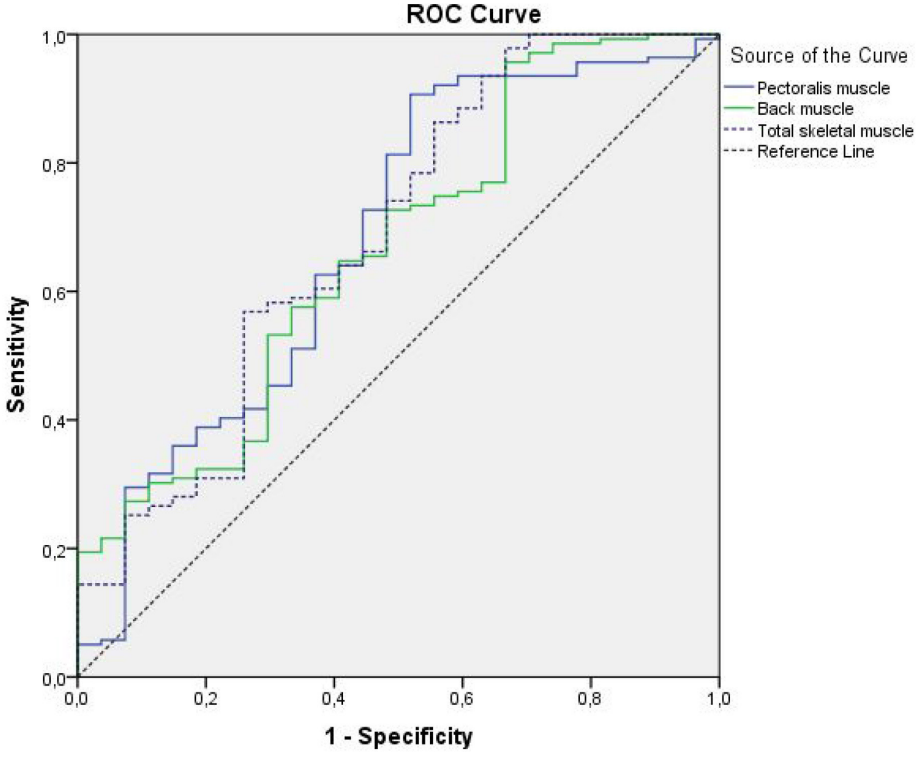

Figure 2. ROC curve analysis of mortality outcome and pectoralis, back and skeletal muscle area.

Table 5. Multivariate Cox regression analyses for mortality.

LOS	Mortality		Univariate		Multivariate	
	Survived (n:140)	Exitus (n:27)	HR (95% CI)	p	HR (95% CI)	p
	Mean ± SD (Median)	*Mean ± SD (Median)*				
Age (year)	60.8±16.7	73.4±11.4	1.044 (1.010 - 1.078)	***0.011***	1.025(0.986-1.065)	***0.212***
	n (%)	*n (%)*				
Pectoralis muscle (≤***2800***)	36 (25.9)	14 (51.9)	4.105 (1.834-9.187)	***0.001***	3.138 (1.171-8.413)	***0.001***
Back muscle (≤***5400***)	43 (30.7)	14 (51.9)	1.444 (0.675-3.086)	***0.343***	0.835(0.263-2.650)	***0.760***
Total skeletal muscle (≤***8000***)	37 (26.4)	13 (48.1)	2.232 (1.026-4.857)	***0.043***	1.046(0.277-1.066)	***0.472***
HR: Hazard Ratio, CI: Confidence Interval, DM: diabetes mellitus.						

Table 6. Multivariate Cox regression analyses for ICU.

LOS	ICU		Univariate		Multivariate	
	No ICU (n=139)	Yes ICU(n=28)	HR (95% CI)	p	HR (95% CI)	p
	Mean ± SD (Median)	*Mean ± SD (Median)*				
Age (year)	60.8±16.9	73.4±11.1	1.041 (1.008 - 1.075)	***0.014***	1.029 (0.994-1.065)	***0.106***
	n (%)	*n (%)*				
Pectoralis muscle (≤***2800***)	37 (26.8)	13 (46.4)	3.189(1.454-6.996)	***0.004***	2.361 (1.012-5.505)	***0.047***
Back muscle (≤***5400***)	44 (31.7)	13 (46.4)	1.143 (0.542-2.414)	***0.725***	1.397 (0.450-4.336)	***0.563***
Total skeletal muscle (≤***8000***)	38 (27.3)	12 (42.9)	1.741 (0.808-3.752)	***0.157***	1.012 (0.276-3.719)	***0.985***
HR: Hazard Ratio, CI: Confidence Interval, DM: diabetes mellitus.						

