



# Impact of sarcopenia and obesity on mortality in older adults with SARS-CoV-2 infection: automated deep learning body composition analysis in the NAPKON-SUEP cohort

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## Abstract

**Introduction** Severe respiratory infections pose a major challenge in clinical practice, especially in older adults. Body composition analysis could play a crucial role in risk assessment and therapeutic decision-making. This study investigates whether obesity or sarcopenia has a greater impact on mortality in patients with severe respiratory infections. The study focuses on the National Pandemic Cohort Network (NAPKON-SUEP) cohort, which includes patients over 60 years of age with confirmed severe COVID-19 pneumonia. An innovative approach was adopted, using pre-trained deep learning models for automated analysis of body composition based on routine thoracic CT scans.

**Methods** The study included 157 hospitalized patients (mean age  $70 \pm 8$  years, 41% women, mortality rate 39%) from the NAPKON-SUEP cohort at 57 study sites. A pre-trained deep learning model was used to analyze body composition (muscle, bone, fat, and intramuscular fat volumes) from thoracic CT images of the NAPKON-SUEP cohort. Binary logistic regression was performed to investigate the association between obesity, sarcopenia, and mortality.

**Results** Non-survivors exhibited lower muscle volume ( $p=0.043$ ), higher intramuscular fat volume ( $p=0.041$ ), and a higher BMI ( $p=0.031$ ) compared to survivors. Among all body composition parameters, muscle volume adjusted to weight was the strongest predictor of mortality in the logistic regression model, even after adjusting for factors such as sex, age, diabetes, chronic lung disease and chronic kidney disease, (odds ratio=0.516). In contrast, BMI did not show significant differences after adjustment for comorbidities.

**Conclusion** This study identifies muscle volume derived from routine CT scans as a major predictor of survival in patients with severe respiratory infections. The results underscore the potential of AI supported CT-based body composition analysis for risk stratification and clinical decision making, not only for COVID-19 patients but also for all patients over 60 years of age with severe acute respiratory infections. The innovative application of pre-trained deep learning models opens up new possibilities for automated and standardized assessment in clinical practice.

**Keywords** Geriatric patient · Body composition · Machine learning · Muscle assessment · Computed tomography · Muscle fat infiltration · Covid-19 · Pneumonia

## Abbreviations

|      |                                       |       |                                  |
|------|---------------------------------------|-------|----------------------------------|
| ARDS | Acute Respiratory Distress Syndrome   | CT    | Computed Tomography              |
| BIA  | Bioelectrical Impedance Analysis      | DXA   | Dual-Energy X-ray Absorptiometry |
| BMI  | Body Mass Index                       | ICUAW | ICU-Acquired Weakness            |
| COPD | Chronic Obstructive Pulmonary Disease | IMAT  | Intramuscular Adipose Tissue     |
|      |                                       | LMU   | Ludwig Maximilian University     |

|                 |                                                                        |
|-----------------|------------------------------------------------------------------------|
| NAPKON          | National Pandemic Cohort Network                                       |
| OR              | Odds Ratio                                                             |
| PCR             | Polymerase Chain Reaction                                              |
| SARS-CoV-2      | Severe Acute Respiratory Syndrome<br>Coronavirus 2                     |
| SAT             | Subcutaneous Adipose Tissue                                            |
| SHIP-AI         | Smart Hospital Information Platform –<br>Artificial Intelligence       |
| SD              | Standard deviation                                                     |
| SO              | Sarcopenic Obesity                                                     |
| SPSS            | Statistical Package for the Social<br>Sciences                         |
| SUEP            | cross-sectoral platform (in German<br>Sektorenübergreifende Plattform) |
| T4, T12, L2, L3 | Thoracic and Lumbar Vertebrae                                          |
| TAT             | total adipose tissue                                                   |

## Background

### Muscle loss as an underestimated factor in infectious medicine

Severe respiratory infections play a central role in clinical practice, especially in the aging population. They do not only pose an acute threat to survival but also have long term consequences. In recent years, there has been growing awareness that body composition – especially low muscle mass – plays a central role in the course and prognosis of infections [1, 2]. Sarcopenia, the age-related loss of muscle mass and strength, often remains unaddressed in clinical practice [3]. While fever, inflammatory markers and organ function are routinely monitored, muscle weakness is often overlooked as a potentially critical marker of disease progression [3].

### COVID-19 as a model for muscle weakness in infections

Coronavirus disease (COVID-19) has highlighted that infections not only affect organs but also body composition [4]. Numerous studies show that low muscle mass is associated with a poorer prognosis, longer ventilation times and higher mortality [4, 5]. The review by Wang et al. postulates that the link between sarcopenia and adverse COVID-19 outcomes is based on chronic inflammation, immune dysfunction and respiratory muscle weakness [4]. However, it remains unclear whether this is a specific phenomenon of COVID-19 or a general characteristic of severe infections. Current findings reveal strong parallels to sepsis, influenza and bacterial pneumonia [2, 6–8]. In sepsis patients, the massive inflammatory response leads to a catabolic metabolic

state that contributes to rapid muscle atrophy [1, 2]. ICU-acquired weakness (ICUAW) is a well-known syndrome in intensive care patients that significantly impairs functional recovery after infections [1]. In acute respiratory distress syndrome (ARDS), too, there are indications that severely ill patients develop pronounced muscle weakness that can persist for years [9, 10]. These observations raise the question of whether muscle weakness should be considered as an independent risk factor for severe courses of infections and whether its early detection could enable targeted therapeutic intervention.

### Muscle tissue as an immunological player

Besides its mechanical function, the musculature also has a direct immunological significance. Muscle tissue produces myokines, which have inflammation-regulating properties and influence the systemic immune response [11, 12]. Reduced muscle mass could thus not only be a passive marker for a severe course of infection, but could actively contribute to the dysregulation of the immune system [13]. Patients with low muscle mass may have a weakened immune system, making them more susceptible to secondary infections and prolonged illness [13]. In addition, the musculature plays a crucial role in the storage of essential micronutrients, including vitamin D and iron, which are necessary for an effective immune response [14, 15]. A reduced muscle mass could thus indirectly lead to a weakened immune response [13].

