

## Original Article

# Diaphragm thickness on computed tomography for nutritional assessment and hospital stay prediction in critical COVID-19

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**Background and Objectives:** To evaluate the significance of diaphragm thickness (DT) in assessing the nutritional status and predicting the length of hospital stay (LOS) of patients with COVID-19. **Methods and Study Design:** The data of 212 patients with severe and critical COVID-19 in Wuhan, China, were retrospectively analyzed. Computed tomography (CT)-obtained DT was measured in cross-sectional images of the mediastinal window at the level of the outlet of the celiac trunk at admission and at 2 weeks, then the rate of change in DT (RCDT) at 2 weeks was calculated. Nutritional risk and malnutrition were evaluated at admission. **Results:** A total of 91 patients were involved in the study. The mean DT was 3.06±0.58 mm (3.15±0.63 mm in male and 2.93±0.50 mm in female). DT was significantly negatively correlated with malnutrition based on Global Leadership Initiative on Malnutrition (GLIM) criteria ( $r=-0.324$ ,  $p=0.002$ ), Nutritional Risk Screening 2002 (NRS-2002) score ( $r=-0.364$ ,  $p=0.000$ ) and the Malnutrition Universal Screening Tool (MUST) score ( $r=-0.326$ ,  $p=0.002$ ) at admission. For the prediction of LOS  $\geq 4$  weeks in patients with COVID-19, the area under the ROC curve (AUC) of the RCDT at 2 weeks was 0.772, while the AUCs of DT, NRS-2002, MUST and Nutrition Risk in Critically Ill scores at admission were 0.751, 0.676, 0.638 and 0.699 respectively. According to the model of multiple linear regression analysis, the DT at admission ( $\beta=-0.377$ ,  $p=0.000$ ), RCDT at 2 weeks ( $\beta=-0.323$ ,  $p=0.001$ ), and mechanical ventilation ( $\beta=0.192$ ,  $p=0.031$ ) were independent risk factors contributed to LOS. **Conclusions:** CT-obtained DT can be used as a dynamic assessment tool for evaluating the nutritional status of patients in isolation wards for COVID-19.

**Key Words:** coronavirus disease 2019, nutritional screening, skeletal muscle, diaphragm thickness, length of hospital stay

## INTRODUCTION

The global coronavirus disease (COVID-19) epidemic has been present for longer than a year, posing a serious threat to human health worldwide. As of Nov 15, 2021, more than 250 million people have been reported to be infected and more than 5 million people have died.<sup>1</sup> Studies have reported that the prevalence of malnutrition is about 40% of COVID-19 pneumonia patients,<sup>2</sup> while a higher nutritional risk was observed in 61% of the severe COVID-19 pneumonia patients in ICU.<sup>3</sup> Nutritional assessment and support are indispensable components of the treatment regimen for COVID-19. Although many researchers have proposed that nutritional assessment and support in the context of COVID-19 are of great significance,<sup>4,5</sup> there are few studies on the topic. Several traditional nutritional risk scoring tools, such as the Nutritional Risk Screening (NRS), Malnutrition Universal Screening Tool (MUST), and Nutrition Risk in the Critically Ill (NUTRIC) scores, have been used for screening nutritional risks in COVID-19 pneumonia patients.<sup>3,6,7</sup> Considering that COVID-19 usually has an acute onset and rapid

progress, these tools have certain limitations and are unable to accurately monitor the nutritional status of the patient throughout the course of the disease. Challenging periods like the COVID-19 pandemic require fast and efficient adaptations of the healthcare system.<sup>8</sup> Therefore, we are interested in determining a novel convenient objective indicator that can accurately and dynamically evaluate the nutritional status of patients with COVID-19.

