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Relationship between skeletal muscle area and density and clinical outcome in adults receiving veno-venous extracorporeal membrane oxygenation

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Abstract

Objective

To investigate the prevalence of low skeletal muscle index (area normalised for height) and density, their trajectory of change and to determine associations with clinical outcome in adults with severe respiratory failure requiring veno-venous extracorporeal membrane oxygenation (VV-ECMO).

Design

Prospective observational study.

Patients

Adults receiving VV-ECMO for a minimum of 72 hours and a maximum of 6-months between September 2010 – June 2017, who had a computed tomography (CT) scan which included the third lumbar vertebra (L3).

Intervention

None

Measurements and main results

Skeletal muscle index and density was determined using Slice-O-Matic V5.0 (TomoVision, Montreal, Canada). Low skeletal muscle index and density were defined using published criteria. Regression models were used to assess for associations between muscle index and density and clinical outcome. 215 patients, median (IQR) age 46 (35.0-57.0) years were included. Forty-five (21.1%) patients had low skeletal muscle index and 48 (22.3%) had low skeletal muscle density on commencement of VV-ECMO. Low skeletal muscle index was more prevalent in males (28.8% vs. 11.6%, X^2=9.4, p = .002) and was associated with a longer duration of VV-ECMO (B 5.0, 95% CI 0.2-9.9, p = .042). Higher skeletal muscle density was independently associated with ICU survival (OR 1.6 per 10 Hounsfield Units, 95% CI 1.1-2.5, p

= .025). No relationship was observed between skeletal muscle index nor density and physical function. Adequacy of energy and protein did not influence change in skeletal muscle index or density.

Conclusions

Low skeletal muscle index at the commencement of VV-ECMO was associated with a longer duration of VV-ECMO, whereas preserved skeletal muscle density was associated with improved survival.

Keywords (4-6)

Critical illness, muscle mass, muscle quality, ECMO, nutrition, physical function

Introduction

Veno-venous extracorporeal membrane oxygenation (VV-ECMO) is a support therapy used in patients with severe refractory respiratory failure. Recent studies confirm outcome benefits compared with conventional strategies (1-3). As survival rates from severe critical illness increase, a significant proportion of patients becomes deconditioned and may require prolonged rehabilitation. Although ICU-acquired weakness is multi-factorial, skeletal muscle atrophy is a significant contributor. Patients receiving VV-ECMO have been shown to lose muscle at a similar rate to critically ill, non-ECMO patients (4) in whom there is direct relationship between hypoxaemia and muscle wasting (5).

Additionally, patients may have pre-existing low skeletal muscle mass (6, 7), and further reduction in strength which may influence recovery. For example, low skeletal muscle area (SMA) and skeletal muscle density (SMD), measured using computed tomography scans (CT) at the third lumbar vertebra (L3), has been associated with adverse outcomes including longer duration of mechanical ventilation and length of ICU stay (7); increased in-hospital (6, 7) and 6-month mortality (8). However, patients requiring VV-ECMO are often younger with fewer comorbidities compared to the general ICU population (9, 10). It is not known whether skeletal muscle area or density at the commencement of VV-ECMO is associated with similar outcomes, but it is hypothesized that lower skeletal muscle area or density influence the trajectory of recovery analogously to patients who do not receive ECMO.

The aim of this study was to assess skeletal muscle area and density at commencement of VV-ECMO, their trajectory of change and to investigate the relationship between skeletal muscle quantity and quality and clinical outcome, nutrition delivery and physical function.

Materials and Methods

Design and setting

We performed a retrospective observational study on patients who received VV-ECMO between September 2010 – June 2017. Patients were identified from a prospectively held database. The need for written informed consent was waived by the ethical committee (Research Ethics Committee reference 17/WA/0166) and the study was registered (NCT03269825).

Eligibility criteria

Patients were eligible for inclusion if they were ≥ 18 years, received a minimum 72 hours to a maximum 6 months of VV-ECMO, and underwent a CT scan at the level of L3 of sufficient quality to analyse, within 24 hours of commencing VV-ECMO.

Data collection

Demographic, anthropometric, nutritional, physical function and clinical data were collected from electronic medical records (Phillips, ICIP, Baltimore, USA). These included admission reason, age, sex, Acute Physiology and Chronic Health Evaluation (APACHE) II score, admission Sequential Organ Failure Assessment (SOFA) score, weight, body mass index (BMI), degree of malnutrition using the Global Leadership initiative on Malnutrition (GLIM) criteria (11) (retrospectively collected), Nutrition Risk in the Critically Ill (NUTRIC) score (12), duration of VV-ECMO, duration of ICU and hospital stay at Guy's and St Thomas' (GSTT), survival status (ECMO, ICU and 6-month), number of co-morbidities, and days in hospital prior to commencement of VV-ECMO.

Nutritional data

Daily and cumulative energy and protein delivery was calculated for days spent on VV-ECMO, for the post-ECMO period, the total duration of ICU admission at GSTT and compared

with estimated targets which were set by the specialist ICU dietitian (**Supplementary Digital Content**). Additionally, if a second CT was undertaken during the ICU admission, energy and protein delivery was considered up until the full day before the second scan. Data included both nutritional (e.g. enteral and parenteral nutrition) and non-nutritional (e.g. intravenous glucose and propofol) sources. Energy and protein intake was considered adequate if a patient achieved a cumulative delivery of $\geq$ 80% of estimated targets (13).

Physical function data

A specialist physiotherapy service embedded within critical care aims to achieve early mobilization as soon as safe. Patients are individually assessed, and progression follows through typically hierarchical functional levels including bed-based exercises, sitting on the edge of the bed, standing and walking.

The ICU mobility scale (IMS) was used to determine the highest level of mobility that each patient surviving ICU achieved in the 48 hours preceding GSTT ICU discharge. The Chelsea Physical Assessment (CPAx) Score (14) was collected within 7 days from decannulation from VV-ECMO in a sub-group of patients who survived to ICU discharge.

CT scan analysis

CT scans were imported into OSIRIX (V8.0, pixmeo, Geneva, Switzerland) from Picture Archiving and Communication System (PACS; IDS7, Sweden) to facilitate landmarking of the mid-point of L3. The isolated L3 slice was anonymised, re-labelled with a patient identifier and exported in DICOM format to be analysed using Slice-O-Matic V 5.0 (TomoVision, Montreal, Canada) by trained personnel (DEB). A second CT scan was also collected where one was undertaken after day 3 of admission and whilst still in the ICU. Where a second CT scan was available, the initial slice was visible to the researcher when landmarking the second to reduce variability.