### The impact of obesity and sarcopenia on health outcomes

While sarcopenia is increasingly recognized as a negative prognostic factor, it has been known for a long time that obesity is also associated with unfavorable disease progression, especially in critically ill patients [16]. Papadimitriou-Olivgeris et al. were able to show that obese patients with sepsis had a dramatically lower survival rate compared to patients of normal weight (survival rate 44% vs. 76%,  $p < 0.001$ ) [17]. So far, it is unclear which nutritional condition – obesity or sarcopenia – is associated with a poorer prognosis [18]. Both conditions may interact in a complex way with inflammatory processes and the body's immune response, which is why a differentiated analysis is necessary.

### Automated CT analysis as an innovative tool for infectious medicine

Determining body composition is challenging in the context of acute illnesses. Methods such as dual-energy X-ray absorptiometry (DXA) or bioelectrical impedance analysis

(BIA) are hardly practical in acute medicine [19]. With the increasing use of deep learning technologies as part of machine learning, the automated analysis of CT scans offers a new way to quantify muscle volume in patients with infections precisely and in a standardized manner [20]. Thoracic CT scans are already part of routine imaging for severe infections such as COVID-19 or sepsis. The ability to automatically analyze body composition from these already existing image data opens up new avenues for risk stratification. Such an analysis could help infectious disease specialists to identify patients at increased risk early on and make targeted treatment decisions.

## Objective

Therefore, the main objective of this study was to investigate the effects of body composition on the survival rate of patients over 60 years of age with severe COVID-19 using a pre-trained deep learning model. In particular, it was analyzed whether obesity or sarcopenia was associated with a poorer prognosis. In addition, the extent to which these patient groups differed in terms of their comorbidities was investigated.

## Methods

### Study design and sample

The cross-sectoral platform (SUEP) cohort of the National Pandemic Cohort Network (NAPKON) recruited SARS-CoV-2-positive patients of all age groups from all sectors of the healthcare system in Germany (university hospitals, non-university hospitals and GP practices). Since November, 2020, the cohort has included both inpatients and outpatients. The SUEP cohort collects primary health data, basic clinical phenotyping information, imaging data, biospecimens and patient-reported outcome measures at 57 study sites. The main inclusion criterion was a polymerase chain reaction (PCR)-confirmed SARS-CoV-2 infection at the time of study participation. Detailed information on the study has been published elsewhere [21].

Our sample was recruited between November 1, 2020 and July 17, 2022. The dataset was exported on December 1, 2022. For the purposes of our research question, only patients aged >60 years with thoracic CT imaging were included in our study. Only CT images obtained during the acute phase of hospitalization were included. The study protocol was approved by the LMU Munich Ethics Committee (study no. 22–0671).

## Data acquisition

The following NAPKON-SUEP variables were analyzed at baseline: age, gender, risk factors, blood pressure, SARS-CoV-2 vaccination status, life expectancy, restrictions on medical interventions, oxygen support, pre-existing conditions and time of CT imaging. Anthropometric data (height and weight) were collected at baseline through patient self-report during anamnesis, as part of the standardized NAPKON SUEP protocol. For each patient, a single axial chest CT image was selected and the position of the arms during the CT was documented.

In the NAPKON-SUEP cohort, patient mortality was documented through systematic recording of clinical outcomes during the acute phase. This information was recorded in electronic case report forms and verified through regular quality controls. In addition, follow-up visits were conducted in the SUEP cohort three and twelve months after the initial infection, supplemented by telephone interviews every six weeks. These follow-ups enabled continuous monitoring of the patients' health status and contributed to the validation of the mortality data.

## Body composition analysis

The thoracic CT images were used for deep learning-based body composition analysis. Before the extraction of body composition markers, the CT images were resampled to a slice thickness of 5 mm to ensure a uniform database for further analysis. The body composition markers were then calculated using a fully automated evaluation pipeline. The analysis focused on the thorax, excluding the extremities. As described by Hosch et al., the thoracic cavity was defined as the chamber enclosed by the rib cage, extending from the superior thoracic aperture to the diaphragm, and includes the trachea up to the level of the cricoid cartilage [22]. For this region, the volumes of the relevant body structures were determined individually, allowing for the separate assessment of muscle mass, total fat mass, and intramuscular fat mass in alignment with our research objectives. All raw parameters were given as volumes (mL).

Further details about the Smart Hospital Information Platform (SHIP)-AI software of the University Hospital Essen have been documented elsewhere [23, 24].

## Clinical definitions

According to the WHO definition, obesity was defined as  $\text{BMI} \geq 30 \text{ kg/m}^2$  [25]. Sarcopenia was assessed via normalized muscle volume (to weight and height<sup>2</sup>) based on CT data.

## Statistics

IBM® SPSS® Statistics version 29 was used for statistical analysis and R studio was utilized for graph design. Metric variables were presented as means and standard deviations (SDs), while categorical variables were presented as frequencies and percentages. Metric variables were compared between the two groups using Student's t-test, while categorical variables were analyzed using the chi-square test or, if applicable, the exact Fisher test. The parameters from pretrained automated body composition analysis were all extracted as volumes. In order to follow current consensus statements for sarcopenia and sarcopenic obesity the muscle volumes were additionally normalized to weight and height squared [26, 27]. Furthermore, body composition parameters were visualized as density plots for the survivors and non-survivors groups.

Also, we conducted a binary logistic regression with death as the dependent variable. The metric independent variables were standardized to their SDs for comparability. Four regression models were formulated for the analysis. Each model considered either muscle volume or its normalized variants, total fat volume, intramuscular fat volume or BMI as an independent variable. Model 1 remained unadjusted, while model 2 was adjusted for age and sex. Model 3 was additionally adjusted for diabetes and chronic lung disease. Model 4 was additionally adjusted for chronic kidney disease. The results were expressed as odds ratios (OR) with confidence intervals and visualized in OR plots. A  $p$ -value  $< 0.05$  was considered statistically significant in the entire analysis.