Skeletal muscle atrophy is an important manifestation of malnutrition and is closely related to the prolonged duration of mechanical ventilation, ICU stay and hospital

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stay, and the increased 1-year mortality.<sup>9</sup> The dynamic monitoring of skeletal muscle indicators, that has received widespread attention, allows for the assessment of nutritional status in real time and can guide nutrition therapy.<sup>10</sup> The diaphragm is a skeletal muscle closely related to respiratory function. More than 60–80% of the tidal volume in spontaneous breathing is produced by diaphragm contraction, which declines under severe disease conditions.<sup>11,12</sup> Diaphragm atrophy has a considerable impact on the prognosis of patients with pneumonia.<sup>13</sup> Therefore, monitoring changes in the diaphragm thickness (DT) may be of clinical significance for the dynamic assessment of nutritional status and guidance of nutritional therapy in patients with COVID-19. We hypothesize that DT is a useful nutritional assessment parameter in severe COVID-19. Bedside ultrasound was recommended to measure respiratory muscles in COVID-19 patients,<sup>14</sup> nevertheless it increased the working hours of medical staff in isolation wards and consumed more personal protective equipment. DT can also be obtained remotely from completed chest computed tomography (CT), which is an important diagnostic method for COVID-19 pneumonia. However, no data to date is available about changes in DT of patients with COVID-19 on CT. We simplified the protocol for DT measured from CT images,<sup>15</sup> and made the data to be obtained more quickly and clinic-friendly. The objectives of this study were to observe the dynamic changes in the CT-obtained DT of patients with COVID-19 along the course of the disease, evaluate the consistency between nutritional screening tools and assessing DT, and assess the correlation between the change in DT and the length of hospital stay (LOS) of patients with severe COVID-19.

## METHODS

### Study population

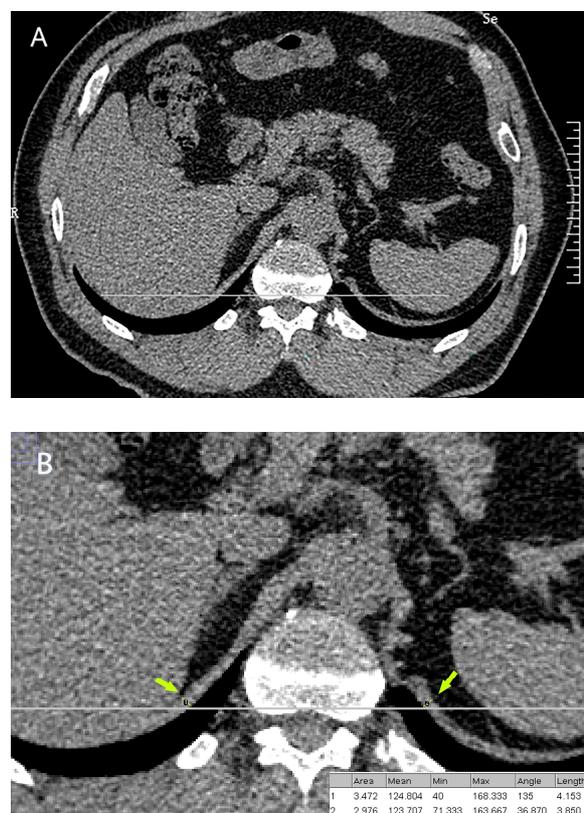
We retrospectively analyzed patients with a confirmed diagnosis of severe and critical COVID-19 who were admitted to three wards at Wuhan No. 1 Hospital and the Guanggu Branch of Tongji Hospital, Wuhan City, Hubei Province, China, supported by two medical teams from February 9 to March 31, 2020. The COVID-19 diagnostic criteria were as follows: 1) a history of residence in an epidemic area, or a history of contact with individuals infected with COVID-19; 2) fever and/or respiratory symptoms; 3) imaging revealing multiple small patchy shadows, interstitial changes, ground-glass opacities, infiltration shadows, and consolidation in both lungs; 4) a normal or decreased total white blood cell count (WBC) and a normal or decreased lymphocyte count in the early stage of the disease; 5) a positive real-time fluorescent reverse transcription polymerase chain reaction test for COVID-19 nucleic acid on nasopharyngeal swab; and 6) severe COVID-19, which was assessed using the following criteria: a) shortness of breath with a respiratory rate  $\geq 30$  bpm; b) a resting-state finger pulse oxygen saturation  $\leq 93\%$ ; and c) an arterial partial pressure of oxygen or inhaled oxygen concentration  $\leq 300$  mmHg. Patients who met one of the following criteria were diagnosed with critical COVID-19: a) respiratory failure occurred and mechanical ventilation was required; b) shock occurred; or c) complicated failure of organs other than the lungs occurred, which required intensive care unit monitoring

and treatment. The inclusion criteria for participation in this study were an age  $\geq 18$  years and a diagnosis of severe or critical COVID-19. Patients who refused to participate in the study, those with a hospital length of stay of  $< 2$  weeks, and those with missing study data were excluded.

