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Cross-sectional area of erector spinae muscles is associated with activities of daily living at discharge in middle- to older-aged patients with coronavirus disease 2019

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ABSTRACT

Objectives: Measurement of skeletal muscle wasting using computed tomography (CT) is widely known to be useful in predicting prognosis. Although some reports have been found in patients with coronavirus disease 2019 (COVID-19), few reports have focused on the ability to perform activities of daily living (ADLs). This study retrospectively investigated the relationship between the erector spinae muscle area measured from CT images and ADL at the time of hospital discharge in patients with COVID-19.

Methods: Among patients aged 40 years or older, 271 patients (median age, 65 years; 180/271 male patients) who had CT cross-sectional images of the 12th thoracic vertebral level on admission were included. The Katz index was used to assess ADLs, and patients who were not completely independent were defined as dependent. Multivariable logistic and Poisson regression analyses were applied to examine the relationship between the cross-sectional area of the erector spinae muscles and the onset of ADL dependence at discharge.

Results: A total of 75 (27.7%) patients became dependent on ADL at the time of hospital discharge. Decreased erector spinae muscle area was significantly related to dependent ADL at discharge (adjusted odds ratio: 0.886, 95% confidence interval: 0.805–0.975). In addition, the erector spinae muscle area was significantly related to the number of ADL items for which independence was not achieved (adjusted incidence rate ratio: 0.959, \( P < 0.001 \)).

Conclusions: The cross-sectional area of the erector spinae muscles from the thoracic CT image was associated with the ability to perform basic ADL at hospital discharge.

1. Introduction

During the coronavirus disease 2019 (COVID-19) pandemic, frailty in older patients with COVID-19 is a critical issue worldwide (Hewitt et al., 2020; Petermann-Rocha et al., 2020; Yang et al., 2021).

Unfortunately, clinical decision-making is often done case by case for individual frailty patients (Moug et al., 2020) because of the lack of established treatment. One of the reasons for this is the difficulty in predicting the clinical course of critically ill patients with frailty, especially those with COVID-19. In particular, prolonged hospitalization and...
intensive care unit (ICU) stay may lead to a decrease in the ability of any activity due to disuse, which may interfere with their daily life (Bell et al., 2020; Leite et al., 2021; Pizzarro-Penaroli et al., 2021). In addition, hospitalization events in the older adult population with frailty are the most significant risk factor for the decline in ADLs (Gill et al., 2010), and lower ADL participation promoted by inactivity during hospitalization is directly associated with their prognosis such as death and institutionalization (Brown et al., 2004). Therefore, it is essential to predict the decline in ADL in the clinical course from an early stage to provide adequate rehabilitation to patients with COVID-19 who need it.

Age-related muscle wasting is commonly observed in older adults (Johannesdottir et al., 2018), and it induces frailty and adverse outcomes. In particular, the measurement of muscle wasting using computed tomography (CT) images is known to provide a quantitative and accurate measure of skeletal muscle and is well related to disability, physical function, and mortality (Amini et al., 2019; Meyer et al., 2021; Johannesdottir et al., 2018), and it induces frailty and adverse outcomes. Based on the contents of the medical records, and C-reactive protein) were collected on admission. These factors included age, sex, height, body weight at hospital admission, body mass index (BMI), comorbidities (hypertension, diabetes mellitus, and dyslipidemia), history of cardiovascular disease, history of cerebrovascular disease, history of cancer, dementia, chronic obstructive pulmonary disease (COPD), need for intensive care (ICU admission or not), and the severity of disease (oxygen only, using the nasal high-flow, and need for intubation therapy) were collected. Blood sample data (white blood cell, total lymphocytes, hemoglobin, albumin, creatinine, HbA1c, ferritin, and C-reactive protein) were collected on admission. These factors included patient background and confounding factors.

The Kats Index defines basic ADL at admission and hospital discharge (Katz and Akpom, 1976). Based on the contents of the medical records, the status of the execution of feeding, continence, transferring, toileting, dressing, and bathing were investigated. Patients who were discharged dead were considered non-independent for all the items. “Independent” is defined as that when patients could perform all the items alone, and “dependent” was defined as that when patients found it impossible to perform one or more of the items or needed to be monitored. In addition, the number of items that became non-independent was investigated using incidence rate analysis.