Tissues were differentiated by setting the appropriate Hounsfield Unit (HU) boundaries. This was -29 to +150 HU for muscle, -190 to -30 HU for intermuscular adipose tissue (IMAT) and subcutaneous adipose tissue (SAT) and -150 to -50 HU for visceral adipose tissue (VAT) (6, 8). Skeletal muscle area (SMA) was adjusted for available height (cm^2/m^2) and recorded as the skeletal muscle index (SMI). Skeletal muscle density (SMD), the average radiological density muscle attenuation, was recorded as a marker of muscle quality. Although SMA and SMI are both considered markers of skeletal muscle quantity, it was considered more appropriate to use SMI in the analysis due to the availability of published cut-off values for the definition of low muscle mass. Values for SMI and SMD were categorised as low or normal according to published literature which are adjusted for sex, age and BMI (15). The actual and percentage loss of body composition parameters between two CT scans was calculated in a sub-set of patients where this was available. The same researcher analysed all CT scans. Intra-observer agreement was excellent for the measurements of SMA (**Supplemental Digital Content).**

Statistical analysis

Data are presented as median (IQR), mean (SD) or number (%). Assessment for normality was performed using the Shapiro-Wilks Test. Linear and logistic regression were used to determine the association between skeletal muscle index and skeletal muscle density on the clinical outcomes of duration of VV-ECMO and survival (ECMO, ICU and 6-month). Univariate regression was undertaken first using variables chosen *a priori* based on their clinical significance to the clinical outcomes and included APACHE II, SOFA, sex, hospital days prior to commencing ECMO, BMI, visceral adipose tissue (per 10 cm^2) and subcutaneous adipose tissue (per 10cm^2). To avoid the effects of collinearity, age was not included as a

variable as it is already included in the calculation for APACHE II score. Similar to others, body composition measurements per 10 units were entered into the regression models as this is felt to be more clinically relevant than using a 1 HU value (8). Multivariate regression models were built with adjustment for variables that were found to be statistically significant ($p \leq .1$) in univariate analysis (Model 2). In addition, due to collinearity between BMI, visceral adipose tissue and subcutaneous adipose tissue, if the latter two variables were statistically significant in univariate analysis, they replaced BMI in Model 3 to determine their relationship with the outcome. Absolute values for SMI (per 10cm^2) and SMD (per 10 HU) were considered separately to categorical variables for low SMI and SMD. If these were significant in univariate analysis, they were entered into multivariate analysis in Model 4.

Chi-squared or Mann-Whitney U tests were used to determine the relationship between SMI, SMD and the physical function outcomes and the change in body composition and nutritional adequacy as appropriate. Analysis were performed using SPSS 24 and SPSS 26.

Results

In total, 371 patients were screened for eligibility with 215 included in the final analysis (**Figure 1**). Baseline demographics are shown in **Table 1.** Data for nutrition delivery are presented in **Table S1** of the **Supplemental Digital Content**. The median (IQR) age was 46 (35-57) years and the majority were male (123 (57.2%)). Overall, patients received 91.0 (82.2-98.4) % of their energy targets and 86.0 (75.8-95.3) % of their protein targets during their GSTT ICU admission. SMI at commencement of VV-ECMO was 46.6 (40.6-54.9) cm^2/m^2 and SMD 36.6 (10.4) HU (**Table S2 – Supplemental Digital Content**). All other body composition data are presented in **Table S2 (Supplemental Digital Content)**.

Prevalence of low skeletal muscle index (SMI) and density (SMD) on commencement of VV-ECMO based on sex and BMI

The prevalence of low SMI, based on sex, age and BMI, on commencement of VV-ECMO was 45/213 (21.1%) and SMD 48/215 (22.3%). Low SMI was more prevalent in males (28.8% vs. 11.6%, $X^2 = 9.4$, $p = .002$) with no difference in SMD.

19 (23.5%) obese patients (BMI $\geq$ 30 kg/m^2) had low SMI and 17 (21.0%) had low SMD. Of the patients considered to be normally nourished using the GLIM criteria (11), the prevalence of low SMI or SMD was 8 (17.8%) and 11 (23.4%) respectively. 12 (25.5%) patients with stage 2 malnutrition had low SMD, but none had low SMI.

Change in skeletal muscle area, index (SMI) and density (SMD) over time

54 patients underwent a second CT scan (median day 9 (7-18)) (**Table S3 in Supplemental Digital Content**). There was a 17.7% (-23.9 to -8.2) reduction in total SMA, 17.7% (-23.9 to -8.2) in total SMI and a 10.6% (-23.6 to 13.4) reduction in SMD.

30/54 (55.5%) patients received adequate (≥80%) energy and 22 /54 (40.7%) received adequate (≥80%) protein up to the day before the second CT scan. There was no difference in the trajectory of skeletal muscle quantity or quality parameters in patients who received adequate energy ($p = .951$) or protein ($p = .410$) compared to those who did not (**Table S4 in Supplemental Digital Content**).

Relationship between skeletal muscle index (SMI) and density (SMD) and clinical outcome

Low SMI was associated with an increased duration of VV-ECMO both in univariate analysis (B 7.3, 95% CI 2.3-12.3, $p = .005$) and when adjusted for BMI and length of stay prior

to VV-ECMO (Model 4) (B 5.0, 95% CI 0.2-9.9, *p* = .042) (**Table 2, Table S5 in Supplemental Digital Content**).

SMD was significantly associated with ICU survival both in univariate analysis (OR 1.8 per 10 HU, 95% CI 1.2-2.8, *p* = .004) and when adjusted for APACHE II and SOFA (Model 2) (OR 1.6, 95% CI 1.1-2.5, *p* .025) (**Table 2, Table S5 in Supplemental Digital Content**).

In VV-ECMO survivors, the duration of VV-ECMO was longer in patients with low SMI (13.0 (8.0-20.0) vs. 9.0 (7.0-12.0), *p* = .008), while there was no difference in the duration of VV-ECMO between patients with low SMD and those with normal SMD (10.0 (6.3-14.8) vs 9.0 (7.0-14.0), *p* = .398).

Relationship between skeletal muscle index (SMI) and density (SMD) and physical function

ICU Mobility Scale (IMS) was collected for all 181 ICU survivors. The IMS score in the 48 hours preceding ICU discharge was 4 (3-6). 112 patients (61.9%) achieved an IMS score of more than three (i.e. achieved out of bed activities). There was no difference in IMS scores between those with low SMI on admission and those with normal SMI (4 (3-6) vs. 4 (3-6), *p* = .212) and those who had low SMD and those who did not (4(3-6) vs. 4(3-6), *p* = .355).

A sub-group of 49 ICU survivors had CPAx scores calculated within 7 days of VV-ECMO decannulation. The median CPAx score was 14 (6.0-26.5). There was no difference in CPAx scores between those with low SMI and those with normal SMI (6 (4-12) vs. 14 (6-29), *p* = .062) or those with low SMD and those with normal SMD (*p* = .285).

Discussion

Almost one quarter of adult patients with severe respiratory failure have low skeletal muscle index and density at the commencement of VV-ECMO. Preserved skeletal muscle

density, but not index, was independently associated with improved ICU survival, whereas low skeletal muscle index at the commencement of VV-ECMO was associated with a longer duration of VV-ECMO. Measurements of skeletal muscle index or density could not discriminate between levels of physical function in ICU survivors and adequacy of nutrition did not influence the trajectory of muscle wasting.