The protocol of this study has passed the review of the ethics committee of NanJing Drum Tower Hospital, the affiliated Hospital of Nanjing University Medical School. (NO.2020-012)

### Assessments

The Acute Physiology and Chronic Health Evaluation II (APACHE II), the Sequential Organ Failure Assessment (SOFA), NRS-2002 score, MUST score, NUTRIC score, number of comorbidities, white blood cell, lymphocyte, hemoglobin, prealbumin, albumin and C-reactive protein (CRP) were collected at admission. The patients were diagnosed with malnutrition based on Global Leadership Initiative on Malnutrition (GLIM) criteria at admission. To measure DT based on CT imaging, Image J software was used. The CT cross-sectional images were evaluated in the mediastinal window at the level of the outlet of the celiac trunk, and the intersection between the horizontal tangent line of the anterior edge of the spinal canal and the lateral margins of the diaphragm was selected as the measuring point. The DT was measured vertically to the surface of the diaphragm (Figure 1); each measurement of



**Figure 1.** Measurement of DT on chest CT. (A) The CT cross-sectional images were evaluated in the mediastinal window at the level of the outlet of the celiac trunk, and the intersection between the horizontal tangent line of the anterior edge of the spinal canal and the lateral margins of the diaphragm was selected as the measuring point. (B) Image J software was used to measure DT based on CT imaging. The DT was measured vertically to the surface of the diaphragm.

the thickness on the left and right sides of the diaphragm was recorded independently by 3 doctors, and the mean DT of the left and right sides measured 3 times was calculated. The rate of change in DT (RCDT) at 2 weeks was calculated using the following equation:

$$\text{RCDT at 2 weeks} = \frac{[(\text{diaphragm thickness at 2 weeks} - \text{diaphragm thickness at admission}) / \text{diaphragm thickness at admission}]$$

### **Nutritional support programmes**

The attending physicians in isolation wards assessed the nutritional risk and status for each individual at admission, and then set nutrition prescriptions that were online reviewed by dietitians within 24 hours after admission. Oral diet is proposed as the first therapeutic option, and oral enteral nutrition is replenished to achieve nutritional goals. When there is a decrease in oral intake, enteral nutrition will be supplemented by tube feeding. Parenteral nutrition is supplemented in the case of enteral nutrition intolerance over 3 days, from partial dose to full dose as appropriate.

### **Discharge criteria**

The patient discharge criteria were as follows: 1) improved clinical manifestations; 2) chest CT infiltrates were absorbed when compared to the previous examination; 3) two consecutive nucleic acid test results, with an interval of 24 hours, were negative; and 4) the blood lymphocyte count was within the normal range. Patients were divided into two groups based on whether the LOS was  $\geq 4$  weeks. A prolonged hospitalization was defined as LOS  $\geq 4$  weeks.

### **Statistical analyses**

Normally distributed data are represented as mean  $\pm$  standard deviation and non-normally distributed data as median. Data on patient characteristics were compared using the  $\chi^2$  test and measurement data using analysis of variance and the t-test. Spearman's correlation analysis was conducted to assess the relationship between DT at admission, RCDT at 2 weeks, and the NRS-2002 score, MUST score and NUTRIC score. Receiver operating characteristic (ROC) curves were performed to evaluate the value of DT at admission, RCDT at 2 weeks, and the

NRS-2002 score, MUST score, and NUTRIC score at admission in predicting prolonged hospitalization. Moreover, the effect of several variables on LOS was considered with multiple linear regression analysis. The data were processed using statistical software SPSS 22.0 and a two-tailed  $p < 0.05$  was considered to indicate a statistically significant difference.