2.3. Skeletal muscle measurement

The skeletal muscle cross-sectional area of the erector spinae muscles was assessed from a thoracic CT image with two consecutive slices at the level of the bilateral 12th ribs attached to the thoracic vertebrae based on a previous study (Feng et al., 2021). CT was determined as the earliest image during hospitalization or at the time of hospital admission. The tube potential was set to 120 kV with a 512 × 512 matrix. The electrical current (mA) and slice thickness were used as confounding factors because they were not standardized when CT images were taken. The observers (M.Y., K.U., K.O., D.N., T.M., and S.S.) measured the muscle area after being sufficiently trained, until their measurement results exceeded 0.95 in intraclass correlation coefficients, using 20 randomly selected slices. The right and left erector spinae muscle areas were measured semiautomatically in this study using the Slice-O-Matic ver. 5.0 (Tomovision, Canada). The measurements were conducted blindly; participants could not be identified to avoid measurement bias, and assessments were performed after the patient was discharged. The Hounsfield unit (HU) range of the skeletal muscle was from –29 to 150. The area (cm²) was calculated as the average of two slices after the measurement value was obtained.

2.4. Statistical analysis

Continuous variables are expressed as median and interquartile range (IQR). Categorical variables are expressed as n (%). Before performing regression analysis, multiple imputations were performed using the chained equation method from 20 imputed datasets using Rubin's formula for missing data. Other analyses (e.g., concordance statistics) were performed without missing data.

Logistic and Poisson regression analyses were performed before and after adjusting for confounding factors (model 1: independent or dependent ADL at hospital admission, electrical current, and CT slice thickness; model 2: model 1 + age, sex, and BMI at the time of hospital admission; model 3: model 2 + comorbidities and prior disease; and model 4: model 3 + blood sample data at admission, ICU admission or not, and severity of disease). Logistic regression analysis showed the odds ratio of increasing erector spinae muscle area for independent or dependent ADL at hospital discharge with a 95% confidence interval (CI). In addition, the same analyses were performed for independent or dependent ADL sub-items as sensitivity analyses. Moreover, to visualize the relationship between skeletal muscle area and ADL at hospital discharge, a multivariable three-dimensional spline curve was drawn based on the logistic regression analysis results. The results of Poisson regression analysis showed the incidence rate ratio (IRR) of increasing erector spinae muscle area for the number of ADL sub-items that became non-independent with a 95% CI limit.

Additionally, to compare differences in the ability to predict ADL at hospital discharge between the baseline model (model 4 of the regression analyses) and the baseline model plus the erector spinae muscle area, reclassification improvement was calculated using the continuous net reclassification improvement (cNRI) and integrated discrimination improvement index (IDI) (Cook and Ridker, 2009; Luís-Ganella et al., 2012). The cNRI distinguishes movements in the correct direction (upper for cases and lower for non-cases). The IDI is the difference in the YATES slopes between the two models and the mean difference in predicted probabilities between cases and non-cases. We used these methods to quantify the improvement of a model when an erector spinae muscle was added.

All analyses were performed using JMP (version 15.1; SAS Institute Inc., Cary, NC, USA), R version 4.0.2 (R Foundation for Statistical Computing, Vienna, Austria), and Stata version 16.0 (Stata Corp., College Station, TX, USA).
College Station, TX). Two-tailed *P* values < 0.05 were indicative of statistical significance.

### 3. Results

During the patient recruitment period, a total of 411 patients diagnosed with COVID-19 were admitted. After excluding patients, 271 patients were enrolled in this study. The details of the patient enrollment flowchart are shown in Fig. 1. The median age of the study population was 65 years, and 66.4% of the patients were men. The number of patients who did not perform independent ADL at the time of hospital admission and at the time of hospital discharge was 110 (40.6%) and 75 (27.7%), respectively. Approximately 90% of the patients did not require high-flow nasal cannula or intubation therapy, but 27 (10.0%) patients were in the ICU during hospitalization. The median date from hospital admission to the first CT imaging was 0 [IQR: 0–1] day. The patient background factors, including the aforementioned items, are presented in Table 1.

