Harder to Breath: Diaphragm ultrasound shows continued dysfunction in post-COVID-19 patients

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Introduction

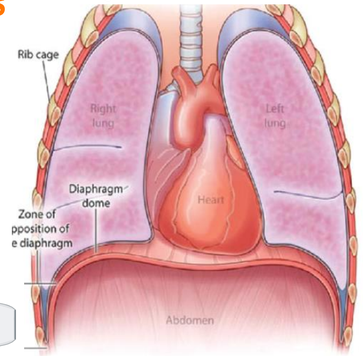
The substantial burden of chronic disability post-hospitalization for coronavirus disease 2019 (COVID-19) is increasingly clear. In a recent study, nearly half of COVID-19 patients were not able to return to work 60 days after hospital discharge.[1] Survivors of severe COVID-19 frequently report persistent shortness of breath, cough and fatigue post-hospitalization.[1,2] While these symptoms may stem from direct involvement of the lung parenchyma itself, the possibility of underlying neuromuscular respiratory weakness should be considered. Neurological manifestations of COVID-19 are increasingly recognized with prominent involvement of the neuromuscular system ranging from mild creatine kinase (CK) elevation to flaccid tetraplegia requiring tracheostomy.[3] Here we report neuromuscular ultrasound findings that define the unexpectedly high prevalence of structural and functional alterations to the diaphragm muscle after hospitalization for COVID-19.

Materials & Methods

Participants

- 25 patients upon admission to acute patient rehabilitation with prior diagnosis of COVID-19
- Admitted from 14 separate acute care hospitals between July 21st, 2020 and September 24th, 2020

Figure 1. Location of scan



Procedure

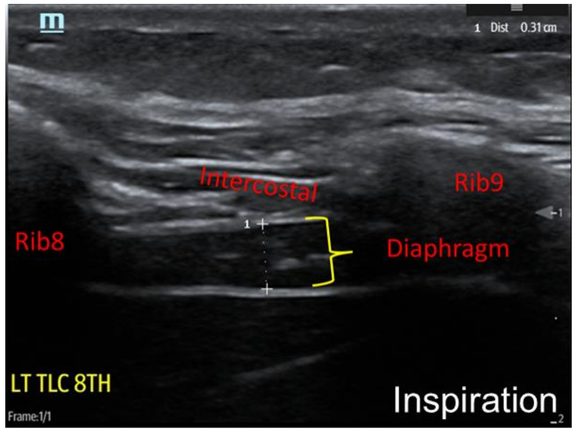
- Acute care data obtained through chart review of medical records and summarized in **Table 1**.
- The diaphragm muscle was assessed on a portable ultrasound system (TE7, Mindray, Mahwah, USA) with either a 6- to 14-MHz linear array or 2- to 5-MHz curvilinear array selected to maximize image clarity on the basis of individual characteristics such as body habitus.
- Each hemi-diaphragm was identified in the zone of apposition, and thickness was measured at end-expiration and maximal inspiration (**Figures 1 & 2**).
- Normal values have been established for diaphragm end-expiratory muscle thickness (>0.14 cm) and thickening ratio (>1.2), calculated as thickness at maximal inspiration/thickness at end-expiration.[4]

Results

Table 1 Baseline characteristics, lab values, and lengths of stay of post-COVID-19 patients in inpatient rehabilitation

Subject Characteristics	
Age	59.1±13.2 (33-89)
Sex M:F (n=25)	19:6
BMI	30.8±6.1 (21-48)
Comorbidities	Hypertension 68% (17/25) Diabetes Mellitus or Pre-Diabetes Mellitus 56% (14/25) Hyperlipidemia 30.4% (7/25) Asthma and/or COPD 20% (5/25) Cancer 13.4% (3/25) Cerebrovascular Accident 13.4% (3/25) Acquired Immunodeficiency 13.4% (3/25)
Days in ICU	38±21.7 (2-83)
Days Hospitalized	45.6±25.5 (10-92)
Days of Mechanical Ventilation	43.1±33.5 (10-153)
Days Since Onset*	72.2±46.5 (3-184)
Days Since ICU	32.4±22.9 (2-80)
CRP (mg/L)	180.2±135.9 (3.5-423)
Troponin (ng/mL)	0.7±2.0 (0.003-8.09)
CK (U/L)	753.3±976.2 (39-3090)
A1c (%)	7.9±2.5 (5.1-13.7)