obtained was determined as 6.1%. The cut-off point was determined as 5400 mm^2 and below for the measurements of the back muscle area according to mortality. For the 5400 mm^2 cut-off value of the back muscle area; sensitivity was 51.85%, specificity was 69.29%, positive predictive value was 24.56% and negative predictive value was 88.19%. The standard error of the area under the ROC curve obtained was 66.4% and 5.9%. The cut-off point for total SMA measurements according to mortality was 8000 mm^2 and below. For the 8000 mm^2 cut-off value of the total SMA value; sensitivity was 48.14%, specificity was 73.57%, positive predictive value was 26% and negative predictive value was 88.03%. The area under the ROC curve obtained was 68.7% with a standard error of 6.1%. 81 patients were >65 years of age. Among those patients, pectoral (p=0.034, AUC=0.656) and SMA (p=0.039, AUC=0.652) were found to be lower in patients with a mortality outcome. Same relationship was not observed for patients younger than 65 years.

For mortality, age, pectoralis muscle area, back muscle area and total SMA variables, which were significant in univariate evaluations, were evaluated with Cox regression analysis, taking into account LOS. Age, pectoralis muscle area and total SMA measurements were significantly included in Univariate Cox regression evaluations (p<0.05). It was observed that HR value of one unit increase in age was 1.044 (95% CI: 1.010-1.078); having pectoralis muscle area below 2800 had an HR risk of 4,105 (95% CI: 1,834-9.187), and having total skeletal muscle value below 8000 had a HR risk of 2,232 (95% CI: 1.026-4.857) (Table 5). On the other hand, in the multivariate analysis, only the pectoralis muscle area value remained significant in the model (p<0.01), the HR value for the pectoralis muscle area value below 2800 was found to be 3.138 (95% CI: 1.171-8.413), and pectoralis muscle can be considered as an independent risk factor for mortality (Table 5).

Age, pectoralis muscle area, back muscle area and total SMA variables, which were significant in univariate evaluations for ICU, were evaluated with Cox regression

analysis considering LOS. Age and pectoralis muscle area measurements were significantly included in Univariate Cox regression evaluations (p<0.05). It was seen that the HR value of one unit increase in age was 1.041 (95% CI: 1.008-1.075) and the HR risk of being below pectoralis muscle area 2800 was found to be 3.189 (95% CI: 1.545-6.996) (Table 6). In the multivariate analysis, only the pectoralis muscle area value remained significant in the model (p<0.01), the HR value for the pectoralis muscle area value below 2800 was found to be 2.361 (95% CI: 1.012-5.505), and pectoralis muscle can be considered as an independent risk factor for ICU (Table 6).

Discussion

Clinical behavior of COVID-19 has a large spectrum and even though some patients have classical risk factors and have favorable outcomes, the reverse can also occur, albeit sparingly. World Health Organization reports put overall mortality at 1.38%[19]. In specific populations mortality can be much higher, for example for patients who present with acute renal failure, in-hospital mortality was found to be 22.5%[20].

Sarcopenia is characterized by generalized progressive loss of muscle mass and muscle strength; It has been defined as a syndrome associated with endpoints such as physical disability, deterioration in quality of life, and death[5]. It has been shown as an adverse prognostic factor in the clinical course during most types of medical stress[21,22]. It is estimated that during the COVID-19 pandemic, patients with sarcopenia have increased infection rates and have a worse prognosis. Kim et al. reported that baseline sarcopenia is associated with a prolonged hospital stay in patients with COVID-19[23]. Also in a recent meta-analysis, patients with sarcopenia are reported to have risk of developing poor COVID-19 outcomes[24]. Early recognition and intervention of sarcopenia can change the course of COVID-19 disease and reduce the complications that may develop.