Table 2 shows the relationship between the erector spinae muscle area and independence in basic ADL at discharge. Unadjusted analysis was shown to relate the higher muscle area with lower OR for dependent ADL (OR, 0.864, 95% CI: 0.827–0.902). This relationship was maintained after adjusting for all confounding factors (OR: 0.886, 95% CI: 0.805–0.975). Similar results were obtained for continence (OR: 0.844, 95% CI: 0.719–0.991), transferring (OR: 0.881, 95% CI: 0.794–0.978), toileting (OR: 0.889, 95% CI: 0.800–0.987), and bathing (OR: 0.876, 95% CI: 0.783–0.980), as a sensitivity analysis for sub-items of basic ADL. Furthermore, Fig. 2 shows the visual relationship between the OR for ADL at the time of discharge. As the continuous value of the skeletal muscle area increased, the OR tendency decreased. The results of the

| Table 1 Patients’ characteristics. | (n = 271) | Missing |
|-----------------------------------|----------|---------|
| Age, years                        | 65 [52–76] | 0       |
| Male                              | 180 (66.4) | 0       |
| Body mass index, kg/m²            | 24.1 [21.3–27.1] | 11 (4.1) |
| Comorbidities                     | 1 (0.4)   |         |
| Hypertension                      | 113 (41.7) |         |
| Dyslipidaemia                     | 47 (17.3)  |         |
| Diabetes mellitus                 | 82 (30.3)  |         |
| Cerebrovascular disease           | 25 (9.2)   |         |
| Cardiovascular disease            | 42 (15.5)  |         |
| Cancer                            | 35 (12.9)  |         |
| Dementia                          | 11 (4.1)   |         |
| COPD                              | 5 (1.9)    |         |
| Baseline laboratory data          |           |         |
| White blood cell, 10⁹/μl          | 5.4 [4.3–6.9] | 2 (0.7)  |
| Total lymphocyte count, /μL       | 1015 [725–1355] | 2 (0.7) |
| Albumin, mg/dl                    | 3.8 [3.4–4.1] | 0       |
| Hemoglobin, mg/dl                 | 14.3 [12.7–15.4] | 2 (0.7) |
| C-reactive protein, mg/dl         | 4.16 [0.81–8.98] | 0       |
| Creatinine, mg/dl                 | 0.91 [0.74–1.13] | 0       |
| HbA1c, %                          | 6.2 [5.8–7.2] | 8 (3.0)  |
| Ferritin, mg/dl                   | 301 [120–628] | 10 (3.7) |
| Admitted to ICU                   | 27 (10.0)  | 0       |
| Respiratory management            | 0         |         |
| Only using oxygen inhalation      | 226 (83.4) | 0       |
| High-flow nasal cannula           | 18 (6.6)   |         |
| Mechanical ventilation            | 27 (10.0)  |         |
| Erector spinae muscle area, cm²   | 28.1 [21.7–35.6] | 0       |

Note: Results show the median [interquartile range] or number (%), COPD: chronic obstructive pulmonary disease, ICU: intensive care unit.

![Fig. 1. Patient enrolment flowchart. CT: computed tomography, COVID-19: coronavirus disease 2019.](image-url)
The relationship between erector spinae muscle area and ADL at hospital discharge.

Exposure Outcome

OR (95% CI) OR (95% CI) OR (95% CI) OR (95% CI) OR (95% CI)

**Feeding**

Erector spinae muscle area 46/271 (17.0%) 0.871 (0.828 – 0.915)

**Continence**

Erector spinae muscle area 51/271 (18.9%) 0.855 (0.811 – 0.900)

**Toileting**

Erector spinae muscle area 68/271 (25.2%) 0.871 (0.834 – 0.910)

**Dressing**

Erector spinae muscle area 61/271 (22.6%) 0.863 (0.823 – 0.904)

**Bathing**

Erector spinae muscle area 68/271 (25.2%) 0.856 (0.817 – 0.900)

Note: All the analyses were performed after multiple imputations. The results showed an OR (95% CI) when the erector spinae muscle area increased by 1 cm

Poisson regression analysis are presented in Table 3. For the number of non-independent ADLs, the erector spinae muscle area remained significant even after adjusting for all confounding factors (IRR, 0.959, 95% CI: 0.937–0.980).