Low muscle mass was less prevalent compared to the 40-70% reported in other populations (6, 7, 16-19), and low muscle mass did not increase mortality. However, increased SMD as a marker of skeletal muscle quality was associated with improved ICU survival. Whilst the latter finding is in keeping with others (8) the former is in contrast with data from mixed critically ill patients (6, 7) or data from adult VV-ECMO patients where the 6-month and 1-year survival was significantly lower in patients with low SMI (17). There are several potential reasons for this difference. From a clinical perspective, the current VV-ECMO cohort was younger and had few comorbidities (6, 7, 17). From a technical perspective, it is possible that the approach we used to analyse the CT scans (e.g. total skeletal muscle area *vs*. individual muscle groups, such as the psoas muscle) combined with the cut-off values used to define 'low' muscle mass may have contributed to this observation. Previous studies have used cut-off values from patients with solid tumours that may not accurately reflect critically ill cohort (7, 17-19), or cut-off values which have not been externally validated (6, 16). Given the characteristics of this cohort, we utilised cut-off values recently developed from a healthy population (15). As these values adjust for sex, age and BMI which are all important determinants of muscle mass, the use of this prediction model to characterise SMI and SMD seems appropriate for our cohort.

These data have significant clinical relevance and suggests that depending on the case-mix of critically ill patients, skeletal muscle density and index may both be important determinants of outcome.

The presence of low skeletal muscle index at commencement of VV-ECMO was associated with a longer duration of VV-ECMO. It is possible that this is a reflection of loss of skeletal muscle (5) occurring as a result of a hospital stay prior to the CT scan, given that the number of days in hospital prior to commencing VV-ECMO was longer in the low SMI group and also independently associated with low skeletal muscle area.

Although skeletal muscle index and density are associated with important clinical outcomes, our data did not show an association with mobility level at ICU discharge or global physical function within 7 days of decannulation from VV-ECMO. However, the difference in CPAx scores between patients with low SMI and those with preserved SMI is greater than the CPAx minimal clinically important difference of 6 points, which may indicate clinical, but not statistical relevance (20). Whilst it is possible that our sample size is too small to be able to detect statistical differences, other reasons may also exist. For example, the relationship between muscle mass and strength in critical illness is not linear leading to difficulties in interpreting these associations (21). Further, these measures - specifically the ICU Mobility Scale - may not be sensitive enough to differentiate between patients, especially in an overall well-fed patient group.

The subsample of patients with a second follow-up CT scan demonstrated a loss >10% of their skeletal muscle mass with a decline in skeletal muscle quality. This is in keeping with data reported from studies using ultrasound of quadriceps muscle (4, 5, 22). However, results from this study do not show a difference in the trajectory of skeletal muscle wasting when adequate energy or protein are received which is in contrast to others (19). It is important to

note that in this previous study the overall energy and protein delivery was only 41% for energy and 57% for protein compared with 90% for energy and 83% for protein in the present study which may account for the differences seen.

The strengths of this study are in the rigorous protocol used to analyse the CT scans, the very high intra-observer agreement, and the use of only one assessor to analyse CT scans.

Some limitations are acknowledged. First, just over 40% of scans were excluded, the majority because there was no abdominal CT scan available, and in a third of cases due to insufficient quality for analysis. Second, as a tertiary referral centre, many patients are repatriated back to their referring ICU or hospital precluding a full dataset being collected for use in survival analysis due to missing data. That said, we are confident the remaining sample was sufficient to explore the other aims. Third, as any retrospective observational studies, we cannot exclude residual confounders related to interval rates of change in skeletal muscle and prevented the ability to prospectively acquire measures of physical function which may otherwise be useful for determining the effect of skeletal muscle index and density on physical function and we are unable to make any determination of causality. Finally, we did not collect data on the use of sedation and muscle relaxants. However, use of muscle relaxants is not routine and used at the discretion of the treating consultant. Sedation is used in line with a departmental protocol a Richmond Agitation and Sedation Score (RASS) of -3 to +2, with a goal to achieve spontaneous breathing and lighter sedation within the first 48 hours.

Conclusion

In this cohort of adult patients requiring VV-ECMO, the presence of low skeletal muscle index (SMI) was associated with a longer duration of VV-ECMO whereas preserved skeletal muscle density (SMD) was associated with enhanced ICU survival.

Take home message (2 sentences max)

Low skeletal muscle index was associated with longer VV-ECMO requirement whereas preserved skeletal muscle density was associated with improved survival

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FIGURE LEGEND

Figure 1: Eligibility flowchart for the study

REFERENCES

1. Noah MA, Peek GJ, Finney SJ, et al: Referral to an extracorporeal membrane oxygenation center and mortality among patients with severe 2009 influenza A(H1N1). *JAMA* 2011; 306(15):1659-68.
2. Combes A, Hajage D, Capellier G, et al: Extracorporeal Membrane Oxygenation for Severe Acute Respiratory Distress Syndrome. *N Engl J Med* 2018; 378(21):1965-75.
3. Goligher EC, Tomlinson G, Hajage D, et al: Extracorporeal Membrane Oxygenation for Severe Acute Respiratory Distress Syndrome and Posterior Probability of Mortality Benefit in a Post Hoc Bayesian Analysis of a Randomized Clinical Trial. *JAMA* 2018; 320(21):2251.
4. Hayes K, Holland AE, Pellegrino VA, et al: Acute skeletal muscle wasting and relation to physical function in patients requiring extracorporeal membrane oxygenation (ECMO). *J Crit Care* 2018; 48:1-8.
5. Puthucheary ZA, Rawal J, McPhail M, et al: Acute skeletal muscle wasting in critical illness. *JAMA* 2013; 310(15):1591-600.
6. Weijs PJ, Looijaard WG, Dekker IM, et al: Low skeletal muscle area is a risk factor for mortality in mechanically ventilated critically ill patients. *Crit Care* 2014; 18(2):R12.
7. Moisey LL, Mourtzakis M, Cotton BA, et al: Skeletal muscle predicts ventilator-free days, ICU-free days, and mortality in elderly ICU patients. *Crit Care* 2013; 17(5):R206.
8. Looijaard WG, Dekker IM, Stapel SN, et al: Skeletal muscle quality as assessed by CT-derived skeletal muscle density is associated with 6-month mortality in mechanically ventilated critically ill patients. *Crit Care* 2016; 20(1):386.
9. Vogel DJ, Murray J, Czapran AZ, et al: Veno-arterio-venous ECMO for septic cardiomyopathy: a single-centre experience. *Perfusion* 2018; 33(Suppl 1):57-64.
10. Camporota L, Caricola EV, Bartolomeo N, et al: Lung Recruitability in Severe Acute Respiratory Distress Syndrome Requiring Extracorporeal Membrane Oxygenation. *Crit Care Med* 2019; 47(9):1177-83.
11. Cederholm T, Jensen GL, Correia MITD, et al: GLIM criteria for the diagnosis of malnutrition – A consensus report from the global clinical nutrition community. *Journal of cachexia, sarcopenia and muscle* 2019; 10(1):207-17.
12. Rahman A, Hasan RM, Agarwala R, et al: Identifying critically-ill patients who will benefit most from nutritional therapy: Further validation of the "modified NUTRIC" nutritional risk assessment tool. *Clin Nutr* 2016; 35(1):158-62.
13. MacGowan L, Smith E, Elliott-Hammond C, et al: Adequacy of nutrition support during extracorporeal membrane oxygenation. *Clin Nutr* 2019; 38(1):324-331.
14. Corner EJ, Wood H, Englebretsen C, et al: The Chelsea critical care physical assessment tool (CPAx): validation of an innovative new tool to measure physical morbidity in the