Our study, even though relatively small, was able to capture an inpatient COVID-19 population close to clinical practice in regards to age, gender, and overall comorbidity distribution. Age was a factor assumed to be significant in predicting mortality in COVID-19. In the study of Quinn et al. investigating the effects of age and frailty on COVID-19 mortality, the relationship between age increase and mortality was found to be significant[25]. In the study conducted by Wang et al. on 125 patients with a diagnosis of COVID-19, the mean age was found to be 49.4 years in critical patients and 39.5 years in non-critical patients. It has been observed that the length of hospital stay increases with increasing age[26]. In the meta-analysis study conducted by Pijls et al, admission to ICU was found to be significant with increasing age[27]. In this present study, age, length of stay, and ICU admission were found to be associated with mortality which are in line with the literature.

Hocaoglu et al. examined the effect of pectoral muscle volume and density on the severity of COVID-19 pneumonia and found an association between decreased muscle volume/density and mortality[28]. Pectoral, back and SMA measurement from chest CT images at T4 level has been proposed as a surrogate sarcopenia marker and was found to correlate with L3 level[10].

The literature is not yet sufficient and shows some differences regarding the measured muscle area and the level at which muscle area is evaluated[29-32]. Heusden et al. have recently demonstrated the feasibility of the T4 vertebral level on a chest CT in the measurement of SMA as an alternative to L3 level on abdominal CT[10]. Also in a few recent studies, pectoralis musculature measured at T4 level has been reported to be prognostic in patients with COVID-19[14,15]. Therefore, in this study, the T4 level was used as a newly available method in the evaluation of muscle areas, as previously documented by Koehler et al.[31]. In the present study, we used an open-source software for measurement and were able to capture mortality data.

We found that decreased pectoralis, back and total SMA were related to adverse outcomes (ICU stay and death) but were not closely associated with other in-hospital adverse events like long hospital stay or superimposed bacterial pneumonia. Literature concerning SMA and other radiological sarcopenia markers and various outcomes is not conclusive. For example, pectoralis muscle area and index were previously associated with length of hospital stay and death in COVID-19 patients[33]. Meyer et al. reported an association of SMA identified by CT with in-hospital mortality in COVID-19 patients[34]. Salman et al. also reported that lower skeletal muscle mass measured on an axial CT image at the level of the twelfth thoracic vertebra had a univariate association with mortality in children with COVID-19[35]. In contrast to those findings, no strong correlation was found between skeletal muscle index at the level of T12 and mortality in 519 hospitalized COVID-19 patients and paraspinal muscle index and radiodensity in male hospitalized COVID 19 cases[36,37]. However, in two recent studies, pectoralis musculature measured at T4 level has been shown to be prognostic in COVID-19 patients[14,15]. The diversity in measurement techniques, classification of outcomes etc. may play a role in this variability.

While age is defined as the major risk factor for adverse outcomes in COVID-19, we also observed that, the relationship between pectoralis and skeletal muscle area and mortality persisted after subgroup analysis for patients older than 65 years. Currently, many agents are being evaluated for effectiveness against COVID-19, most of those studies emphasize the need for early intervention before clinical progression and resource prioritization. SMA measurement with 3-D slicer has been shown to have a lower learning curve and excellent inter-observer agreement, pectoral/back muscles at T4 are done from CT scans which are standard of care in COVID-19 patients and do not need extra imaging/redundant studies. Therefore, pectoralis muscle area and SMA calculation on admission Chest CT shows great promise as a prognostic marker to be included in further clinical trials.

This study has several limitations. First of all, this patient collective might be not representative of the current state

of the pandemic. Despite the patient and mortality data collection was done prospectively, identification of relevant radiologic studies and muscle area measurement were done retrospectively. Case numbers are relatively low so generalizability may be limited. We did not observe any relationship between length of hospital stay and either ultimate outcomes or muscle area measurements. This may be the result of components inherent to clinical practice (availability of post-discharge skilled care, social support systems, patient preference etc.) and might be individual country/system dependent. Further studies are needed for standardization of CT-derived sarcopenia measures and predicted clinical outcomes.

Conclusion

Thoracic sarcopenia is found to be associated with mortality and ICU hospitalization in patients with COVID-19. Since calculation of pectoralis muscle area at T4 level on Chest CT images can be used as a surrogate sarcopenia marker in the diagnosis of COVID-19, it may be possible to predict the prognosis at the time of admission.

Ethical approval

All patients consented for use of their anonymized data for scientific purposes. The study design was non-interventional. The study was performed under institutional review board approval (Decision number: 2021/0601) and Ministry of Health permission (decision number: 2021-11-15T11_46_24). This study was performed in line with the principles of the Declaration of Helsinki. Approval was granted by the Ethics Committee of Istanbul Medeniyet University (2021/0601).

