ORIGINAL ARTICLE

Comparison between Effect of Indirect Calorimetry vs Weight-based Equation (25 kcal/kg/day)-guided Nutrition on Quadriceps Muscle Thickness as Assessed by Bedside Ultrasonography in Medical Intensive Care Unit Patients: A Randomized Clinical Trial

Aravind Chandrasekaran[1], Divya Pal[2], Rahul Harne[3], Sweta J Patel[4], Jagadeesh KN[5], Anant V Pachisia[6], Pooja Tyagi[7], Keerti Brar[8], Swagat Pattajoshi[9], Parimal B Patel[10], Ronak Zatakiya[11], Deepak Govil[12]

Received on: 29 February 2024; *Accepted on:* 04 May 2024; *Published on:* 31 May 2024

Abstract

Aim and background: Sarcopenia is a substantial contributor to intensive care unit (ICU)-acquired weakness and is associated with significant short- and long-term outcomes. It can, however, be mitigated by providing appropriate nutrition. Indirect calorimetry (IC) is believed to be the gold standard in determining caloric targets in the dynamic environment of critical illness. We conducted this study to compare the effect of IC vs weight-based (25 kcal/kg/day) feeding on quadriceps muscle thickness (QMT) by ultrasound in critically ill patients.

Materials and methods: A prospective study was conducted on 60 mechanically ventilated patients randomized to two groups [weight-based equation (WBE) group or the IC group] in medical ICU after obtaining institutional ethics committee approval, and fed accordingly. The right QMT measurement using ultrasound and caloric targets were documented on day 1, 3 and 7 and analyzed statistically. The IC readings were obtained from the metabolic cart E-COVX Module™.

Results: The baseline demographics, APACHE-II, NUTRIC score, and SOFA scores on day 1, 3, and 7 were comparable between the two groups. The resting energy expenditure (REE) obtained in the IC group was significantly less than the WBE energy targets and the former were fed with significantly less calories. A significantly less percent reduction of QMT in the IC group compared with the WBE group was observed from day 1 to day 3, day 3 to day 7, and day 1 to day 7.

Conclusion: From our study, we conclude that IC-REE-based nutrition is associated with lesser reduction in QMT and lesser calories fed in critically ill mechanically ventilated patients compared from WBE. CTRI registration-CTRI/2023/01/049119.

Keywords: Caloric target, Critically ill, Indirect calorimetry, Intensive care unit–acquired weakness, Muscle wasting, Nutrition, Quadriceps muscle thickness, Sarcopenia, Ultrasound.

Indian Journal of Critical Care Medicine (2024): 10.5005/jp-journals-10071-24737

Highlights

- Mitigation of sarcopenia by appropriate nutrition as guided by indirect calorimetry (IC) vs weight-based equation (WBE) (25 kcal/kg/day) and assessed by serial bedside ultrasonographic quadriceps muscle thickness (QMT) measurement in mechanically ventilated critically ill patients was studied.
- We observed that IC-based feeding was associated with lesser caloric intake and lesser reduction in QMT compared from feeding based upon WBE.

Introduction

ASPEN, ESPEN, and other Universal societal intensive care unit (ICU) nutritional guidelines strongly recommend Indirect Calorimetry (IC) for assessment of energy requirements in patients who are critically ill with the objective of circumventing the detrimental effects of overfeeding or underfeeding.[1–3] Recent data show feeding based on energy targets obtained through WBE are often inadequate and have weak correlation with measured energy

[1]Department of Critical Care Medicine, K.K. Patel Super Specialty Hospital, Bhuj, Gujarat, India

[2–12]Institute of Critical Care and Anaesthesia, Medanta – The Medicity, Gurugram, Haryana, India

Corresponding Author: Deepak Govil, Institute of Critical Care and Anesthesia, Medanta – The Medicity, Gurugram, Haryana, India, Phone: +91 9818056688, e-mail: drdeepak_govil@yahoo.co.in

How to cite this article: Chandrasekaran A, Pal D, Harne R, Patel SJ, Jagadeesh KN, Pachisia AV, *et al*. Comparison between Effect of Indirect Calorimetry vs Weight-based Equation (25 kcal/kg/day)-guided Nutrition on Quadriceps Muscle Thickness as Assessed by Bedside Ultrasonography in Medical Intensive Care Unit Patients: A Randomized Clinical Trial. Indian J Crit Care Med 2024;28(6):587–594.