## Results

### Patient characteristics

A total of 157 patients (mean age:  $70 \pm 8$  years; 41% women) met our inclusion criteria. The patient characteristics are shown in Table 1.

The patient collective corresponded to a geriatric cohort, since over 90% had at least two comorbidities and were thus classified as multimorbid. The average BMI was  $28.4 \text{ kg/m}^2$ , with about a third of patients with a BMI  $> 30 \text{ kg/m}^2$  considered obese.

All included patients suffered from severe COVID-19, as all required oxygen therapy.

Of the 157 patients, a total of 61 (39%) died. The groups death and control did not differ in terms of age, gender distribution and smoking status. However, the non-survivors had a significantly lower vaccination rate (16% vs. 55%), were more likely to have a medical intervention limitation (39%

vs. 5%) and had a higher BMI ( $29.9 \text{ kg/m}^2$  vs.  $27.5 \text{ kg/m}^2$ ) compared to survivors. In addition, diabetes, chronic lung disease and chronic kidney disease were significantly more common in the non-survivor group.

The majority of CT scans (78%) were performed as baseline examinations. Since arm position in the CT can influence the measurement of muscle mass, this was documented, but did not differ between the two groups. It was found that the majority of patients (95%) stretched both arms above their heads, which meant that the imaging conditions were homogeneous.

### Body composition analysis of survivors and non-survivors

Thoracic CT examination was performed at a mean interval of six days following a positive SARS-CoV-2 swab test. Body composition analyses derived from thoracic CT scans without extremities are shown in Table 2. Non-survivors had significantly lower total muscle volume and higher intramuscular fat volume compared to survivors. This difference was particularly noticeable when muscle volume was considered in relation to body weight. In contrast, no significant differences were found between the two groups in terms of bone and total fat volume. Figure 1 indicates these results as density plots.

Figure 2 shows two examples of thoracic CT scans in coronal and sagittal view. Both subjects presented are in the typical scanning position with their arms raised above their heads. The automated analysis of the CT scan in example (a) indicates a lower muscle volume and a greater amount of subcutaneous adipose tissue (SAT) compared to the second case (b). It should be noted that Fig. 2 shows only a single section, whereas the automated body composition analysis took into account all 5-mm slices of the thoracic CT scan.

### Influence factors on mortality

The results of the binary logistic regression analysis are presented in Table 3, with death as the dependent variable. Four models were evaluated. In the unadjusted model (Model 1) as well as in the model adjusted for age and gender (Model 2), muscle volume, muscle volume normalized to body weight, BMI, and intramuscular fat volume were significantly associated with mortality. In Model 3, which was further adjusted for diabetes and chronic lung disease, these associations remained largely consistent. However, in the fully adjusted model (Model 4), which also included chronic kidney disease, only muscle volume normalized to weight remained a significant predictor of mortality (OR 0.516, 95% CI 0.297–0.896,  $p < 0.01$ ). Absolute muscle volume, BMI, and intramuscular fat volume no longer showed

**Table 1** Patient characteristics

| Characteristics                           | all         | death      | control    | <i>p</i> -value              |
|-------------------------------------------|-------------|------------|------------|------------------------------|
| n (%)                                     | 157 (100.0) | 61 (38.9)  | 96 (61.1)  |                              |
| <b>Demographic variables</b>              |             |            |            |                              |
| age [years]                               | 70 (8)      | 71 (8)     | 69 (8)     | 0.107 <sup>a</sup>           |
| age groups [years]                        |             |            |            |                              |
| 60–69 years                               | 82 (52.2)   | 27 (44.3)  | 55 (57.3)  | 0.280 <sup>a</sup>           |
| 70–79 years                               | 49 (31.2)   | 22 (36.0)  | 27 (28.1)  |                              |
| >80 years                                 | 26 (16.6)   | 12 (19.7)  | 14 (14.6)  |                              |
| women (%)                                 | 65 (41)     | 24 (39)    | 41 (43)    | 0.677 <sup>a</sup>           |
| <b>Risk factors</b>                       |             |            |            |                              |
| BMI [kg/m <sup>2</sup> ]                  | 28.4 (6.0)  | 29.9 (7.3) | 27.5 (5.0) | <b>0.031<sup>b</sup></b>     |
| Obesity (BMI ≥ 30 kg/m <sup>2</sup> ) (%) | 38 (24.2)   | 17 (27.8)  | 21 (21.9)  | 0.165 <sup>b</sup>           |
| Ever smoker (%)                           | 48 (30.6)   | 17 (27.9)  | 31 (32.3)  | 0.253 <sup>c</sup>           |
| <b>Blood pressure</b>                     |             |            |            |                              |
| Systolic [mmHg]                           | 128 (20)    | 122 (22)   | 132 (19)   | <b>0.004<sup>d</sup></b>     |
| Diastolic [mmHg]                          | 70 (14)     | 64 (14)    | 74 (13)    | <b>&lt;0.001<sup>d</sup></b> |
| <b>Vaccination and life expectancy</b>    |             |            |            |                              |
| SARS-CoV-2 vaccination (%)                | 63 (40.1)   | 10 (16.4)  | 53 (55.2)  | <b>&lt;0.001<sup>e</sup></b> |
| Life expectancy of less than one year (%) | 6 (3.7)     | 5 (8.2)    | 1 (1.0)    | <b>0.020<sup>f</sup></b>     |
| Limitation of medical interventions (%)   | 29 (18.5)   | 24 (39.3)  | 5 (5.2)    | <b>&lt;0.001<sup>g</sup></b> |
| <b>Oxygenation support</b>                |             |            |            |                              |
| Conventional oxygen therapy (%)           | 57 (42.2)   | 9 (16.1)   | 48 (60.8)  | <b>&lt;0.001<sup>h</sup></b> |
| High-Flow oxygen therapy (%)              | 10 (7.4)    | 4 (7.1)    | 6 (7.6)    |                              |
| Non-invasive mechanical ventilation (%)   | 24 (17.8)   | 8 (14.3)   | 16 (20.2)  |                              |
| Invasive mechanical ventilation (%)       | 44 (32.6)   | 35 (62.5)  | 9 (11.4)   |                              |
| <b>Disease</b>                            |             |            |            |                              |
| Multimorbidity (≥ 2) (%)                  | 128 (89.5)  | 54 (94.7)  | 74 (86.0)  | 0.097 <sup>i</sup>           |
| High blood pressure (%)                   | 107 (93.9)  | 46 (93.9)  | 61 (92.4)  | 1.000 <sup>j</sup>           |
| Heart disease (%)                         | 117 (75.0)  | 50 (83.3)  | 67 (69.8)  | 0.057 <sup>k</sup>           |
| Diabetes mellitus (%)                     | 56 (36.4)   | 28 (46.7)  | 28 (29.8)  | <b>0.034<sup>l</sup></b>     |
| Chronic lung disease (%)                  | 47 (30.3)   | 24 (40.7)  | 23 (24.0)  | <b>0.028<sup>m</sup></b>     |
| Gastrointestinal disease (%)              | 10 (6.6)    | 6 (10.5)   | 4 (4.3)    | 0.179 <sup>n</sup>           |
| Neurological or psychiatric disease (%)   | 27 (17.4)   | 13 (21.7)  | 14 (14.7)  | 0.268 <sup>m</sup>           |
| Solid tumor disease (%)                   | 32 (20.5)   | 14 (23.3)  | 18 (18.6)  | 0.490 <sup>k</sup>           |
| Hematological malignancy (%)              | 17 (11.1)   | 9 (15.0)   | 8 (8.6)    | 0.219 <sup>o</sup>           |
| Chronic renal disease (%)                 | 32 (21.1)   | 22 (37.3)  | 10 (10.8)  | <b>&lt;0.001<sup>d</sup></b> |
| Chronic liver disease (%)                 | 12 (7.8)    | 6 (10.2)   | 6 (6.4)    | 0.396 <sup>o</sup>           |
| Rheumatologic condition (%)               | 8 (5.1)     | 3 (4.9)    | 5 (5.2)    | 0.936 <sup>a</sup>           |
| Post organ transplantation (%)            | 5 (3.2)     | 3 (5.0)    | 2 (2.1)    | 0.670 <sup>m</sup>           |
| <b>Arm positioning during CT scan</b>     |             |            |            |                              |