## **RESULTS**

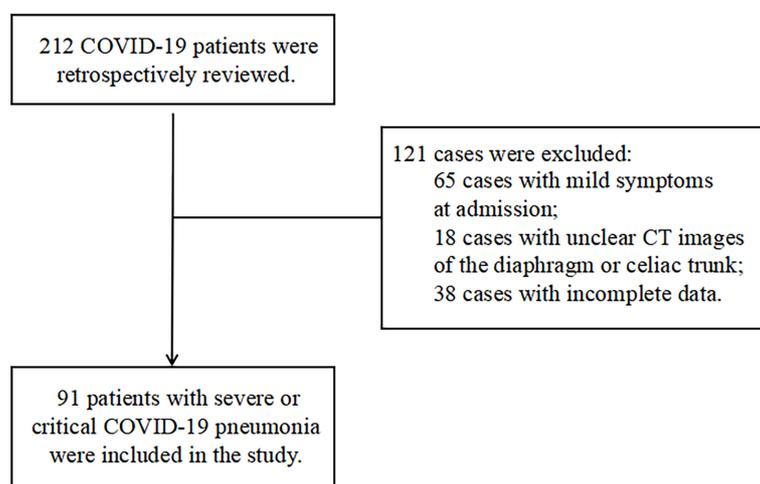
### **Patient baseline data**

A total of 212 COVID-19 patients were retrospectively reviewed; however, 65 cases with mild symptoms at admission, 18 cases with unclear CT images of the diaphragm or celiac trunk, and 38 cases with incomplete data (include 2 cases transferred to ICU and 3 cases died within 2 weeks) were excluded (Figure 2). Finally, 91 patients with severe or critical COVID-19 pneumonia were involved in this study. Mean age was  $60.5 \pm 15.9$  years, 52 patients (57.1%) were male, mean body mass index (BMI) was  $21.9 \pm 2.4$ , and 17 patients (18.9%) were found to have undernutrition. At admission, the median scores of APACHE II and SOFA were 10 and 2 respectively, the mean DT was  $3.06 \pm 0.58$  mm in total patients ( $3.15 \pm 0.63$  mm in male and  $2.93 \pm 0.50$  mm in female), and the mean LOS was  $29.1 \pm 7.7$  days.

There were no deaths in the enrolled patients. 53 patients (58.2%) with NRS-2002 score  $\geq 3$  at admission, were divided into the group with nutritional risk, while 38 patients with NRS-2002 score  $< 3$  at admission, were divided into groups without nutritional risk. There were significant differences in age, APACHE II score, SOFA score, number of comorbidities, WBC, lymphocyte, hemoglobin, albumin, prealbumin, DT at admission, and LOS between the two groups (Table 1).

### **Correlation between DT and nutritional risk and status**

DT at admission was significantly negatively correlated with malnutrition based on GLIM criteria ( $r = -0.324$ ,  $p = 0.002$ ), NRS-2002 ( $r = -0.364$ ,  $p = 0.000$ ) and MUST ( $r = -0.326$ ,  $p = 0.002$ ) at admission. There was no relativity between DT and NUTRIC score, WBC, lymphocyte, prealbumin, albumin, CRP (Table 2).



**Figure 2.** Enrolment of study cases.

**Table 1.** Baseline clinical and biochemical characteristics of 91 COVID-19 patients

Characteristics	Total (n=91)	NRS-2002 $\geq 3$ (n=53)	NRS-2002 $< 3$ (n=38)	<i>p</i>
Age, years	60.5 $\pm$ 15.9	65.5 $\pm$ 15.7	53.6 $\pm$ 13.5	<0.001
Gender				
Male, n (%)	52 (57.1)	33 (62.3)	19(50.0%)	0.244
BMI, kg/m <sup>2</sup>	22.3 $\pm$ 2.6	21.9 $\pm$ 2.78	22.7 $\pm$ 2.37	0.157
APACHE II	10 (8-15)	12 (9-18)	8 (5-10)	<0.001
SOFA	2 (2.0-3.0)	3 (2.0-3.5)	2 (2.0-2.0)	<0.001
Number of comorbidities, n (%)				<0.001
0	41 (45.1)	18 (34.0)	23(60.5%)	
1	26 (28.6)	17 (32.1)	9(23.7%)	
$\geq 2$	24 (26.4)	18 (34.0)	6(15.8%)	
WBC, $\times 10^9/L$	5.05 $\pm$ 2.65	4.23 $\pm$ 2.31	6.20 $\pm$ 2.68	<0.001
Lymphocyte, $\times 10^9/L$	1.20 $\pm$ 0.59	0.99 $\pm$ 0.36	1.49 $\pm$ 0.72	<0.001
Hemoglobin, g/L	123.7 $\pm$ 16.5	120.5 $\pm$ 17.6	128.2 $\pm$ 14.0	0.026
Prealbumin, mg/L	200.8 $\pm$ 87.5	181.1 $\pm$ 90.4	228.2 $\pm$ 76.2	0.011
Albumin, g/L	33.5 $\pm$ 4.7	31.6 $\pm$ 4.1	36.1 $\pm$ 4.4	0.000
CRP, mg/L	81.3 $\pm$ 46.3	84.2 $\pm$ 47.8	77.3 $\pm$ 44.5	0.481
NRS-2002	2.92 $\pm$ 1.52	3.96 $\pm$ 1.02	1.47 $\pm$ 0.69	<0.001
MUST	2.32 $\pm$ 0.94	2.83 $\pm$ 0.73	1.61 $\pm$ 0.72	<0.001
NUTRIC	2.14 $\pm$ 1.47	2.88 $\pm$ 1.40	1.11 $\pm$ 0.80	<0.001
DT at admission, mm	3.06 $\pm$ 0.58	2.90 $\pm$ 0.52	3.27 $\pm$ 0.60	0.002
Male, mm	3.15 $\pm$ 0.63	2.99 $\pm$ 0.59	3.43 $\pm$ 0.60	0.012
Female, mm	2.93 $\pm$ 0.50	2.76 $\pm$ 0.37	3.11 $\pm$ 0.56	0.024
Corticosteroid therapy, n (%)	8 (8.8)	7 (13.2)	1 (2.6)	0.079
Mechanical ventilation, n (%)	7 (7.7)	5 (9.4)	2 (5.3)	0.112
LOS, days	29.1 $\pm$ 7.7	31.9 $\pm$ 6.8	25.1 $\pm$ 7.2	<0.001