Source of support: Nil

Conflict of interest: Dr Deepak Govil is associated as Associate Editor of this journal and this manuscript was subjected to this journal's standard review procedures, with this peer review handled independently of the Associate Editor and his research group.

expenditure (EE), consequence being either over-/under-feeding and worse ICU outcomes. The ESPEN guidelines suggest "if IC is used, isocaloric nutrition rather than hypocaloric nutrition can be progressively implemented after the early phase of acute illness.[2] Hypocaloric nutrition (not exceeding 70% of EE) should be administered in the early phase of acute illness. After day 3, caloric delivery can be increased up to 80–100% of measured EE."

At present, there is no other method more accurate in measuring the dynamic milieu of EE than IC in the continuously changing metabolic requirements of critical illness. Though IC obtained values of EE promise to be an appropriate nutrition target, systematic review of available evidence as of March 2021 by Heyland et al. reveal that the use of IC-based nutrition compared with predictive equations-based nutrition may be associated with better mortality outcome and improved nutritional intake, however, duration of mechanical ventilation, incidence of infections or ventilator associated pneumonia, ICU, and hospital length of stay is similar in both groups.[4]

Muscle wasting or sarcopenia is a substantial contributor to ICU acquired weakness and has been associated with significant short- and long-term morbidity and mortality outcomes. These include increased ICU and hospital length of stay, longer time spent on mechanical ventilation, higher mortality, higher re-admission rates, long-term physical disability, worse quality of life, and increased caregiver burden.[5–8]

Various studies and meta-analysis have shown a trend toward better mortality outcome where IC was used for medical nutrition therapy (MNT) and its use is also recommended by ASPEN and ESPEN to guide nutrition whenever available.[1,2] The SPN study found an improvement in the rate of hospital-acquired infections and a reduction in the length of ventilation.[9] Petros et al. confirmed a decrease in nosocomial infections, but the EAT-ICU study did not confirm these findings.[10,11]

Puthucheary et al. conducted a prospective study on 63 critically ill patients recruited within 24 hours of admission to ICU, with acute physiology and chronic health evaluation (APACHE II) scores of 23.5 to characterize muscle wasting.[12] Serial sonographic measurements of cross-sectional area (CSA) of rectus femoris (RF) on days 1, 3, 7, and 10 were done to determine the muscle loss. A significant attrition in RF CSA was seen on day 10 and it was more in patients who had multiorgan dysfunction compared with those who had single-organ failure. Guerreiro et al. in their prospective study in 2017 among 100 patients concluded that ultrasound as a modality for thigh thickness assessment was easy to use and reproducible and that could predict re-hospitalization or death, even in patients without ambulatory ability.[13] Moreover, functional decline at 3 months post-discharge from hospital was observed in those having a contractile index of <60% as assessed using ultrasound.

Parry et al. in 2015 conducted a single-center prospective observational study to record quadriceps thickness reduction in the initial 10 days of admission to medical/surgical ICU.[14] They included 22 adult patients who were mechanically ventilated for at least 48 hours, and acquired successive quadriceps ultrasound images in the initial 10 day duration, at awakening and at ICU discharge. They also recorded the muscle strength and function at similar times. They concluded that in ICU, muscle wasting happens fast and ultrasound can be successfully used as a modality to identify ensuing damage. They also concluded that the since VI shows the maximum variation in muscle quality and has greatest correlation with voluntary measures, it may be 'the' muscle to focus upon in future studies. They recommended that measurements of RF CSA and VI in the form of thickness and echogenicity may be performed in future ultrasonographic studies.

So, "IC remains a promising investigatory tool only, or does it influence a positive ICU outcome" is the primary question driving this study. In our study, we address the question: "Can indirect calorimetry, that is believed to be gold standard in determining caloric targets in the dynamic environment of critical illness be used effectively to mitigate sarcopenia in ICU?."