**Table 1** (continued)

| Characteristics                  | all        | death     | control   | <i>p</i> -value    |
|----------------------------------|------------|-----------|-----------|--------------------|
| Both arms above the head (%)     | 142 (95.3) | 53 (94.6) | 89 (95.7) | 0.634 <sup>r</sup> |
| One arm above the head (%)       | 4 (2.5)    | 1 (1.8)   | 3 (3.2)   |                    |
| Both arms alongside the body (%) | 3 (1.9)    | 2 (3.6)   | 1 (1.1)   |                    |

BMI: body mass index. CT: computer tomography

<sup>a</sup> Variable was available for 157 patients

<sup>b</sup> Variable was available for 126 patients

<sup>c</sup> Variable was available for 111 patients

<sup>d</sup> Variable was available for 152 patients

<sup>e</sup> Variable was available for 119 patients

<sup>f</sup> Variable was available for 131 patients

<sup>g</sup> Variable was available for 148 patients

<sup>h</sup> Variable was available for 135 patients

<sup>i</sup> Variable was available for 143 patients

<sup>j</sup> Variable was available for 115 patients

<sup>k</sup> Variable was available for 156 patients

<sup>l</sup> Variable was available for 154 patients

<sup>m</sup> Variable was available for 155 patients

<sup>n</sup> Variable was available for 151 patients

<sup>o</sup> Variable was available for 153 patients

<sup>r</sup> Variable was available for 149 patients

**Table 2** Body composition analysis of thoracic CT scans

|                                                        | all           | death         | control       | <i>p</i> -value          |
|--------------------------------------------------------|---------------|---------------|---------------|--------------------------|
| n (%)                                                  | 157 (100.0)   | 61 (38.9)     | 96 (61.1)     |                          |
| Muscle volume [L]                                      | 3.26 (0.94)   | 3.07 (0.81)   | 3.38 (1.00)   | <b>0.043<sup>a</sup></b> |
| Muscle volume/ height <sup>2</sup> [L/m <sup>2</sup> ] | 1.10 (0.27)   | 1.05 (0.26)   | 1.13 (0.27)   | 0.111 <sup>p</sup>       |
| Muscle volume/ weight [L/kg]                           | 0.0399 (0.01) | 0.0364 (0.01) | 0.0417 (0.01) | <b>0.003<sup>q</sup></b> |
| Bone volume [L]                                        | 1.95 (0.40)   | 1.93 (0.35)   | 1.96 (0.44)   | 0.736 <sup>a</sup>       |
| Total fat volume [L]                                   | 6.71 (2.62)   | 6.79 (2.48)   | 6.65 (2.72)   | 0.760 <sup>a</sup>       |
| Intramuscular fat volume [L]                           | 1.28 (0.50)   | 1.39 (0.53)   | 1.22 (0.47)   | <b>0.041<sup>a</sup></b> |