From the results of the cNRI and IDI, the addition of the erector spinae muscle area was the complementary predictive ability for the baseline model (Supplementary Table 1). The results of both analyses show incremental predictive ability with the addition of the erector spinae muscle area when consistently positive values were found. With the addition of muscle area, the cNRI changed by 0.476 (95% CI: 0.198–0.755), and IDI also tended to change by 0.015 (95% CI: -0.003–0.033, P = 0.094).

4. Discussion

The present study mainly showed the relationship between the erector spinae muscle area identified by the thoracic CT image, taken for clinical purposes, and the ability of basic ADL at hospital discharge. When muscle area was higher, the OR of dependent ADL was observed when the muscle area was added. This study has a relatively large sample size compared to that of other reports, and shows the advantage of using antigravity muscles instead of abdominal skeletal muscles in chest CT images obtained for clinical purposes, which is one of the strengths of this study. These results may provide the patient’s progress and assume the living situation after hospital discharge by measuring the muscle mass in the CT image on admission. Furthermore, the identification of cases that are more prone to disability at the time of hospital discharge may facilitate appropriate rehabilitation.

To the best of our knowledge, only one study has focused on the relationship between ADL and CT-based muscle measurements. Giraudo et al. (2021) reported the relationship between the mean density of the right erector spinae muscles measured by thoracic CT imaging and ADL at the same time as CT imaging, as assessed by the Barthel Index (0–100 points) for 150 patients with COVID-19, and their results showed that low muscle density was associated with lower ADL scores.
The present study focused on the erector spinae muscle area; we found similar results showing that skeletal muscle morphology assessment by CT imaging was associated with decreased ADL. Another previous study on the benefits of using the erector spinae muscle has shown the relationship between the measurement of skeletal muscle wasting by CT imaging and critical illness or death in 116 patients with severe symptoms (Feng et al., 2021). In addition, we previously reported in other patients that it is optimal to perform measurement only in the erector spinae muscle but not in other abdominal muscles when assessing for skeletal muscle area (Yamashita et al., 2022). In the same study, only the erector spinae muscle area showed a clinical course similar to that of the density. Consequently, previous studies support the validity of using the erector spinae muscle area for measurement in the present study.

Another previous study (Damanti et al., 2021) in which the assessment of abdominal skeletal muscles was examined for its association with several clinical outcomes (successful extubation, ICU stay, length of hospitalization, number of complications, and in-hospital mortality) supported the results of the present study. Furthermore, the relationship between the skeletal muscle and the severity of disease (Hocagolu et al., 2021), ICU admission (Bunnell et al., 2021), extubation (Ufuk et al., 2020), length of hospital stay (Kim et al., 2021; Ufuk et al., 2020), and mortality (Bunnell et al., 2021; Feng et al., 2021; Ufuk et al., 2020; Yang et al., 2020) using total abdominal or thoracic muscles or other muscles (the pectoralis major, psoas major, etc.) was reported. Although the findings of these reports are not directly comparable to those of the present study because of the use of different muscles and outcomes, they may be helpful for both clinical application and future studies. Furthermore, in addition to the skeletal muscle assessment in this study, further risk stratification may be achieved by assessing the degree of obesity identified in CT images, which is known to be a risk factor for severe COVID-19 (Bunnell et al., 2021; Kottlors et al., 2020; Yang et al., 2020).

In the present study, one of the major antigravity muscles, the erector spinae muscles, was used to assess muscle wasting. The erector spinae muscles are the only antigravity muscles seen on thoracic CT images and have a relatively stable structure because of their paraspinal muscles. Sub-analysis of the present study showed that skeletal muscle area was significantly associated with ADLs requiring standing movements, such as transferring, toileting, and bathing. Conversely, there was no association with ADLs involving more standing movements. On the other hand, because ADLs such as eating and dressing using the upper limbs do not require standing movements and are mostly completed in a sitting position, it would be unlikely to be impaired during progression to the terminal stages of disease. The degree of disability is determined by weakness, mainly in standing activities such as walking and physical activity. Therefore, the antigravity muscle area is expected to predict all standing movements, such as walking and physical activities that lead to disability of ADL performance.