general adult critical care population; an observational proof-of-concept pilot study. *Physiotherapy* 2013; 99(1):33-41.
15. van der Werf A, Langius JAE, de van der Schueren MAE, et al: Percentiles for skeletal muscle index, area and radiation attenuation based on computed tomography imaging in a healthy Caucasian population. *Eur J Clin Nutr* 2018; 72(2):288-96.
16. Toledo DO, Carvalho AM, Oliveira A, et al: The use of computed tomography images as a prognostic marker in critically ill cancer patients. *Clin Nutr ESPEN* 2018; 25:114-20.
17. Cho WH, Choi YY, Byun KS, et al: Prognostic Value of Sarcopenia for Long-Term Mortality in Extracorporeal Membrane Oxygenation for Acute Respiratory Failure. *ASAIO J* 2019. [Epub ahead of print].
18. Sheean PM, Peterson SJ, Gomez Perez S, et al: The prevalence of sarcopenia in patients with respiratory failure classified as normally nourished using computed tomography and subjective global assessment. *JPEN* 2014; 38(7):873-9.
19. Braunschweig CA, Sheean PM, Peterson SJ, et al: Exploitation of diagnostic computed tomography scans to assess the impact of nutrition support on body composition changes in respiratory failure patients. *JPEN* 2014; 38(7):880-5.
20. Corner EJ, Hichens LV, Attrill KM, et al: The responsiveness of the Chelsea Critical Care Physical Assessment tool in measuring functional recovery in the burns critical care population: An observational study. *Burns* 2015; 41(2):241-7.
21. Connolly B, Maddocks M, MacBean V, et al: Nonvolitional assessment of tibialis anterior force and architecture during critical illness. *Muscle Nerve* 2017. 57(6):964-972
22. Parry SM, El-Ansary D, Cartwright MS, et al: Ultrasonography in the intensive care setting can be used to detect changes in the quality and quantity of muscle and is related to muscle strength and function. *J Crit Care* 2015; 30(5):1151.e9-14.

SUPPLEMENTAL DIGITAL CONTENT

Nutritional Data

Energy targets were calculated using a weight based equation (e.g. 20-25 kcal/kg, adjusted as clinically appropriate) and protein targets using a minimum of 1.2 g/kg day with adjustments if clinically indicated (e.g. for continuous renal replacement therapy). Where a range of energy and protein targets were documented, the mid-point was used. Energy and protein targets were adjusted for part days where required (e.g. the first and last days of admission). Data were collected until oral nutrition commenced, discharge from GSTT ICU or death.

Intra-observer agreement for the measurement of skeletal muscle area (SMA) using SliceOmatic

A random sample of 12 CT scans from the larger study sample were used to determine intra-observer agreement. DEB analysed all scans. After a period of training and practice, CT scans were measured in triplicate using the SliceOmatic software on two occasions a minimum of 7 days apart. The mean of the three scans was calculated and used in the analysis.

For measurement reliability, an *a priori* power calculation determined that to compare two observations a minimum of 12 participants were required, anticipating coefficients between 0.6 and 0.9 and using a significance level of 0.05 and power of 80%.

Intraobserver agreement for the measurements of skeletal muscle are was determined using intraclass correlation coefficients (ICC) using a two-way random effects model for absolute agreement. The following reliability criteria was used: 0.00-0.49 indicating poor agreement, 0.50-0.74 indicating moderate agreement and 0.75-1.00 indicating excellent

agreement. Bland-Altman analysis was examined to provide a visual representation of the agreement between measurement occasions and to examine whether there was a systematic error present. Statistical analysis was undertaken using SPSS 26 and PRISM Graphpad (version 8.0).

The ICC was 1.00 (95% CI 0.999 – 1.000), indicating excellent agreement. Bland Altman analysis is shown in **Figure S1** and demonstrates a mean (SD) bias of 0.5 (1.0) cm^2 (95% limits of agreement -1.5 cm^2 to 2.43 cm^2) between the measurements. The average coefficient of variation was 0.5%.

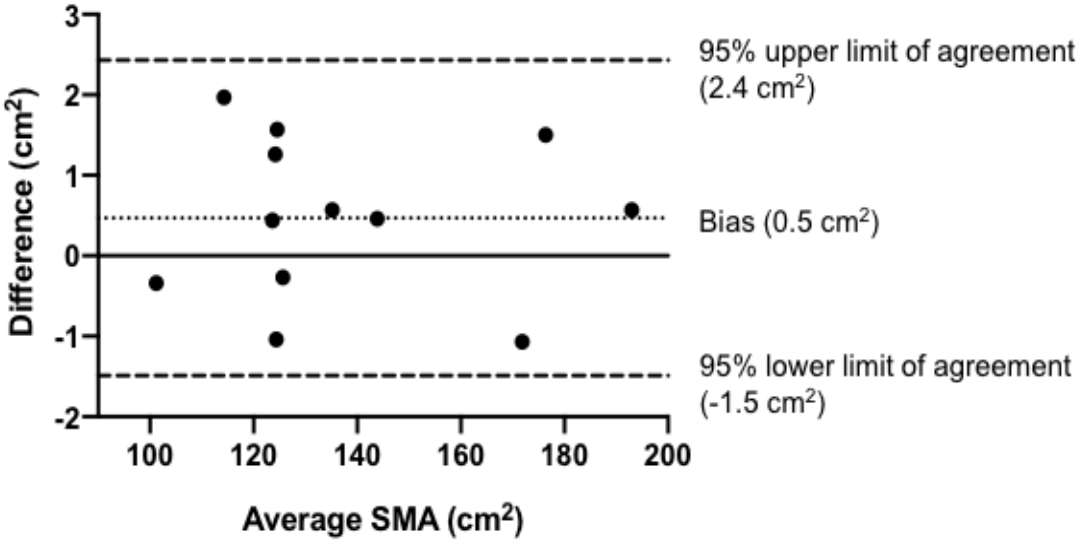

Fig S1: Bland Altman analysis of intra-observer agreement for skeletal muscle area (SMA).