References

1. Elkrief A, Hennessy C, Kuderer NM, Rubinstein SM, Wulff-Burchfield E, Rosovsky RP, Vega-Luna K, Thompson MA, Panagiotou OA, Desai A, Rivera DR, Khaki AR, Tachiki L, Lynch RC, Stratton C, Elias R, Batist G, Kasi A, Shah DP, Bakouny Z, Cabal A, Clement J, Crowell J, Dixon B, Friese CR, Fry SL, Grover P, Gulati S, Gupta S, Hwang C, Khan H, Kim SJ, Klein EJ, Labaki C, McKay RR, Nizam A, Pennell NA, Puc M, Schmidt AL, Shahrokni A, Shaya JA, Su CT, Wall S, Williams N, Wise-Draper TM, Mishra S, Grivas P, French B, Warner JL, Wildes TM. Geriatric risk factors for serious COVID-19 outcomes among older adults with cancer: a cohort study from the COVID-19 and Cancer Consortium. The Lancet Healthy longevity 2022;3(3):e143-e152.
2. Carrillo-Vega MF, Salinas-Escudero G, García-Peña C, Gutiérrez-Robledo LM, Parra-Rodríguez L. Early estimation of the risk factors for hospitalization and mortality by COVID-19 in Mexico. PloS one 2020; 15(9):e0238905.
3. Quitián LM, Rodríguez-Martinez CE, Sossa-Briceño MP, Cortés JA. Disease burden and vaccination priorities in Colombia. Vaccine 2022;40(12):1717–1721.
4. Wen W, Chen C, Tang J, Wang C, Zhou M, Cheng Y, Zhou X, Wu Q, Zhang X, Feng Z, Wang M, Mao Q. Efficacy and safety of three new oral antiviral treatment (molnupiravir, fluvoxamine and Paxlovid) for COVID-19: a meta-analysis. Annals of medicine 2022;54(1):516-523.
5. Santilli V, Bernetti A, Mangone M, Paoloni M. Clinical definition of sarcopenia. Clinical cases in mineral and bone metabolism : the official journal of the Italian Society of Osteoporosis, Mineral Metabolism, and Skeletal Diseases 2014;11(3):177-80.
6. Ferreira AP, Machado MV. Impact of pretransplant frailty and sarcopenia on the post-transplant prognosis of patients with liver cirrhosis: a systematic review. Eur J Gastroenterol Hepatol 2021 2021/12//;33(1S Suppl 1):e883-e897.
7. Huq S, Khalafallah AM, Ruiz-Cardozo MA, Botros D, Oliveira LAP, Dux H, White T, Jimenez AE, Gujar SK, Sair HI, Pillai JJ, Mukherjee D. A novel radiographic marker of sarcopenia with prognostic value in glioblastoma. Clinical neurology and neurosurgery 2021;207:106782.
8. Lee ZY, Ong SP, Ng CC, Yap CSL, Engkasan JP, Barakatun-Nisak MY, Heyland DK, Hasan MS. Association between ultrasound quadriceps muscle status with premorbid functional status and 60-day mortality in mechanically ventilated critically ill patient: A single-center prospective observational study. Clinical nutrition (Edinburgh, Scotland) 2021;40(3):1338-1347.
9. Cavayas YA, Eljaiek R, Rodrigue É, Lamarche Y, Girard M, Wang HT, Levesque S, Denault AY. Preoperative Diaphragm Function Is Associated With Postoperative Pulmonary Complications After Cardiac Surgery. Critical care medicine 2019;47(12):e966-e974.
10. van Heusden HC, Swartz JE, Chargi N, de Jong PA, van Baal M, Wegner I, de Bree R. Feasibility of assessment of skeletal muscle mass on a single cross-sectional image at the level of the fourth thoracic vertebra. Eur J Radiol 2021;142:109879.
11. Dong X, Dan X, Yawen A, Haibo X, Huan L, Mengqi T, Linglong C, Zhao R. Identifying sarcopenia in advanced non-small cell lung cancer patients using skeletal muscle CT radiomics and machine learning. Thoracic Cancer 2020;11(9): 2650–2659.
12. Negroni D, Zagaria D, Paladini A, Falaschi Z, Arcoraci A, Barini M, Carriero A. COVID-19 CT Scan Lung Segmentation: How We Do It. Journal of Digital Imaging 2022;35(3):424-431.
13. Fedorov A, Beichel R, Kalpathy-Cramer J, Finet J, Fillion-Robin J-C, Pujol S, Bauer C, Jennings D, Fennessy F, Sonka M, Buatti J, Aylward S, Miller J, Pieper S, Kikinis R. 3D Slicer as an Image Computing Platform for the Quantitative Imaging Network. Magnetic resonance imaging 2012;30:1323-41.
14. Surov A, Kardas H, Besutti G, Pellegrini M, Ottone M, Onur MR, Atak F, Erdemir AG, Hocaoglu E, Yıldız Ö, Inci E, Cingöz E, Cingöz M, Dursun M, Korkmaz İ, Orhan Ç, Strobel A, Wienke A, Pech M. Prognostic Role of the Pectoralis Musculature in Patients with COVID-19. A