APACHE II: acute physiology and chronic health evaluation II; SOFA: sequential organ failure assessment; WBC: while blood cell; CRP: C-reactive protein; NRS-2002: nutritional risk screening 2002; MUST: malnutrition universal screening tool; NUTRIC: nutrition risk in critically ill; DT: diaphragm thickness; LOS: length of hospital stay.

**Table 2.** Spearman correlation analysis for DT at admission

	Total		Male		Female	
	<i>r</i>	<i>p</i>	<i>r</i>	<i>p</i>	<i>r</i>	<i>p</i>
GLIM	-0.324	0.002	-0.303	0.029	-0.347	0.030
NRS-2002	-0.364	<0.001	-0.426	0.002	-0.375	0.019
MUST	-0.326	0.002	-0.371	0.007	-0.326	0.043
NUTRIC	-0.164	0.119	-0.214	0.128	-0.183	0.265
WBC	0.106	0.318	0.045	0.752	0.267	0.101
Lymphocyte	0.155	0.143	0.040	0.778	0.391	0.014
Prealbumin	0.105	0.320	0.090	0.525	0.166	0.313
Albumin	0.223	0.034	0.322	0.020	0.063	0.704
CRP	0.171	0.105	0.249	0.075	0.071	0.668

DT: diaphragm thickness; *r*: correlation coefficient; GLIM: Diagnosis of malnutrition based on Global Leadership Initiative on Malnutrition criteria; NRS-2002: nutritional risk screening 2002; MUST: malnutrition universal screening tool; NUTRIC: nutrition risk in critically ill; WBC: while blood cell; CRP, C-reactive protein.

### Clinical and nutritional parameters affecting LOS

The patients were divided into two groups according to LOS:  $\geq 4$  weeks and  $< 4$  weeks. 53 patients (58.2%) were hospitalized for more than 4 weeks, with an average DT at admission of 2.83 $\pm$ 0.48 mm, an average DT at 2 weeks of 2.65 $\pm$ 0.41 mm, and an average RCDT at 2 weeks of -5.0 $\pm$ 15.1%, which were significantly increased in those who were hospitalized for less than 4 weeks, 3.37 $\pm$ 0.57 mm, 3.56 $\pm$ 0.54 mm, and 6.2 $\pm$ 9.7% respectively. 14 patients (26.4%) were diagnosed with malnutrition based on GLIM criteria in the prolonged LOS group, while only 3 patients (7.9%) in the LOS  $< 4$  weeks group. There were also significant differences in age, SOFA, APACHE II, NRS-2002 score, MUST score, and NUTRIC score at admission between the two groups (Table 3).

### ROC Curves in predicting prolonged hospitalization

For the prediction of LOS  $\geq 4$  weeks in patients with COVID-19, the area under the ROC curve for the RCDT at 2 weeks was 0.772, for DT at admission was 0.751, for the NRS-2002 was 0.676, for the MUST was 0.638, and for the NUTRIC score was 0.699 (Table 4).