Table S1: Nutritional delivery

Variable	All (n=210)		Normal SMI (n=168)	Low SMI (n=45)	*p* Value		Normal SMD (n=167)	Low SMD (n=48)	*p* value
Duration of ECMO									
Patients receiving adequate energy	156 (74.3%)		116[4] (70.3%)	39[2] (88.6%)	**.014***		117[8] (72.2%)	39 (81.3%)	.209*
Patients receiving adequate protein	123 (58.6%)		90[4] (54.5%)	32[2] (72.7%)	**.030***		91[8] (56.2%)	32 (66.7%)	.195*
% energy targets met	90.4 (79.7-97.5)		89.7[4] (68.2-93.5)	91.6[2] (82.1-96.5)	.514		90.0[8] (79.3-67.0)	91.1 (80.67-102.7)	.259
% protein targets met	83.4 (72.1-93.5)		82.6[4] (25.0)	85.2[2] (78.4-92.1)	.159		82.6[8] (69.8-92.9)	85.0 (75.4-95.7)	.241
Energy kcal/kg/day	18.0 (14.7-21.2)		17.7[4] (14.1-21.4)	18.2[2] (16.4-19.8)	.432		18.0[8] (14.7-21.1)	17.8 (14.9-21.5)	.726
Protein g/kg/day	1.1 (0.9-1.2)		1.0[4] (0.9-1.2)	1.1[2] (0.9-1.3)	.118		1.0[8] (0.9-1.2)	1.1 (0.9-1.3)	.102
Duration of ICU stay at ECMO Centre									
Patients receiving adequate energy	166 (79.0%)		126[4] (76.4%)	39[2] (88.6%)	.076*		128[7] (79.0%)	38 (79.2%)	.982*
Patients receiving adequate protein	144 (68.6%)		108[4] (65.5%)	35[2] (79.5%)	.074*		106[7] (65.4%)	38 (79.2%)	.072*
% energy targets met	91.0 (82.2-98.4)		90.8[4] (80.7-98.4)	91.3[2] (84.8-97.5)	.431		91.0 [7] (81.7-97.0)	91.0 (83.9-102.2)	.565
% protein targets met	86.0 (75.8-95.2)		85.9[4] (74.0-95.3)	88.0[2] (84.8-97.5)	.342		85.5 [7] (75.0-95.1)	90.0 (82.6-96.0)	.106
Energy kcal/kg/day	19.5 (16.0-22.7)		19.5 (15.0-22.8)	19.2 (16.5-21.9)	.849		19.5[7] (15.4-22.2)	18.7 (15.3-23.7)	.412
Protein g/kg/day	1.1 (1.0-1.3)		1.1 (1.0-1.3)	1.1 (1.1-1.2)	.399		1.1[7] (1.0-1.2)	1.2 (1.1-1.3)	.069
Post-ECMO									
Patients receiving adequate energy	136[1] (76.4%)		102[5] (73.9%)	33[3] (84.6%)	.165*		103[9] (76.9%)	33 (75.0%)	.800*
Patients receiving adequate protein	126[1] (70.8%)		95[5] (68.8%)	31[3] (79.5%)	.195*		92[9] (68.7%)	34 (77.3%)	.276*
% energy targets	93.6[1] (80.7-99.6)		93.6[5] (78.8-99.5)	94.6[3] (84.9-100.0)	.497		93.8[9] (80.7-99.2)	93.5 (79.4-100.9)	.737
% protein targets met	89.5[1] (76.7-100.0)		91.5[5] (73.8-100.0)	88.9[3] (80.8-100.7)	.774		89.0[9] (73.8-99.5)	92.9 (82.0-108.7)	.107
Energy kcal/kg/day	19.6[1] (15.4-23.5)		20.3[6] (15.1-23.8)	19.3[3] (15.5-23.3)	.816		19.6[9] (15.6-23.3)	20.3 (14.4-24.7)	.561
Protein g/kg/day	1.2[1] (1.0-1.4)		1.2[5] (1.0-1.4)	1.2[3] (1.0-1.3)	.286		1.2[9] (1.0-1.3)	1.3 (1.1-1.4)	.155

Data are presented as median (IQR) or number (%)

ECMO Extracorporeal Membrane Oxygenation*, g* gram, *ICU* Intensive Care Unit*, Kg* kilogram, *kcal* kilocalorie, *SMI* Skeletal Muscle Index

[1]N=178 32 patients did not have a post-ECMO period in the study ICU, [2]N=44, [3]N=39, [4]N=165, [5]N=138, [6]N=139, [7]N= 167, [8]N=162, [9]N=134
all other missing data are those patients where energy and / or protein targets were not set for their ICU stay.
*Chi squared test. All other P values are the result of Mann-Whitney U test.

Table S2: CT analysis of body composition at commencement of VV-ECMO

Body composition component	All (n=215)		Normal SMI (n=168)	Low SMI (n=45)	*p* value		Normal SMD (n=167)	Low SMD (n=48)	*p* value
Skeletal muscle area cm^2	138.6 (115.8-166.1)		140.9 (116.0-170.3)	131.5 (106.8-147.9)	**.013**		143.6 (118.3-169.2)	127.1 (100.1-146.0)	**.004**
Skeletal muscle index cm^2/m^2	46.6[1] (40.6-54.9)		49.1 (42.3-57.4)	40.3 (36.6-44.8)	**.000**		48.5[6] (41.7-56.4)	41.9 (38.6-48.4)	**.001**
Intermuscular adipose tissue cm^2	6.9 (4.0-12.6)		6.7 (4.0-12.1)	7.2 (4.2-16.7)	.326		5.9 (3.2-9.6)	12.8 (7.5-21.0)	**.000**
Visceral adipose tissue cm^2	117.5 (40.0-199.3)		113.0 (33.9-194.0)	145.3 (65.2-220.4)	.160		102.6 (34.2-190.4)	146.8 (71.8-230.1)	**.032**
Subcutaneous adipose tissue[5] cm^2	167.7 (92.8-259.1)		153.1[3] (95.0-256.7)	198.8[4] (74.3-294.3)	.530		168.3[7] (91.3-269.8)	148.0[8] (71.8-252.5)	.859
Skeletal muscle density HU	36.6[2] (10.4)		37.1[2] (9.6)	34.9[2] (13.0)	.069*		39.8[2] (8.9)	25.3[2] (6.3)	**.000***

Data are presented as median (IQR) unless otherwise specified. *p* values are the result of Mann-Whitney U test or *Independent samples t-test

Abbreviations: *cm* centimetre*, CT* computed tomography, *HU* Hounsfield Units *SMI* Skeletal Muscle Index, *VV-ECMO* veno-venous extracorporeal membrane oxygenation

[1]N=213, [6]N=166 patients missing as no height recorded, [2]Mean (SD), [3]N=131, [4]N=31, [5]N=163, [7]N=126, [8]N=37 Patients for subcutaneous adipose tissue missing due to area missing from the Computed Tomography Scan

There was no difference in the trajectory of skeletal muscle quantity or quality.