Multicenter Study. Academic radiology 2022:S1076-6332(22)00299-92.
15. Kardas H, Thormann M, Bär C, Omari J, Wienke A, Pech M, Surov A. Impact of Pectoral Muscle Values on Clinical Outcomes in Patients With Severe Covid-19 Disease. *In vivo* (Athens, Greece) 2022;36(1):375-380.
16. Fuchs G, Chretien YR, Mario J, Do S, Eikermann M, Liu B, Yang K, Fintelmann FJ. Quantifying the effect of slice thickness, intravenous contrast and tube current on muscle segmentation: Implications for body composition analysis. Eur Radiol 2018;28(6):2455-2463.
17. van der Werf A, Dekker IM, Meijerink MR, Wierdsma NJ, de van der Schueren MAE, Langius JAE. Skeletal muscle analyses: agreement between non-contrast and contrast CT scan measurements of skeletal muscle area and mean muscle attenuation. Clinical physiology and functional imaging 2018;38(3):366-372.
18. van Vugt JLA, Coebergh van den Braak RRJ, Schippers HJW, Veen KM, Levolger S, de Bruin RWF, Koek M, Niessen WJ, JNM IJ, Willemsen F. Contrast-enhancement influences skeletal muscle density, but not skeletal muscle mass, measurements on computed tomography. Clinical nutrition (Edinburgh, Scotland) 2018;37(5):1707-1714.
19. WHO. WHO Coronavirus Disease (COVID-19) Dashboard. 2022.
20. Costa RLD, Sória TC, Salles EF, Gerecht AV, Corvisier MF, Menezes MAM, Ávila CDS, Silva ECF, Pereira SRN, Simvoulidis LFN. Acute kidney injury in patients with Covid-19 in a Brazilian ICU: incidence, predictors and in-hospital mortality. Jornal brasileiro de nefrologia : 'orgao oficial de Sociedades Brasileira e Latino-Americana de Nefrologia 2021;43(3):349-358.
21. Anjanappa M, Corden M, Green A, Roberts D, Hoskin P, McWilliam A, Choudhury A. Sarcopenia in cancer: Risking more than muscle loss. Technical innovations & patient support in radiation oncology 2020;16:50-57.
22. Pipek LZ, Baptista CG, Nascimento RFV, Taba JV, Suzuki MO, do Nascimento FS, Martines DR, Nii F, Iuamoto LR, Carneiro-D'Albuquerque LA, Meyer A, Andraus W. The impact of properly diagnosed sarcopenia on postoperative outcomes after gastrointestinal surgery: A systematic review and meta-analysis. PloS one 2020;15(8):e0237740.
23. Kim JW, Yoon JS, Kim EJ, Hong HL, Kwon HH, Jung CY, Kim KC, Sung YS, Park SH, Kim SK, Choe JY. Prognostic Implication of Baseline Sarcopenia for Length of Hospital Stay and Survival in Patients With Coronavirus Disease 2019. The journals of gerontology Series A, Biological sciences and medical sciences 2021;76(8):e110-e116.
24. Siahaan YMT, Hartoyo V, Hariyanto TI, Kurniawan A. Coronavirus disease 2019 (Covid-19) outcomes in patients with sarcopenia: A meta-analysis and meta-regression. Clinical nutrition ESPEN 2022;48:158-166.
25. Welch C. Age and frailty are independently associated with increased COVID-19 mortality and increased care needs in survivors: results of an international multi-centre study. Age Ageing 2021;50(3):617-630.
26. Wang R, Pan M, Zhang X, Han M, Fan X, Zhao F, Miao M, Xu J, Guan M, Deng X, Chen X, Shen L. Epidemiological and clinical features of 125 Hospitalized Patients with COVID-19 in Fuyang, Anhui, China. International Journal of Infectious Diseases 2020;95:421-428.