### Multivariate linear regression analysis of LOS

LOS was significantly correlated with age ( $r=0.382$ ,  $p=0.000$ ), APACHE II ( $r=0.434$ ,  $p=0.000$ ), number of Comorbidities  $\geq 2$  ( $r=0.222$ ,  $p=0.035$ ), NRS-2002 score  $\geq 3$  ( $r=0.435$ ,  $p=0.000$ ), and mechanical ventilation ( $r=0.306$ ,  $p=0.003$ ), while LOS was significantly negatively correlated with DT at admission ( $r=-0.339$ ,  $p=0.001$ ), RCDT at 2 weeks ( $r=-0.480$ ,  $p=0.000$ ), lymphocyte at admission ( $r=-0.464$ ,  $p=0.000$ ), prealbumin at admission ( $r=-0.459$ ,  $p=0.000$ ). Multiple regression analysis showed DT at

**Table 3.** Clinical and nutritional parameters affecting LOS

	LOS $\geq$ 4 weeks (n=53)	LOS <4 weeks (n=38)	<i>p</i>
Age, years	65.2 $\pm$ 15.6	54.1 $\pm$ 14.0	0.001
Gender			
Males, n (%)	30 (56.6)	22 (57.9)	0.902
BMI, kg/m <sup>2</sup>	21.8 $\pm$ 2.8	22.7 $\pm$ 2.3	0.129
SOFA at admission	3.0 $\pm$ 1.5	2.3 $\pm$ 1.0	0.011
APACHE II at admission	12.8 $\pm$ 6.2	9.9 $\pm$ 5.2	0.023
GLIM at admission, n (%)	14 (26.4)	3 (7.9)	0.030
NRS-2002 at admission	3.3 $\pm$ 1.4	2.4 $\pm$ 1.6	0.004
MUST at admission	2.5 $\pm$ 0.9	2.0 $\pm$ 1.0	0.011
NUTRIC at admission	2.6 $\pm$ 1.5	1.6 $\pm$ 1.2	0.001
DT at admission, mm	2.83 $\pm$ 0.48	3.37 $\pm$ 0.57	<0.001
Male, mm	2.88 $\pm$ 0.51	3.52 $\pm$ 0.58	<0.001
Female, mm	2.77 $\pm$ 0.45	3.16 $\pm$ 0.49	0.015
DT at 2 weeks, mm	2.65 $\pm$ 0.41	3.56 $\pm$ 0.54	<0.001
Male, mm	2.67 $\pm$ 0.37	3.69 $\pm$ 0.63	<0.001
Female, mm	2.63 $\pm$ 0.47	3.38 $\pm$ 0.35	<0.001
RCDT at 2 weeks, %	-5.0 $\pm$ 15.1	6.2 $\pm$ 9.7	<0.001

LOS: length of hospital stay; SOFA, sequential organ failure assessment; APACHE II, acute physiology and chronic health evaluation II; GLIM, Diagnosis of malnutrition based on Global Leadership Initiative on Malnutrition criteria; NRS-2002, nutritional risk screening 2002; MUST, malnutrition universal screening tool; NUTRIC, nutrition risk in critically ill; DT, diaphragm thickness; RCDT, the rate of change in diaphragm thickness.

**Table 4.** ROC curves in predicting prolonged hospitalization

	Sensitivity	Specificity	AUC (95% CI)	<i>p</i>
DT at admission	0.553	0.868	0.751 (0.649-0.854)	<0.001
RCDT at 2 weeks	0.895	0.698	0.772 (0.673-0.871)	<0.001
NRS-2002 at admission	0.605	0.717	0.676 (0.560-0.792)	0.004
MUST at admission	0.711	0.472	0.638 (0.522-0.754)	0.025
NUTRIC at admission	0.605	0.717	0.699 (0.591-0.807)	0.001

ROC: receiver operating characteristics; AUC: area under the curve; CI: confidence interval; DT: diaphragm thickness; RCDT: the rate of change in diaphragm thickness; NRS-2002: Nutritional Risk Screening 2002; MUST: malnutrition universal screening tool; NUTRIC: nutrition risk in critically ill.