We aimed to analyze if there is reduction in sarcopenia in critically ill mechanically ventilated medical ICU patients fed based on IC when compared with critically ill mechanically ventilated ICU patients fed based on weight-based caloric targets (25 kcal/kg/day).

Materials and Methods

We conducted as a prospective randomized controlled trial (RCT)–pilot study in 60 mechanically ventilated patients who were admitted to the medical ICU in our institute. Informed written consent was obtained from the attendants of the 60 patients who were enrolled (Fig. 1) in the study if they met the following criteria:

Inclusion Criteria

- Critically ill patients admitted to the medical ICU.
- Expected to stay >3 days in ICU.
- Mechanically ventilated.
- Age >18 years.

Exclusion Criteria

- No air leak (ICD, bronchopleural fistula, etc.).
- Contraindications for enteral feeding.
- Patients with thigh injury, thigh deformity, focal neurological deficits involving either of the lower limbs.
- Postoperative patients.

Withdrawal Criteria

- Intolerance to enteral feeding (early morning gastric aspiration volume > 500 mL despite appropriate prokinetic therapy).
- Severe refeeding deemed to require reduction in calorie administration despite electrolyte correction measures.

Sample Size

- The study of Parry et al. observed 24.9% reduction in thickness at day 7 in weight-based formula.[14] With this reference and assumption of difference of 24% between weight-based group and IC group in reduction of thickness, 80% power of study and 5% level of significance, the minimum required sample size was estimated to be 27 patients in each study group. Considering loss to follow-up to be around 10%, a sample size of 60 (30 patients in each group) was taken.

Block Randomization with Sealed Envelope System

We prepared 10 sealed opaque envelopes assigning A and B in five envelopes each, where A represents WBE group and B represents IC group. Once a patient/attendant agreed to participate in the study, an envelope was picked and the patient was allocated to the group according to the alphabet in the envelope. In this system, patients were randomized in a series of blocks of ten.