<sup>a</sup> Variable was available for 157 patients

<sup>p</sup> Variable was available for 141 patients

<sup>q</sup> Variable was available for 134 patients

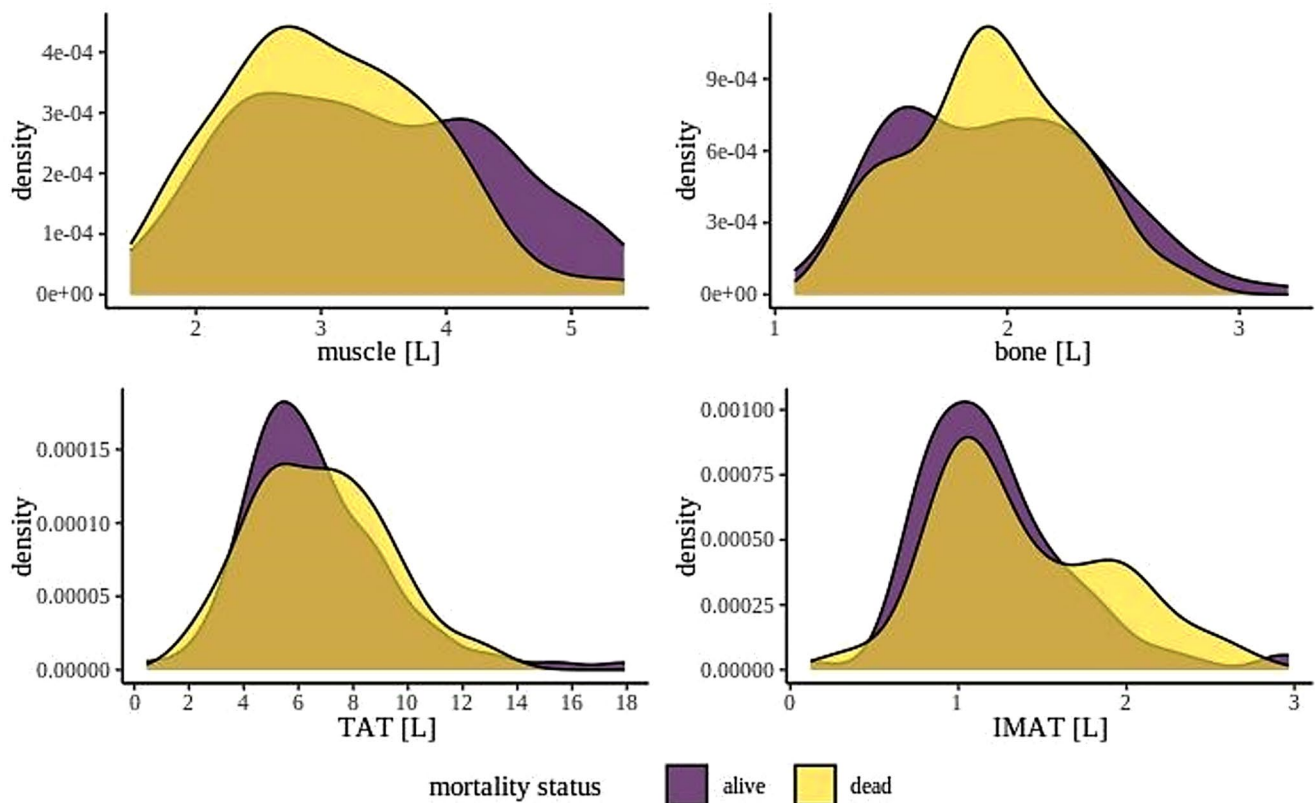
significant associations. These findings suggest that muscle volume relative to body weight may be a more robust and independent marker of mortality risk in this cohort. The results are further illustrated by the odds ratio plots in Fig. 3.

## Discussion

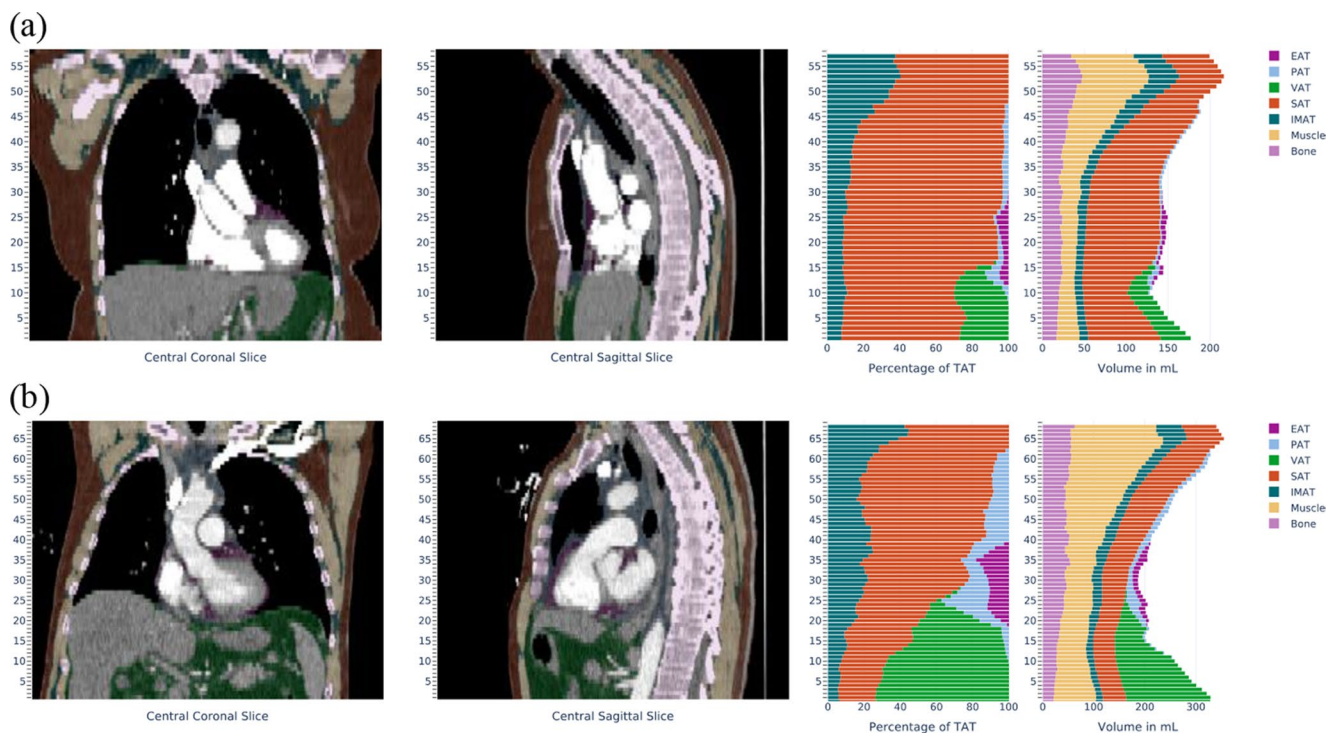
A total of 157 patients from the NAPKON-SUEP cohort (mean age: 70 ± 8 years; 41% women) were included in our study. To the best of our knowledge, we are the first to investigate muscle and fat volume using automated 3D-CT-Thorax analysis in a cohort of COVID-19 patients aged > 60 years. Our results showed that muscle mass was the most relevant body composition factor in relation to mortality.