**Table 5.** Multivariate linear regression analysis of LOS

	Spearman correlation analysis		Enter regression model			
	<i>r</i>	<i>p</i>	B	$\beta$	95% CI of B	<i>p</i>
Age	0.382	<0.001	0.041	0.101	-0.045-0.128	0.342
Gender	0.052	0.624	---	---	---	---
BMI	-0.201	0.056	---	---	---	---
APACHE II	0.434	<0.001	0.131	0.101	-0.163-0.426	0.387
Comorbidities $\geq$ 2	0.222	0.035	0.206	0.012	-2.756-3.169	0.890
NRS-2002 $\geq$ 3	0.435	<0.001	0.887	0.057	-2.123-3.898	0.559
DT at admission	-0.339	0.001	-5.008	-0.377	-7.432-(-2.585)	<0.001
RCDT at 2 weeks	-0.480	<0.001	-17.574	-0.323	-28.113-(-7.035)	0.001
Lymphocyte at admission	-0.464	<0.001	-1.531	-0.117	-4.271-1.209	0.270
Prealbumin at admission	-0.459	<0.001	-8.735	-0.099	-24.334-6.864	0.268
CRP at admission	0.143	0.178	---	---	---	---
Mechanical ventilation	0.306	0.003	5.524	0.192	0.523-10.524	0.031
Corticosteroid therapy	0.123	0.246	---	---	---	---

LOS: length of hospital stay; *r*: correlation coefficient; B: Partial regression coefficient;  $\beta$ : Standardized  $\beta$ ; CI: confidence interval; APACHE II: acute physiology and chronic health evaluation II; NRS: nutritional risk screening; DT: diaphragm thickness; RCDT: the rate of change in diaphragm thickness; CRP, C-reactive protein.

admission, RCDT at 2 weeks and mechanical ventilation had a significant influence on LOS (Table 5).

## DISCUSSION

The appropriate nutritional monitoring method for patients in infectious isolation wards is still unknown. It is the first study to evaluate the relationship between CT-obtained DT and nutritional risk and nutritional status in

COVID-19 pneumonia isolation wards. Our study indicated that CT-obtained DT was significantly correlated with the patient's nutritional risk, nutrition status and LOS, changes in DT occurred dynamically during the course of the disease in patients with COVID-19, and the RCDT at 2 weeks predicted the prolonged hospitalization, after excluding the influence of mechanical ventilation. It suggested that CT-obtained DT might reflect whole-body

muscle mass and the dynamic changes of CT-obtained DT could be a favorable nutritional status assessment tool for rapidly increasing number of patients in isolation wards for COVID-19 pneumonia in this pandemic or potential acute viral pneumonia in the future.

Up to present, symptomatic support is still regarded as an important treatment for COVID-19, especially nutritional therapy, while the body's immune system recovers and regains its defense activity, so as to achieve elimination of the virus.<sup>16</sup> However, patients with COVID-19 often experience different degrees of gastrointestinal symptoms, inflammatory reactions and oxidative stress, resulting in reduced nutrient intake and synthesis, increased catabolism, a high nutritional risk,<sup>17,18</sup> myasthenia and muscular atrophy,<sup>19,20</sup> a prolonged hospital stay, and a high mortality rate for patients with severe disease.<sup>21</sup> More importantly, malnutrition may play a critical role in promoting the transition from mild pneumonia to severe pneumonia.<sup>22</sup> Therefore, timely nutritional assessment and support are crucial when managing COVID-19. Nevertheless, due to the emergence of a multitude of cases, including numerous cases of severe disease in a short period of time, medical workers and hospitals have been placed under extreme pressure and the assessment of nutritional status may have been delayed or neglected.