In spite of this, antigravity muscles are prone to atrophy arising from inactivity due to hospitalization (Clark, 2009). In particular, prolonged bed rest causes deconditioning (Kortebein et al., 2007) of the antigravity muscles of the trunk (Ikemoto et al., 2012). Atrophy of skeletal muscle tissues associated with a few days of bed rest is more likely to occur in type I fibers (Demangel et al., 2017), predominantly in antigravity muscles (Johnson et al., 1973). In addition, the invasive nature of intensive care may lead to muscle atrophy, such as mechanical ventilation, steroids, and sedatives (Zorowitz, 2016). Deconditioning is thought to cause a more pronounced decline in ADL during hospitalization. Moreover, it is thought to be caused by increased protein catabolism associated with the inflammatory response to infection (Piotrowicz et al., 2021). To prevent physical deterioration associated with hospitalization and treatment, it is desirable to provide rehabilitation similar to that for other diseases from an early stage.

In Argentina, an online survey of physical rehabilitation in patients with COVID-19 who were admitted to the ICU was performed by physical therapists (Bertozzi et al., 2021). The results showed that almost all therapists set the goal of performing ADL in patients who were not on mechanical ventilation, but only half of the therapists focused on ADL in patients who were weaned from mechanical ventilation. In contrast, a systematic review of 43 studies focusing on the intervention effects of rehabilitation showed that exercise, early mobilization, and multicomponent programs might improve recovery, including ADL following ICU admission for severe respiratory illness that could be generalizable to those with COVID-19 (Goodwin et al., 2021). Furthermore, although few reports are available for hospitalized patients, some intervention trials have focused on morphological changes in skeletal muscles (Aas et al., 2020; de Almeida et al., 2020; Smeuninx et al., 2021). Further studies focused on the effect of in-hospital rehabilitation on ADL with the recovery of muscle wasting would help in clinical decision-making about the progress of patients’ ADL and might help predict their quality of life after hospital discharge.

Along with some strong points, this study had several limitations. First, this was performed retrospectively in a single-center study. All data, except for those obtained from CT image analysis, were obtained from the medical records. Therefore, the definition of ADL may be a contrived assessment. However, the measurement of ADL is straightforward and can be assessed by most medical staff (e.g., doctor, nurse, physical therapist), so it has relatively consistent views among all healthcare providers. Further prospective studies with larger sample sizes would complement the errors in the subjective assessment. Second, this study was not compared with other frailty scales, such as visualizing (Hewitt et al., 2020), scoring from the medical record (Kündl et al., 2020; Petermann-Rocha et al., 2020), or measuring muscle strength (Cheval et al., 2021; Kara et al., 2021b), and assessing for the presence of sarcopenia (Eikz et al., 2021). Evaluation of both muscle wasting using CT and lower muscle function may lead to enhanced prediction of the prognosis of hospitalized patients (Yamashita et al., 2021). In our clinical setting, we performed the physical assessment in detail for only severely affected patients to prevent the spread of infection. The severity of muscle wasting should be screened based on the medical information.
obtained, such as CT images, and the use of multiple scales and a thorough physical function assessment may be useful for further stratification of disease severity. Third, we measured only the erector spinae muscle identified by thoracic CT imaging, but measurements on the thigh muscles are also desirable for a more detailed evaluation (Kara et al., 2021a). On the other hand, we believe it is not desirable to measure only the muscle mass during imaging because CT is invasive. Clinical decisions about muscle wasting should be based on the images taken for clinical purposes. Finally, the influence of the relevant factors, such as social conditions (e.g., hospital admission control, lockdown) and the variant of COVID-19, was not considered in the present study.

5. Conclusions

The cross-sectional area of the erector spinae muscles was associated with the ability to perform basic ADLs at hospital discharge and provided additive information about predictive ADLs. In addition, this relationship tended to show the items that required standing activities. Based on these findings, it may be helpful to identify prognoses, such as readmissions, mortality, physical dependence, and functionality, and determine the need for post-discharge care from CT images taken for medical purposes. Further studies are needed on the usefulness of the erector spinae muscle area in patients with COVID-19.

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CRediT authorship contribution statement

M.Y., T.K., T.W., and K.K. were performed conception and design in this study. M.Y., N.H., S.U., K.O., D.N., and T.M. collected the data. M.Y., N.H., and K.U. performed the analysis. M.Y. drafted the article, and the other co-authors revised and edited it. All authors approved final of the study.

Declaration of competing interest

All authors have no conflicts of interest to declare.

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