Table S3: Change in body composition in patients who had a second CT scan after day 3 of admission

Variable	During ICU admission (n=54)
Day of second scan	9.0 (7.0-18.0)
SMA change cm^2	-24.6 (-37.3 to -12.0)
SMA change (%)	-17.7 (-23.9 to -8.2)
SMI change cm^2	-9.0 (-12.1 to -4.0)
SMI change (%)	-17.7 (-23.9 to -8.2)
IMAT change cm^2	1.2 (-0.4 to 3.4)
IMAT change (%)	17.3 (-10.1 to 51.9)
VAT change cm^2	-8.7 (-31.0 to 1.1)
VAT change (%)	-9.3 (-16.6 to 2.1)
SAT change cm^2	-19.4[2] (-28.0 to -5.5)
SAT change (%)	-10.6[2] (-17.7 to -2.3)
SMD change HU	-4.0 (-9.6 to 3.2)
SMD change (%)	-10.6 (-23.6 to 13.4)

Data are presented as median (IQR)

Abbreviations: *cm* centimetre, *CT* computed tomography, *HU* Hounsfield Units, *IMAT* intermuscular adipose tissue, *IQR* interquartile range, SMA skeletal muscle area, *SMD* skeletal muscle density, *SMI* skeletal muscle index, *SAT* subcutaneous adipose tissue, *VAT* visceral adipose tissue

[1]n=18, [2]n=34data are missing due to subcutaneous adipose tissue compartment being cut-off on CT scan and therefore not able to be analysed.

Table S4: Table of the trajectory of change in skeletal muscle area and density according to adequacy of energy and protein delivery

Variable	Energy			Protein		
	Adequate (n=30)	**Not adequate (n=24)**	***p* value**	**Adequate (n=22)**	**Not adequate (n=32)**	***p* value**
SMA change	-17.6 (-23.9 to -8.6)%	-17.5 (-25.4 to -6.9)%	.951	-18.9 (-23.9 to -13.4)%	-14.5 (-25.4 to -6.9)%	.410
SMD change	-11.9 (-20.1 to 13.7)%	-8.0 (-29.2 to 13.8)%	.951	-6.7 (-19.7 to 15.6)%	-14.2 (-24.1 to 7.9)%	.410

Adequacy of energy and protein was defined as ≥ 80% of the estimated target.
Data are expressed as median (IQR)
Abbreviations: *IQR* interquartile range; *SMA* skeletal muscle area; *SMD* skeletal muscle density.

Table S5: Full Logistic and Linear regression for the association between skeletal muscle index, skeletal muscle density and outcome

Variable	Univariate		Model 2		Model 4	
	Unstandardised B/OR (95% CI)	*p* value	Unstandardised B / OR (95% CI)	*p* value	Unstandardised B / OR (95% CI)	*p* value
ECMO Survival						
SMI (per 10 cm^2)	1.0 (0.7 to 1.5)	.964	-	-	-	-
SMD (per 10 HU)	1.6 (1.0 to 2.5)	**.035**	1.406 (0.9 to 2.3)	0.179	-	-
IMAT (per 10 cm^2)	1.1 (0.6 to 2.0)	.666	-	-	-	-
APACHE II	0.9 (0.8 to 1.0)	**.005**	0.8 (0.8 to 1.0)	**.033**	-	-
SOFA	0.9 (0.8 to 1.0)	**.036**	0.9 (0.8 to 1.0)	.114	-	-
BMI	1.0 (1.0 to 1.1)	.835	-	-	-	-
Hospital days prior to ECMO	0.9 (0.9 to 1.0)	**.025**	0.9 (0.8 to 0.98)	**.010**	-	-
Sex (male)	1.5 (0.6 to 3.7)	.357	-	-	-	-
VAT (per 10 cm^2)	1.0 (1.0 to 1.0)	.892	-	-	-	-
SAT (per 10 cm^2)	1.0 (0.9 to 1.0)	.845	-	-	-	-
Low SMI	0.7 (0.2 to 2.1)	.506	-	-	-	-
Low SMD	0.6 (0.2 to 1.9)	.422	-	-	-	-
ICU Survival						
SMI (per 10 cm^2	1.0 (0.7 to 1.4)	.992	-	-	-	-
SMD (per 10 HU)	1.8 (1.2 to 2.8)	**.004**	1.6 (1.1 to 2.5)	**.025**	-	-
IMAT (per 10 cm^2)	1.2 (0.7 to 1.9)	.541	-	-	-	-
APACHE II	0.9 (0.8 to 0.9)	**.002**	0.9 (0.8 to 0.9)	**.025**	-	-
SOFA	0.9 (0.8 to 0.9)	**.002**	0.9 (0.8 to 1.0)	.071	-	-
BMI	1.0 (0.9 to 1.04)	.641	-	-	-	-
Hospital days prior to ECMO	1.0 (0.9 to 1.0)	.140	-	-	-	-
Sex (male)	1.9 (0.9 to 4.0)	.120	-	-	-	-
VAT (per 10 cm^2)	1.0 (0.9 to 1.0)	.530	-	-	-	-
SAT (per 10 cm^2)	1.0 (0.9 to 1.0)	.151	-	-	-	-
Low SMI	1.4 (0.6 to 3.3)	.407	-	-	-	-
Low SMD	1.3 (0.6 to 3.0)	.528	-	-	-	-
6-month survival						

SMI (per 10 cm^2	0.9 (0.7 to 1.3)	.710	-	-	-	-
SMD (per 10 HU)	1.5 (1.0 to 2.1)	**.042**	1.2 (0.8 to 1.8)	.299	-	-
IMAT (per 10 cm^2)	1.3 (0.8 to 2.1)	.301	-	-	-	-
APACHE II	0.9 (0.8 to 0.9)	**.009**	0.9 (0.8 to 1.0)	.087	-	-
SOFA	0.9 (0.8 to 0.9)	**.005**	0.9 (0.8 to 0.9)	**.019**	-	-
BMI	1.0 (0.9 to 1.0)	.587	-	-	-	-
Hospital days prior to ECMO	0.9 (0.8 to 0.9)	**.036**	0.2 (0.8 to 0.9)	**.010**	-	-
Gender (male)	1.8 (0.9 to 3.7)	.103	-	-	-	-
VAT (per 10 cm^2)	1.0 (0.9 to 1.0)	.825	-	-	-	-
SAT (per 10 cm^2)	1.0 (0.9 to 1.0)	.196	-	-	-	-
Low SMI	1.7 (0.8 to 3.6)	.190	-	-	-	-
Low SMD	0.9 (0.4 to 2.1)	.876	-	-	-	-
Duration of ECMO						
SMI (per 10 cm^2)	-2.7 (-4.6 to -0.9)	**.004**	-1.3 (-3.6 to 0.9)	.244	-	-
SMD (per 10 HU)	-0.02 (-2.0 to 1.9)	.986	-	-	-	-
IMAT (per 10 cm^2)	-1.3 (-3.9 to 1.2)	0.317	-	-	-	-
APACHE II	-0.1 (-0.6 to 0.4)	0.635	-	-	-	-
SOFA	-0.04 (-0.5 to 0.5)	0.876	-	-	-	-
BMI	-0.2 (-0.5 to 0.0)	**0.097**	-0.03 (-0.3 to 0.03)	0.851	-0.1 (-0.4 to 0.1)	.348
Hospital days prior to ECMO	1.04 (0.6 to 1.4)	**0.000**	1.0 (0.5 to 1.4)	**0.000**	0.9 (0.5 to 1.4)	**.000**
Gender	-0.3 (-4.5 to 3.9)	0.886	-	**-**	-	**-**
VAT (per 10 cm^2)	-0.1 (-0.3 to 0.1)	0.198	-	**-**	-	**-**
SAT (per 10 cm^2)	-0.1 (-0.3 to 0.1)	0.263	-	**-**	-	**-**
Low SMI	7.3 (2.3 to 12.3)	**0.005**	-	**-**	5.0 (0.2 to 9.9)	**.042**
Low SMD	-0.5 (-5.5 to 4.5)	0.842	-	**-**	-	-