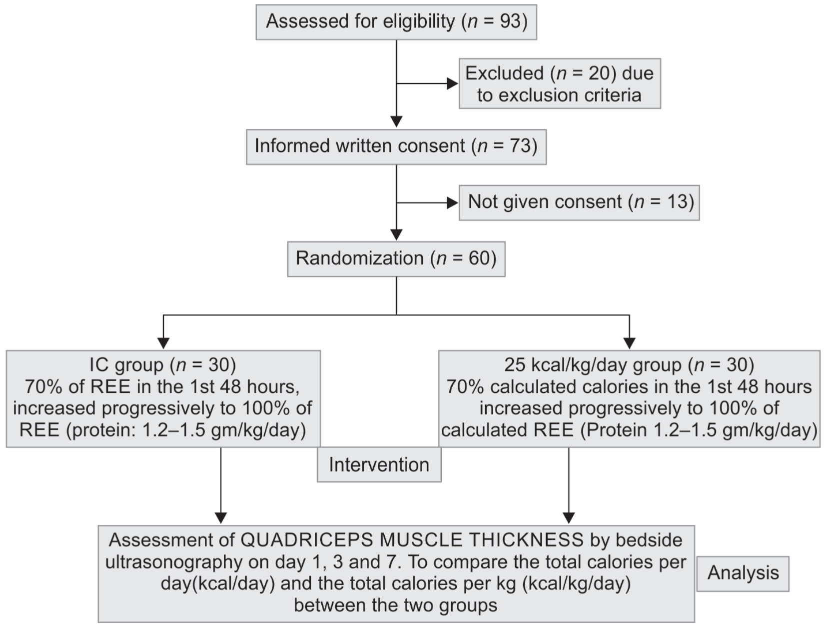

Fig. 1: Flow diagram of the study

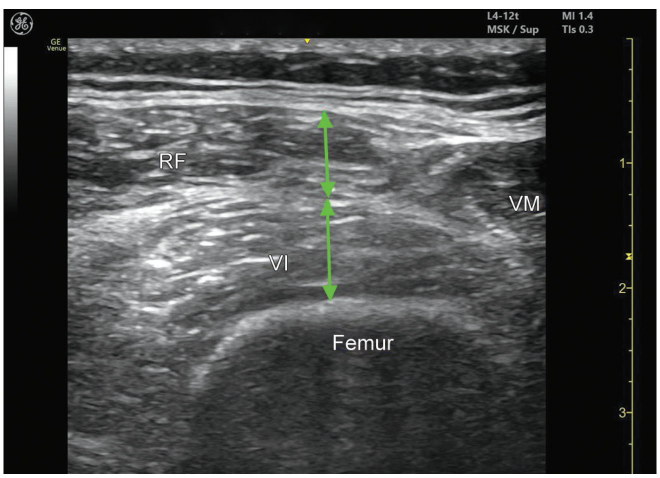

Fig. 2: Assessment of quadriceps muscle thickness (RF, rectus femoris plus; VI, vastus intermedius; VM, vastus medialis) using ultrasound

Fig. 3: Reference points for measurement of quadriceps muscle thickness. At the junction of upper 2/3rd and lower 1/3rd of the distance between anterior superior iliac spine and superior border of patella

Primary Objective

To compare the difference in reduction of QMT (by ultrasound) on day 1, 3 and 7 between the IC Group and the weight-based (25 kcal/kg/day) nutrition target group.

Secondary Objective

To compare the total calories per day (kcal/day) and the total calories per kg (kcal/kg/day) between the two groups.

Data Collection and Analysis

The recruited patient was randomly allocated to either the WBE or the IC group. The right QMT (rectus femoris plus vastus intermedius) was measured using sonography at the point of intersection between superior 2/3rd and inferior 1/3rd of the line connecting ASIS (anterior superior iliac spine) and the superior border of patella (Figs 2 and 3). The first (day 1) measurement was done on day of intubation or on the day of ICU admission if already intubated.

The patients were fed based on WBE or resting EE (REE) calorie targets obtained through IC, according to the random group that the patient was allocated to. In both the groups, the feed was initiated at 70% of the energy target in the initial 48 hours and then progressively increased to 100% of the energy targets after 48 hours.

The IC readings were obtained from the metabolic cart module (E- COVX Module™) applied on the Datex-Ohmeda GE Carescape R860 ventilator connected to the patients' endotracheal tube (ET) through a D-lite Sensor™ (Fig. 4). Once the patient was stabilized with no recent change in ventilatory parameters like FiO_2, PEEP or minute ventilation, REE readings were noted down from the ventilator and was set as the calorie target for the patient. While measuring the REE, care was taken that there was no leak around the ET tube cuff by comparing the inspiratory and the expiratory

Fig. 4: ECOV-X module with D-lite gas sampling line and sensor, attachment to the patient

tidal volumes and also viewing at the flow-volume loops and volume-time scalars. Also, it was ensured that air leaks in the form of broncho-pleural fistulas or ICD air leaks were not present since they would result in gross variation in the measurement of REE.

The patients were fed through the enteral route if there were no contraindications for enteral route.

The sonographic QMT measurements were repeated at the same point on the anterior thigh on days 3 and 7 in both the groups and compared between the two groups.

Stastistical Analysis

Number and percentage (%) were used for presentation of the categorical variables. For the quantitative data, the means ± SD and median with 25th and 75th percentiles (interquartile range) were recorded. We used Kolmogorov–Smirnov test to check the data normality. Nonparametric tests were used where the data were not normal. For the results, we applied following statistical tests:

1. Quantitative variables with non-normal distribution were compared and analyzed using Mann–Whitney test, while quantitative variables with normal distribution were analyzed using independent *t*-test.
2. The qualitative variables were compared and analyzed using Chi-square test. We used Fisher's exact test for an expected value of <5 for any cell. Microsoft Excel spreadsheet was used for data entry and Statistical Package for Social Sciences (SPSS) software, IBM manufacturer, Chicago, USA, version 25.0 was used for the ultimate analysis.