## Low muscle mass as marker for severe courses of infection

Our regression analysis showed that muscle volume adjusted to weight had the strongest influence on survival, even after adjustment for age, sex, diabetes mellitus, chronic lung and kidney disease. This suggests that muscle volume adjusted to weight plays a central role in the prognosis of severe COVID-19 pneumonia. Additionally, we could show that for BMI and as well total muscle fat this effect did not remain significant after adjusting for comorbidities. Therefore, we postulate that sarcopenia plays a greater role than obesity in patients aging over 60 years with severe respiratory infection and that muscle volume is the most reliable body composition marker for predicting mortality.



**Fig. 1** Density plot of body composition TAT=total adipose tissue, IMAT=intramuscular adipose tissue. The color scheme was specifically chosen so that it is easily distinguishable even for patients with red-green color deficiency



**Fig. 2** Reports of the body composition analysis of two examples: (a) with low muscle volume and (b) with sufficient muscle volume EAT=epicardial adipose tissue, PAT=pericardial adipose tissue,

VAT=visceral adipose tissue, SAT=subcutaneous adipose tissue, IMAT=intramuscular adipose tissue

**Table 3** Logistic regression analysis with death as dependent variable

| Independent variables              | model 1                                      | model 2                                      | model 3                                      | model 4                                      |
|------------------------------------|----------------------------------------------|----------------------------------------------|----------------------------------------------|----------------------------------------------|
| Muscle volume                      | <b>0.708</b><br>(0.506–0.992) <sup>a</sup> * | <b>0.508</b><br>(0.304–0.847) <sup>a**</sup> | <b>0.526</b><br>(0.310–0.892) <sup>n</sup> * | 0.607<br>(0.352–1.045) <sup>z</sup>          |
| Muscle volume/ weight              | <b>0.563</b><br>(0.379–0.836) <sup>q**</sup> | <b>0.456</b><br>(0.277–0.752) <sup>q**</sup> | <b>0.475</b><br>(0.278–0.811) <sup>s**</sup> | <b>0.516</b><br>(0.297–0.896) <sup>t**</sup> |
| Muscle volume/ height <sup>2</sup> | 0.752<br>(0.529–1.069) <sup>p</sup>          | 0.714<br>(0.457–1.116) <sup>p</sup>          | 0.790<br>(0.495–1.261) <sup>u</sup>          | 0.891<br>(0.551–1.440) <sup>v</sup>          |
| Total fat volume                   | 1.052<br>(0.763–1.449) <sup>a</sup>          | 1.112<br>(0.798–1.549) <sup>a</sup>          | 1.050<br>(0.743–1.485) <sup>n</sup>          | 1.124<br>(0.785–1.611) <sup>z</sup>          |
| Intramuscular fat volume           | <b>1.400</b><br>(1.009–1.943) <sup>a</sup> * | <b>1.416</b><br>(1.012–1.980) <sup>a*</sup>  | 1.328<br>(0.932–1.894) <sup>n</sup>          | 1.334<br>(0.922–1.929) <sup>z</sup>          |
| BMI                                | <b>1.500</b><br>(1.024–2.197) <sup>b*</sup>  | <b>1.614</b><br>(1.075–2.422) <sup>b*</sup>  | 1.411<br>(0.916–2.172) <sup>e</sup>          | 1.491<br>(0.931–2.386) <sup>w</sup>          |

BMI: body mass index

Model 1 is unadjusted

Model 2 is adjusted for age and gender

Model 3 is adjusted for age, gender, diabetes and chronic lung disease

Model 4 is adjusted for age, gender, diabetes, chronic lung disease and chronic renal disease

Significance levels are expressed as \* &lt;0.05 and \*\*&lt;0.01

<sup>a</sup> Variable was available for 157 patients<sup>b</sup> Variable was available for 126 patients<sup>c</sup> Variable was available for 122 patients<sup>n</sup> Variable was available for 153 patients<sup>p</sup> Variable was available for 141 patients<sup>q</sup> Variable was available for 134 patients<sup>s</sup> Variable was available for 130 patients<sup>t</sup> Variable was available for 128 patients<sup>u</sup> Variable was available for 137 patients<sup>v</sup> Variable was available for 135 patients<sup>w</sup> Variable was available for 135 patients<sup>z</sup> Variable was available for 151 patients

Our findings align with previous studies, although most of these focused either on muscle or fat tissue and examined thoracic or abdominal CT scans in COVID-19 patients [5, 28–33]. Moreover, the vast majority relied on two-dimensional measurements of a single cross-sectional slice, typically assessing muscle structures at the thoracic vertebrae T4 and T12, the lumbar vertebrae L2 and L3 and the pectoralis muscle [5, 28–33]. Due to different anatomical reference points, the findings of these studies were sometimes inconsistent. A recent review including 22 studies on the association between sarcopenia and mortality in COVID-19 patients found that 17 studies reported a direct correlation, whereas five showed no significant association [5]. However, none of these studies employed a three-dimensional approach [5], which may have led to inconsistent findings.