27. Pijls BG, Jolani S, Atherley A, Derckx RT, Dijkstra JIR, Franssen GHL, Hendriks S, Richters A, Venemans-Jellema A, Zalpuri S, Zeegers MP. Demographic risk factors for COVID-19 infection, severity, ICU admission and death: a meta-analysis of 59 studies. BMJ Open 2021;11(1):e044640.
28. Hocaoglu E, Ors S, Yildiz O, Inci E. Correlation of Pectoralis Muscle Volume and Density with Severity of COVID-19 Pneumonia in Adults. Academic radiology 2021;28(2):166-172.
29. Schiaffino S, Albano D, Cozzi A, Messina C, Arioli R, Bnà C, Bruno A, Carbonaro LA, Carriero A, Carriero S, Danna PSC, D'Ascoli E, De Berardinis C, Della Pepa G, Falaschi Z, Gitto S, Malavazos AE, Mauri G, Monfardini L, Paschè A, Rizzati R, Secchi F, Vanzulli A, Tombini V, Vicentin I, Zagaria D, Sardanelli F, Sconfienza LM. CT-derived Chest Muscle Metrics for Outcome Prediction in Patients with COVID-19. Radiology 2021;300(2):E328-e336.
30. Ali AM, Kunugi H. Screening for Sarcopenia (Physical Frailty) in the COVID-19 Era. International journal of endocrinology 2021;2021:5563960.
31. Koehler J, Boirie Y, Bensid L, Pereira B, Ghelis N, Dupuis C, Tournadre A, Boyer L, Cassagnes L. Thoracic sarcopenia as a predictive factor of SARS-COV2 evolution. Clinical nutrition (Edinburgh, Scotland) 2022;S0261-5614(22)00032-2.
32. Menozzi R, Valoriani F, Prampolini F, Banchelli F, Boldrini E, Martelli F, Galetti S, Fari R, Gabriele S, Palumbo P, Forni D, Pantaleoni M, D'Amico R, Pecchi AR. Impact of sarcopenia in SARS-CoV-2 patients during two different epidemic waves. Clinical nutrition ESPEN 2022;47:252-259.
33. Ufuk F, Demirci M, Sagtas E, Akbudak IH, Ugurlu E, Sari T. The prognostic value of pneumonia severity score and pectoralis muscle Area on chest CT in adult COVID-19 patients. Eur J Radiol 2020;131:109271.
34. Meyer HJ, Wienke A, Surov A. Computed tomography-defined body composition as prognostic markers for unfavourable outcomes and in-hospital mortality in coronavirus disease 2019. J Cachexia Sarcopenia Muscle 2022;13(1):159-168.
35. Salman R, Sammer MB, Serrallach BL, Sangi-Haghpeykar H, Annapragada AV, Paul Guillerman R. Lower skeletal muscle mass on CT body composition analysis is associated with adverse clinical course and outcome in children with COVID-19. La Radiologia medica 2022;127(4):440-448.
36. Moctezuma-Velázquez P, Miranda-Zazueta G, Ortiz-Brizuela E, González-Lara MF, Tamez-Torres KM, Román-Montes CM, Díaz-Mejía BA, Pérez-García E, Villanueva-Reza M, Tovar-Méndez VH, Medrano-Borromeo C,

Martínez-Valenzuela A, Jandete-Medina M, Martínez-Guerra BA, Uscanga-Domínguez L, Sifuentes-Osornio J, Ponce-de-León A, Olivas-Martinez A, Moctezuma-Velázquez C. Low Thoracic Skeletal Muscle Area Is Not Associated With Negative Outcomes in Patients With COVID-19. American journal of physical medicine & rehabilitation 2021;100(5):413-418.

37. Feng Z, Zhao H, Kang W, Liu Q, Wu J, Bragazzi NL, Ma X, Wang W, Rong P. Association of Paraspinal Muscle Measurements on Chest Computed Tomography With Clinical Outcomes in Patients With Severe Coronavirus Disease 2019. The journals of gerontology Series A, Biological sciences and medical sciences 2021; 76(3):e78-e84.