The *p*-value of less than 0.05 was considered statistically significant.

Results

The baseline demographic parameters namely age, sex, weight, and BMI were comparable between the two groups with no statistical significance; mean age being 47.77 ± 14.8 years, with $n = 31$ (51.67%) males and had mean BMI of 27.26 ± 4.69 kg/m^2 (Table 1).

The NUTRIC score was comparable between the two groups with no statistical significance with median score (25th–75th percentile) being 5 (5–5) in both groups (Table 1).

The Acute Physiology and Chronic Health Evaluation (APACHE II) scores are comparable between the two groups with no statistical significance with mean ± SD score being 21.17 ± 5.76 (Table 1).

The SOFA scores on the days of USG measurement of QMT were comparable between the two groups with no statistical significance (Table 2).

There was a statistically significant difference in the Energy targets (kcal/day) between the two groups on all the days of measurements (Table 2), requirements being significantly less in IC group as compared from WBE group.

Also, a statistically significant difference in the per kg energy targets between the two groups on all the 3 days of measurements was observed (Table 2, Fig. 5).

There was a statistically significant difference in QMT between the two groups on the 1st day of measurement and not on the 3rd or the 7th days (Table 2). However, the percent reduction in QMT from day 1 to day 3, day 3 to day 7, and day 1 to day 7 was significantly lower in the IC group (Table 3, Figs 6 to 8).

Discussion

In 1892, Sir William Osler described that patients with severe infections suffer a "rapid loss of flesh."[15] In the present day, it is a known fact that critical illness results in muscle wasting and that longer ICU stay patients may experience more of it. Sarcopenia in ICU leads to ICU-acquired weakness (ICUAW) and is proven to be associated with worse short- and long-term outcomes. Not less than 25% of mechanically ventilated patients requiring more than a week of intubation suffer ICUAW as do around 100% of those patients who are diagnosed with systemic inflammatory

Table 1: Comparison of age, BMI, gender, APACHE II, NUTRIC score between indirect calorimetry and weight-based equation groups

	Indirect calorimetry (n = 30)	*Weight-based equation (n = 30)*	*Total*	*p-value*
Age (years)				
Mean ± SD	50.47 ± 14.41	45.07 ± 14.93	47.77 ± 14.8	0.159‡
Body mass index (kg/m²)				
Mean ± SD	26.74 ± 4.85	27.78 ± 4.55	27.26 ± 4.69	0.392‡
Gender				
Male/Female (%)	(46.67%)/(53.33%)	(56.67%)/(43.33%)	(51.67%)/(48.33%)	0.438†
APACHE II score on admission				
Mean ± SD	19.97 ± 5.95	22.37 ± 5.4	21.17 ± 5.76	0.107‡
NUTRIC score on admission				
Median (25th–75th percentile)	5 (5–5)	5 (5–5)	5 (5–5)	0.748§

‡Independent *t* test; §Mann–Whitney test; †Chi-square test

Table 2: Comparison of SOFA score, quadriceps muscle thickness, energy target kcal/kg, energy target kcal/day on day 1, 3, 7 between indirect calorimetry and weight-based equation groups

	Indirect calorimetry (n = 30)	*Weight-based equation (n = 30)*	*Total*	*p-value*
SOFA score				
Median (25th–75th percentile)				
On day 1	11 (9–13)	12 (10–15)	12 (9–15)	0.196§
On day 3	9.5 (8–12)	11 (9–13.75)	10 (9–13)	0.122§
On day 7	8 (8–10.75)	9.5 (8–12)	9 (8–12)	0.15§
Energy target (kcal/kg)				
Median (25th–75th percentile)				
On day 1	15.09 (13.762–18.638)	17.35 (17.078–17.62)	17.11 (14.632–17.925)	0.027§
On day 3	17.63 (16.04–19.432)	25 (25–25.298)	23.66 (17.268–25)	<0.0001§
On day 7	18.8 (17.51–20.815)	25.82 (25–26.68)	24.2 (18.532–26.19)	<0.0001§
Quadriceps muscle thickness (cm)				
Mean ± SD				
On day 1	1.63 ± 0.31	1.81 ± 0.38	1.72 ± 0.35	0.044‡
On day 3	1.53 ± 0.3	1.56 ± 0.4	1.55 ± 0.35	0.749‡
On day 7	1.46 ± 0.29	1.38 ± 0.41	1.42 ± 0.35	0.374‡
Energy target (kcal/day)				
Mean ± SD				
On day 1	1172.47 ± 329.39	1340.48 ± 229.75	1256.47 ± 294.03	0.026‡
On day 3	1318.17 ± 297.61	1913.33 ± 284.87	1615.75 ± 416.51	<0.0001‡
On day 7	1427.33 ± 311.78	1980.83 ± 301.98	1704.08 ± 412.91	<0.0001‡