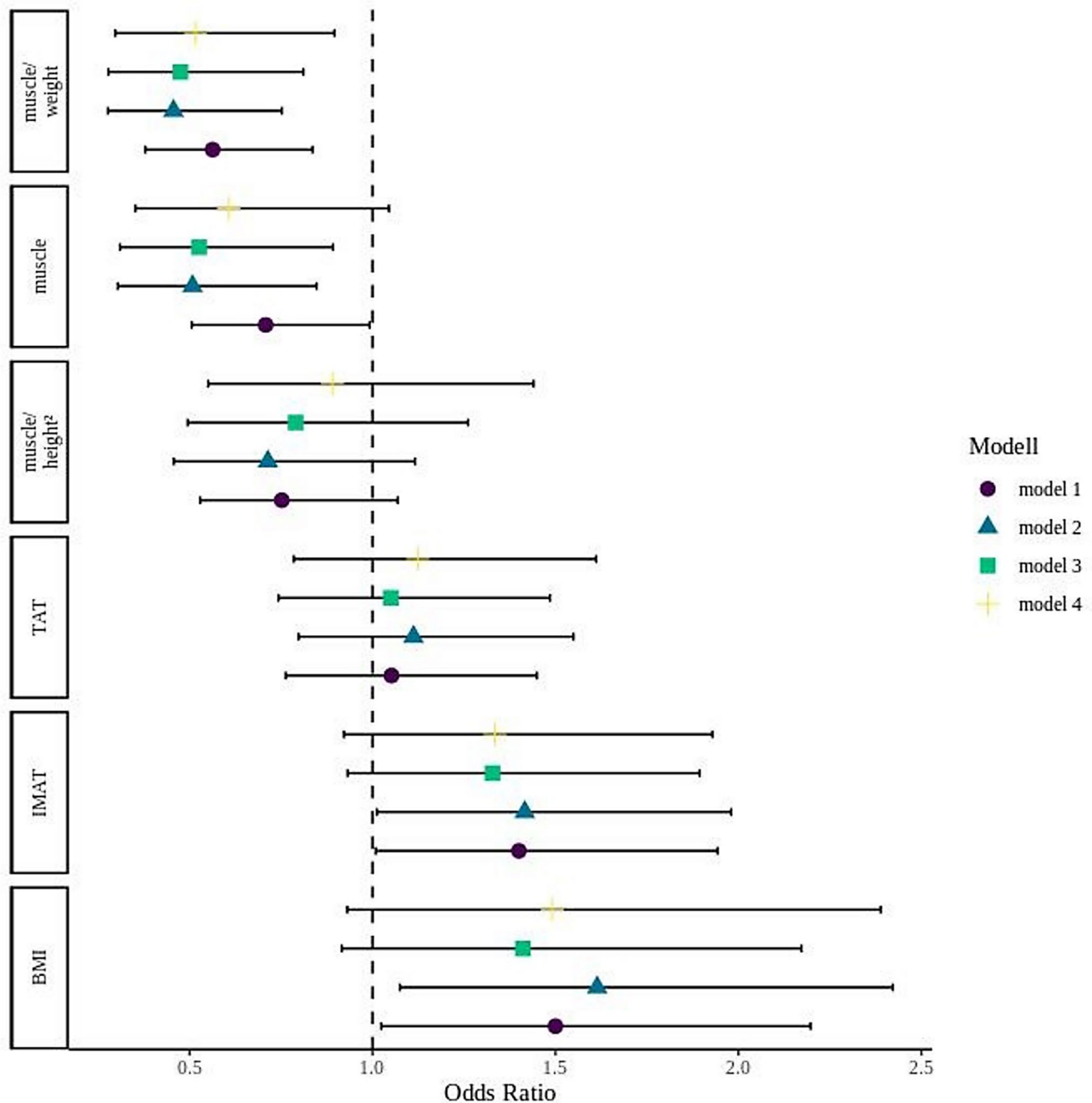
Nevertheless, the results show that obesity and sarcopenia need to be considered carefully. When both conditions are present at the same time, this condition is referred to as sarcopenic obesity (SO), which is associated with particularly unfavorable health consequences. Long-term studies

have shown that patients with SO have the poorest survival prognosis, followed by patients with sarcopenia alone and finally by obese patients without sarcopenia [34].

Another noteworthy finding is the significant difference in intramuscular fat content in our cohort. Non survivors showed significantly higher amounts of intramuscular fat. This observation is consistent with the long-term study by Pishgar et al., which showed that increased intermuscular fat was associated with higher mortality, while subcutaneous fat had less of an impact – a pattern also observed in patients with chronic obstructive pulmonary disease (COPD) [35]. In view of these results, intramuscular fat could be used as a potential prognostic marker in future studies and in clinical practice [36].

### Normalization of muscle volume

Another relevant aspect is the normalization of muscle volume. For decades, there has been discussion – similar to that regarding BMI – about which method of normalizing



**Fig. 3** Odds ratio plot for the binary logistic regression BMI: body mass index, TAT=total adipose tissue, IMAT=intramuscular adipose tissue. Model 1: unadjusted. Model 2: adjusted for age and sex. Model

3: adjusted for age, sex, diabetes and chronic lung disease Model 4: adjusted for age, sex, diabetes, chronic lung disease. and chronic kidney disease

muscle volume is most useful. According to the definition of sarcopenia, normalization to height squared is recommended [26]. However, recent studies on sarcopenic obesity indicate that this method may lead to an overestimation of muscle mass in obese patients ( $\text{BMI} \geq 30 \text{ kg/m}^2$  and/or increased waist circumference). This is because obese patients often have greater muscle mass due to their higher body weight, but this is not necessarily associated

with sufficient muscle strength and function [27]. For this reason, since 2022, normalization to body weight has been increasingly favored [27]. In our study, only muscle volume normalized to weight remained a significant predictor of mortality in the fully adjusted model, while absolute muscle volume and muscle volume normalized to height<sup>2</sup> lost statistical significance. This supports the notion that normalization to weight may be more appropriate in cohorts

with a higher prevalence of overweight and obesity. Indeed, the average BMI in our cohort was 28 kg/m<sup>2</sup>, compared to 25 kg/m<sup>2</sup> in our previous study [37], where no clear advantage was found for weight-based normalization. This difference might explain the shift in results and highlights the importance of tailoring normalization strategies to the specific characteristics of the population under study.

Interestingly, in both studies, absolute muscle volume showed strong correlations with normalized values, although its predictive value was not robust after full adjustment in the current analysis. This underscores the potential value of simple absolute measures, but also the importance of adjusting for body composition when assessing clinical risk.