Mean ± SD (Range) or % as appropriate.
*As defined by first positive test, onset of symptoms, or hospital admission where available



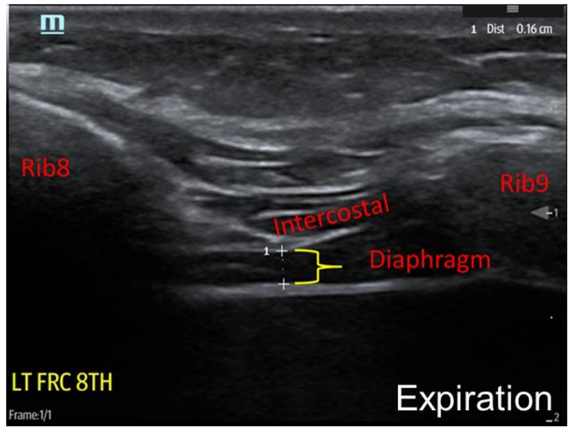


Figure 2. Examples of normal diaphragm scan measurements

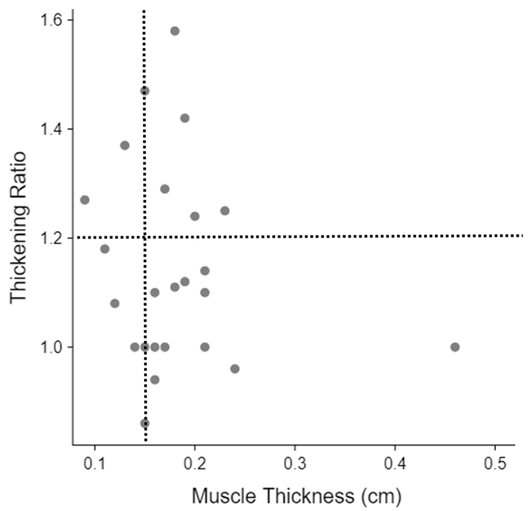


Figure 3. Sonographic diaphragm muscle thickness versus thickening ratio in survivors of COVID-19 that require inpatient rehabilitation. Individual cases plotted to the left of the vertical dotted line have abnormal thickness (i.e. muscle atrophy). Those plotted below the horizontal dotted line have abnormal thickening ratio (i.e. impaired contractility). Taken together, only the 5 cases (out of 25) located in the upper right quadrant fall within normal limits across both parameters.

Results

Of the 25 patients, 5 (20%) had an end-expiration thickness value below the normal cut off, 19 (76%) had a reduced thickening ratio on at least one side, and 10 (49%) had reduced thickening ratio bilaterally. Overall, 20 patients (80%) had at least one structural or functional abnormality on diaphragm ultrasound (**Figure 3**)

Discussion & Conclusion

To our knowledge this is the first study utilizing ultrasound to evaluate the diaphragm in COVID-19 survivors and demonstrates that patients who require inpatient rehabilitation after acute hospitalization have a very high prevalence of diaphragm dysfunction. These findings are remarkably similar to a previous report of sonographically identified diaphragm dysfunction in patients with confirmed myopathy.[5] In contrast, diaphragm ultrasound findings in patients with chronic dyspnea related to COPD largely resembled the healthy population.[6] Given the large number of COVID-19 survivors who suffer from persistent dyspnea months after onset of disease [7], it is possible that diaphragm muscle dysfunction is a major contributing factor.

Limitations

Our study is limited by several factors. This data is only representative of patients admitted to acute inpatient rehabilitation after hospitalization and mechanical ventilation (MV) due to COVID-19. Additionally, no controls were available due to the difficulty in matching patients for length of mechanical ventilation. Our study had an average of 43 days of MV while a study by Seneff et al. in 1996 showed an average of 3-8 days in over 5,000 ICU patients surveyed.[8]

References

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