Table showing the full logistic and linear regression models for associations between SMI, SMD and outcome.
Model 2: Adjusted for significant variables from univariate analysis
Model 3: As per model 2, but BMI substituted for VAT. Not shown in this table as Vat not significant in univariate analysis
Model 4: Cut-off values for low SMI and SMD as a categorical variable replace absolute values (per 10 cm^2 or HU).

Abbreviations*: cm* centimetre*, CI* Confidence Interval, *ECMO* Extracorporeal Membrane Oxygenation, *HU* Hounsfield Units, *ICU* Intensive Care Unit, *SAT* Subcutaneous adipose tissue, *SMD* Skeletal Muscle Density, *SMI* Skeletal Muscle Index, *OR* Odds ratio, *VAT* Visceral adipose tissue.

Table 1: Baseline characteristics

Variable	All (n=215)		Normal SMI (n=168)	Low SMI (n=45)	*p* value		Normal SMD (n=167)	Low SMD (n=48)	*p* value
Age	46.0 (35.0-57.0)		46.0 (38.0-57.0)	41.0 (30.0-53.5)	0.79		46.0 (35.0-57.0)	45.5 (38.0-55.8)	0.955
Sex (male)	123 (57.2%)		84 (50.0%)	34 (75.6%)	**0.002***		98 (58.7%)	21 (43.8%)	0.067*
APACHE II	18.0 (15.0-21.0)		19.0 (15.3-21.0)	18.0 (14.0-20.0)	0.112		18.0 (15.0-21.0)	19.0 (16.0-20.8)	0.443
SOFA (admission)	7.0 (4.0-11.0)		7.0 (4.0-11.0)	6.0 (4.0-11.0)	0.410		7.0 (4.0-11.0)	7.0 (4.0-11.0)	0.739
SOFA (ECMO)	7.0 (4.0-11.0)		7.0 (4.0-11.0)	7.0 (4.0-11.0)	0.548		7.0 (4.0-11.0)	8.5 (4.0-11.8)	0.311
Weight, kg	82.0 (68.0-101.0)		80.0 (65.0-99.5)	88.0 (65.0-99.5)	**0.036**		82.0 (70.0-100.0)	80.0 (63.0-105.7)	0.525
BMI, kg/m^2	27.7[a] (24.0-33.2)		27.7 (23.7-33.7)	28.4[g] (23.7-33.7)	0.758		27.7 (24.0-33.0)	27.5 (22.9-105.7)	0.808
NUTRITION STATUS[b] Normal Stage 1 Stage 2 Overweight Obese	 59 (27.7%) 8 (3.8%) 3 (1.4%) 62 (29.1%) 81 (38.0%)		 51 (30.4%) 5 (3.0%) 3 (1.8) 47 (28.0) 62 (36.9)	 8 (17.8%) 3 (6.7%) 0 15 (33.3%) 19 (42.2)	 n/a n/a n/a 0.482* 0.514*		 48 (28.9%) 1 (0.6%) 3 (1.8%) 50 (30.1%) 64 (38.6%)	 11 (23.4%) 7 (14.9%) 12 (25.5%) 17 (36.2%) 17 (36.2%)	 0.556* n/a n/a 0.541* 0.766*
NUTRIC Score	4.0[b] (33.0-6.0)		5.0 (3.0-6.0)	4.0 (3.0-6.0)	**0.013**		4.0 (2.0-6.0)	5.0 (3.0-6.0)	
High NUTRIC on admission	103[b] (48.1%)		84[e] (50.3%)	17 (37.8%)	0.136*		76 (45.8%)	25 (52.1%)	0.441*
Energy target ECMO (kcal/day)	1825.0[c] (1623.2-2050.0)		1800.0[e] (1600.0-200.0)	2000.0 (1725.0-2125.0)	**0.006**		1862.5 (1625.0-2050.0)	1800.0 (1500.0-2018.8)	0.294
Protein target ECMO (g/day)	90.0[c] (78.5-102.6)		90.0[e] (78.0-102.0)	95.0 (85.0-113.5)	0.053		90.0 (79.0-102.5)	90.0 (75.8-105.5)	0.810
Energy target non-ECMO (kcal/day)	1875.0[d] (1600.0-2101.0)		1833.8[f] (1599.7-2100.0)	2000.0 (1619.0-2200.0)	0.154		1851 (1580.6)	1920.5 (1631.0-2129.3)	0.446
Protein target non-ECMO (g/day)	88.0[d] (72.0-104.3)		87.8[f] (70.0-103.1)	90.0 (75.0-111.6)	0.211		87.8 (73.5-102.8)	90.0 (70.1-109.0)	0.594
Duration of ECMO	10.0 (7.0-15.0)		9.0 (6.3-14.0)	13.0 (8.0-22.0)	**0.007**		9.0 (7.0-15.0)	10.0 (6.0-15.0)	0.541

ECMO centre ICU stay	21.0 (14.0-32.0)		21.0 (70.0-103.1)	26.0 (16.0-41.0)	0.051		20.0 (14.0-30.0)	25.5 (16.0-35.5)	0.054
ECMO centre hospital stay	23.0 (16.0-33.0)		22.0 (15.3-31.8)	27.0 (16.0-44.5)	0.066		22.0 (15.0-31.0)	29.5 (17.3-42.8)	**0.037**
Hospital days prior to ECMO	3.0[c] (1.0-7.0)		3.0 (1.0-6.0)	7.0 (2.0-10.5)	**0.03**		3.0 (1.0-7.0)	4.0 (1.0-8.0)	0.505
Number of co-morbidities	1 (0-3)		1 (0-3)	1 (2-10.5)	0.185		1 (0-3)	1 (0-2)	0.844
Survival (ECMO)	187 (87.0%)		147 (87.5%)	41 (91.1%)	0.504*		146 (87.4%)	44 (91.7%)	0.419*
Survival (ICU)	181 (84.2%)		143 (85.1%)	36 (80.0%)	0.405*		142 (85.0%)	39 (81.3%)	0.527*
Survival (6 months)	173 (80.5%)		138 (82.1%)	33 (73.3%)	0.187*		134 (80.2%)	39 (81.3%)	0.876*