### **Additional factors influencing mortality beyond muscle mass**

The analysis of the patient groups shows significant differences in several clinical and demographic factors that are potentially associated with mortality and are already well described in recent publications [38, 39]: The vaccination status differed significantly between the groups: in the group of non-survivors, it was only 16%, while in the survivors it was 55%. Additionally, life expectancy of less than one year and limitation of medical interventions was significant higher in the non-survivor group.

In term of comorbidities, the two groups differed significantly in terms of three concomitant diseases: diabetes mellitus, chronic renal failure and chronic lung disease. Recent major studies confirm this correlation and show that these comorbidities increase the mortality risk in the event of severe Covid-19-infections [40–42]. Interestingly, no significant differences were found with regard to cardiovascular diseases, including arterial hypertension. In addition, the mean blood pressure in the group of non-survivors was significantly lower. This could be explained by severe septic processes with consecutive blood pressure drop. However, this raises the question of whether diabetes, chronic renal insufficiency and lung diseases play a greater role than cardiovascular risk factors in severe respiratory infections but cannot be answered by this study design.

### **Therapeutic consequences and clinical relevance**

The realization that low muscle mass is associated with higher mortality highlights the importance of preventive and therapeutic measures to maintain muscle mass, especially in infectious medicine. It is therefore crucial to take measures that promote muscle maintenance – both preventively and therapeutically. Early detection of patients with lower muscle mass could help to counteract this. The use

of automated methods as showed in our study from routine CT scans could prove to be a valuable tool for risk assessment. This would allow the early identification of patients with low muscle mass, who could then be monitored more closely [20]. In addition to diagnostic options, nutrition plays a central role [14, 15, 43]. A protein-rich diet combined with essential amino acids can help to slow down muscle breakdown and at the same time strengthen the immune system. Likewise, the targeted intake of micronutrients such as vitamin D and iron could have a positive influence on the course of the disease [14, 15]. Physiotherapy is also of great importance. Especially for seriously ill patients, it is essential to integrate early exercise programs to minimize muscle loss [44]. For ventilated patients in particular, respiratory muscle training programs could help to stabilize respiratory function and accelerate recovery [45]. Future studies should also focus on the automated analysis of diaphragm and respiratory muscle composition to gain better insight into respiratory sarcopenia [46].

### **Automated body composition analysis in other medical contexts**

The automated, AI-based analysis of body composition using CT imaging has gained increasing importance across various medical disciplines in recent years. Several studies have demonstrated a strong correlation between muscle and fat measurements derived from thoracic CT scans and those obtained from abdominal CT at the L3 vertebral level, which is considered the gold standard in body composition analysis [47]. The SHIP-AI system used in this study was first described 2021 by Koitka et al. and showed a high degree of agreement with established reference methods such as DXA and BIA – particularly with regard to fat distribution and muscle mass [23]. In a follow-up study by Kroll et al., SHIP-AI was successfully used for quantitative assessment in patients with neuroendocrine tumors [24]. In addition, it has recently been shown that SHIP-AI-based indices such as the sarcopenia or fat index also have prognostic relevance in patients with idiopathic pulmonary fibrosis [48]. These studies illustrate the broad spectrum of application and clinical relevance of automated CT-based body composition analyses in numerous medical contexts. With regard to sarcopenia and obesity, the determination of standardized cut-off values remains a key objective for future research in the field of automated body composition analysis. Overall, the method provides a reliable, reproducible, and clinically practical alternative to conventional anthropometric diagnostics.

## Strength and limitations

One of the strengths of the study is the innovative approach by applying pre-trained deep learning models for the automated analysis of body composition using thoracic CT scans in the NAPKON-SUEP cohort. This enables an objective and standardized evaluation that avoids subjective assessments and ensures a high degree of reproducibility. Compared to manual measurement methods, this technique offers more precise measurement of muscle, fat and bone volume, which is particularly advantageous in clinical applications. Another key aspect of the study is the holistic view of body composition. While previous research often focused on BMI or individual cross-sectional images, a 3D-approach was used here.

Despite these strengths, the study has some limitations. One important point is that body composition was only measured at a single point in time. There is a lack of data on how muscle mass changes over the course of the disease. Long-term observation would be helpful to better understand the extent to which such changes influence prognosis. Another limitation of the study is that height and weight were not objectively measured but were obtained through patient self-report during anamnesis, which may introduce reporting bias or inaccuracy.

Furthermore, the study focuses on muscle volume without considering functional aspects. However, for the diagnosis of sarcopenia the measurement of muscle strength is essential. Supplementing the study with a measurement of handgrip strength or other functional tests could help to further substantiate the clinical relevance of the results.

Overall, additional studies with long-term follow-up data and measurement of muscle strength would be necessary to further substantiate these findings.

## Conclusion

In summary, the NAPKON-SUEP cohort examined for the first-time muscle and fat volume of COVID-19 patients aged over 60 years in relation to mortality using automated 3D CT thorax analysis. The results showed that sarcopenia has a stronger influence on survival than obesity. The early identification of patients with critical muscle mass could be a key factor in improving survival rates and shortening the course of the disease. In this context, automated CT-based muscle mass determination offers a promising, innovative diagnostic tool. Further studies are needed to validate its usefulness in clinical practice and to enable its implementation.

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**Data availability** No datasets were generated or analysed during the current study.

## Declarations

**Ethical approval** This study was performed in line with the principles of the Declaration of Helsinki. For the NAPKON SUEP, a primary ethics vote was obtained at the Ethics Committee of the Department of Medicine at Goethe University Frankfurt (local ethics ID approval 20–924). All further study sites received their local ethics votes at the respective ethics commissions. The NAPKON SUEP is registered at ClinicalTrials.gov (Identifier: NCT04768998). Approval for this study was granted by the Ethics Committee of LMU Munich, Germany (study no. 22–0671).

**Informed consent** Informed consent was obtained from all individual participants included in the study.

**Competing interests** The authors declare no competing interests.

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