Nutritional risk screening tools such as NRS-2002, MUST, NUTRIC, are widely used to assess the nutritional risk of patients with COVID-19.<sup>3,6,7</sup> However, these tools assess the nutritional risk of the patient, not the nutritional status, and do not evaluate skeletal muscle atrophy. There are obvious shortcomings in using nutritional risk screening tools to monitor dynamic nutritional status during hospitalization. More than half of patients with sarcopenia and myosteatosis are assessed to be at low nutritional risk.<sup>23</sup> Traditional nutritional assessment parameters, such as prealbumin, transferrin, lymphocyte count, triceps brachii skin fold thickness, and grip strength, are susceptible to volume status and inflammatory response; therefore, they have a low predictive value and are unreliable for monitoring a patient's nutritional status.<sup>24</sup> CT is considered the gold standard for the evaluation of total skeletal muscle quantity.<sup>25</sup> In critically ill patients, the psoas muscle index has proven to be a feasible solution to assess the nutritional status.<sup>26</sup> However, this requires an additional CT scan of the psoas major muscle for patients with COVID-19, which increases the burden of epidemic protection and the cost of treatment. Similarly, ultrasound measurement of limb muscles is an attractive option for diagnosing skeletal muscle atrophy and predicting prognosis,<sup>27</sup> although there are many factors, such as excessive compression by the ultrasound probe, obesity, subcutaneous edema, the direction of the probe, and the position of the muscle, that affect the accuracy and reproducibility of the measurement results.<sup>28</sup>

Since a chest CT examination is recommended for the diagnosis of patients with COVID-19, the DT measurement can be obtained in the mediastinal window of the chest CT image; thus, there is no need to increase the scanning scope. For patients with COVID-19, this is an indicator simple to obtain. In this study we detected that diaphragm atrophy at two weeks existed in some patients with severe COVID-19, and it substantially affected the

LOS. GLIM, nutritional risk screening scores and DT had a congruent trend. For the prediction of LOS, the measurement of DT and the dynamic changes in DT were superior to the use of nutritional risk screening tools. It is a nutritional assessment index worthy of further research and evaluation in COVID-19 isolation wards.

We believe that CT-obtained DT measurements as a tool for assessing nutritional status has several possible advantages. 1) Considering that the diaphragm is a kind of skeletal muscles, early and continuous high catabolism together with the subsequent skeletal muscle atrophy will affect the diaphragm in critical ill.<sup>29</sup> In addition, once the primary disease is treated, anabolism increases and the diaphragm will show growth similar to the muscles of the limbs and the psoas major muscle, thus reflecting the patient's nutritional status in real time. 2) The diaphragm is the most important inhalation muscle, providing more than 60–80% of the momentum required for inhalation.<sup>30</sup> Diaphragm atrophy may have a more direct impact on respiratory function and prognosis as compared to the limb and psoas major muscles. Therefore, the diaphragm as a nutritional assessment parameter may have a greater clinical significance. 3) Apart from some cases where disuse atrophy of the diaphragm may occur, such as with controlled mechanical ventilation, neuromuscular Junction disease, or diaphragm trauma, most patients maintain normal or even enhanced movement of the diaphragm. Diaphragm atrophy is attributed to increased catabolism of the patient's skeletal muscles under the condition of sepsis, trauma and systemic inflammation; therefore, CT-obtained DT can be more accurate for monitoring nutritional status. 4) As a non bedside nutrition assessment tool, the DT measurements can be obtained using completed chest CT images, no additional examination would be required, and rapid results can be obtained in most cases, without adding additional burden to the already overloaded clinical program and excessive medical expenses, which are feasible factors for promotion in light of the current COVID-19 epidemic.

This study had the following limitations. First, it was a retrospective study with a small sample size and, due to the type of isolation wards, patients were screened based on the severity of their disease prior to being enrolled, resulting in a limited number of deaths and patients with severe disease. Clinical studies concerning COVID-19 in these patients would inevitably cause sampling errors. Second, due to establishing different discharge standards than those that are generally used, using LOS as an observation indicator might have affected the credibility of the results. Third, respiratory movement affected the accuracy of DT measurements. Fourth, a reference range for DT at the level of the celiac trunk on CT is still undetermined. Individual characteristics such as gender, race, and height may also affect the results.

### **Conclusion**

In conclusion, this retrospective study revealed the correlation between CT-obtained DT and nutritional risk and status in patients with COVID-19, confirmed the negative predictive significance of LOS of DT at admission and the RCDT at 2 weeks, and demonstrated that decreased DT at admission and RCDT at 2 weeks may independent-

ly contribute to prolonged hospitalization in these patients. Therefore, it's suggested that CT- obtained DT can be used as a dynamic assessment tool for evaluating the nutritional status of patients in isolation wards for COVID-19. More researches on CT-obtained DT as a dynamic nutritional assessment tool can be pursued in patients with other diseases.

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#### AUTHOR DISCLOSURES

We declare that we do not have any commercial or associative interest that represents a conflict of interest in connection with the work submitted.

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