Data are expressed as median (IQR) or number (%)

APACHE Acute Physiology And Chronic Health Evaluation, *BMI* Body Mass Index, *ECMO* Extracorporeal Membrane Oxygenation, *SMI* Skeletal Muscle Index, *SOFA* Sequential Organ Failure Assessment, *NUTRIC* Nutrition Risk in the Critically Ill

[a]N=212 height missing therefore unable to calculate, [b]N=213 height missing for 2 patients, therefore unable to calculate BMI, [c]N=214 data missing for one patient, [d]N=209 6 patients did not have a non-ECMO period at our institution, [e]N=167 data unavailable for one patient, [f]N=162 5 patients did not have a non-ECMO period at our centre, [g]N=44 height missing therefore unable to calculate.
*Chi squared test. All other P values are the result of Mann-Whitney U test

Table 2: Logistic and Linear Regression for association between skeletal muscle index, skeletal muscle density and outcome

Variable	Univariate		Model 2		Model 4	
	Unstandardised B / OR (95% CI)	***p* value**	**Unstandardised B / OR (95% CI)**	***p* value**	**Unstandardised B / OR (95% CI)**	***p* value**
ECMO Survival						
SMI (per 10 cm^2)	1.0 (0.7 to 1.5)	0.964	-	-	-	-
SMD (per 10 HU)	1.6 (1.0 to 2.5)	**0.035**	1.4 (0.9 to 2.3)	0.179	-	-
Low SMI	0.7 (0.2 to 2.1)	0.506	-	-	-	-
Low SMD	0.6 (0.2 to 1.9)	0.422	-	-	-	-
ICU Survival						
SMI (per 10 cm^2	1.0 (0.7 to 1.4)	0.992	-	-	-	-
SMD (per 10 HU)	1.8 (1.2 to 2.8)	**0.004**	1.6 (1.1 to 2.5)	**0.025**	-	-
Low SMI	1.4 (0.6 to 3.3)	0.407	-	-	-	-
Low SMD	1.3 (0.6 to 3.0)	0.528	-	-	-	-
6-month survival						
SMI (per 10 cm^2	0.9 (0.7 to 1.3)	0.710	-	-	-	-
SMD (per 10 HU)	1.5 (1.0 to 2.1)	**0.042**	1.2 (0.8 to 1.8)	0.299	-	-
Low SMI	1.7 (0.8 to 3.6)	0.190	-	-	-	-
Low SMD	0.9 (0.4 to 2.1)	0.876	-	-	-	-
Duration of ECMO						
SMI (per 10 cm^2)	-2.7 (-4.6 to -0.9)	**0.004**	-1.3 (-3.6 to 0.9)	0.244	-	-
SMD (per 10 HU)	-0.02 (-2.0 to 2.0)	0.986	-	-	-	-
Low SMI	7.3 (2.3 to 12.3)	**0.005**	-	-	5.0 (0.2 to 9.9)	**0.042**
Low SMD	-0.5 (-5.5 to 4.5)	0.842	-	-	-	-

Table showing logistic and linear regression model for associations between SMI, SMD and outcome. Model 3 is removed from this table as neither VAT nor SAT were significant in univariate analysis. Full results are displayed in Table S3 of the ESM.
Model 2: Adjusted for significant variables from univariate analysis
Model 4: cut-off values for low SMI and SMD replace absolute values.

cm centimetre*, CI* Confidence Interval, *ECMO* Extracorporeal Membrane Oxygenation, *HU* Hounsfield Units, *ICU* Intensive Care Unit, *SAT* Subcutaneous adipose tissue, *SMD* Skeletal Muscle Density, *SMI* Skeletal Muscle Index, *OR* Odds ratio, *VAT* Visceral adipose tissue

Figure 1

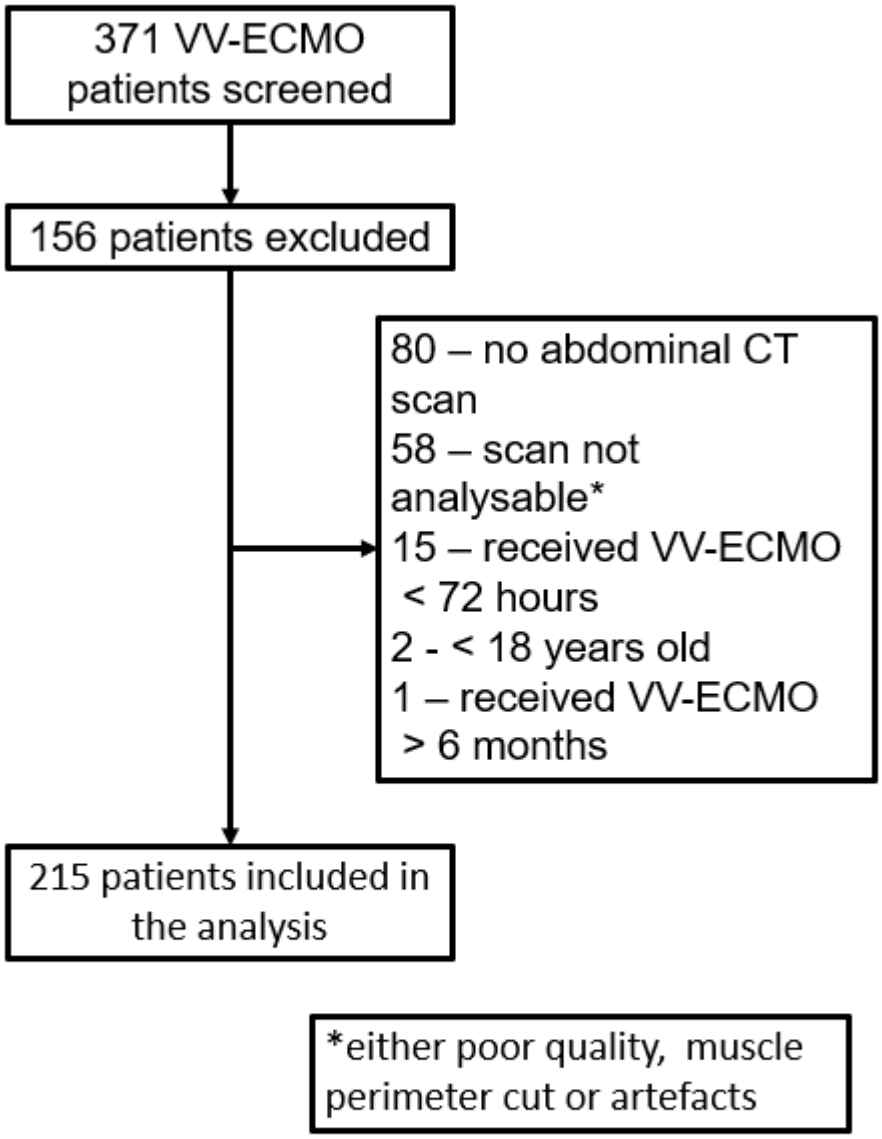

Figure 1: Eligibility flowchart for the study.