‡Independent *t* test; §Mann–Whitney test

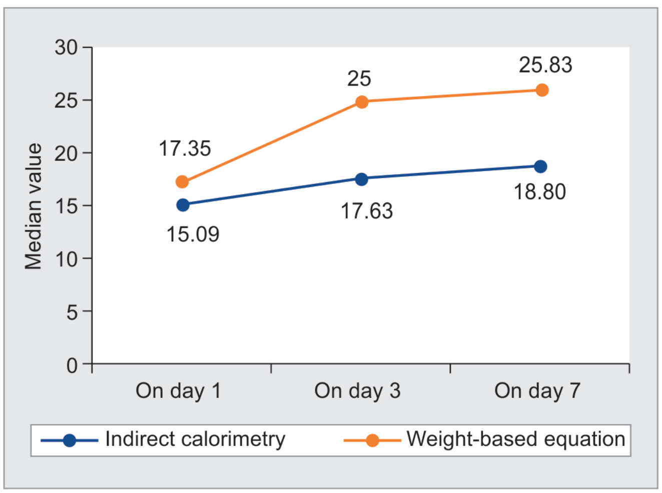

Fig. 5: Comparison of energy target (kcal/kg) between indirect calorimetry and weight-based equation

Table 3: Comparison of percentage reduction in quadriceps muscle thickness from day 1 to day 3, day 3 to 7, and day 1 to 7 between indirect calorimetry and weight-based equation

	Percentage reduction in quadriceps muscle thickness Median (25th–75th percentile)			
	Indirect calorimetry (n = 30)	*Weight-based equation (n = 30)*	*Total*	*p-value*
From day 1 to day 3	5.73 (3.129–7.261)	14.47 (8.374–19.273)	7.41 (4.919–14.674)	<0.0001§
From day 3 to day 7	4.02 (2.884–5.888)	12.69 (5.82–16.197)	5.77 (3.383–12.897)	<0.0001§
From day 1 to day 7	9.67 (7.74–12.321)	29.21 (19.014–31.39)	12.38 (9.05–29.116)	<0.0001§

§Mann–Whitney test

response syndrome (SIRS) and severe sepsis.[16] Appropriate nutrition strategies combined with exercise are considered to be important in preventing and mitigating sarcopenia.[8] Multiple studies have been performed till date comparing nutritional interventions and their effect on sarcopenia or ICU-AW. Our study is one of such kind where we analyzed if indirect calorimetry-based feeding could have effects on preventing the progression or mitigating sarcopenia in the critically ill mechanically ventilated ICU patients.

We followed the nutritional societies, i.e., ESPEN and ASPEN recommendations in determining the energy targets in both the groups (IC and weight based). In order to account for the endogenous energy production in the early phase of critical illness that practically and reliably cannot be measured by any method, the ASPEN and ESPEN strongly urge us to initiate feeds targeting not more than 70% of the energy target in the first 48 hours and then, gradually increase the target to 100% after 48–72 hours.[1,2] Though our energy targets were decided differently between the groups, the patients were fed with the same quantity of protein targeting to achieve a 1.2–1.5 gm/kg/day protein.

We documented the baseline demographics in both groups and found them to be comparable. We ensured that the confounders, that is, the preexisting nutritional status of the patients exhibited by the NUTRIC score, APACHE II, and the number and extent of

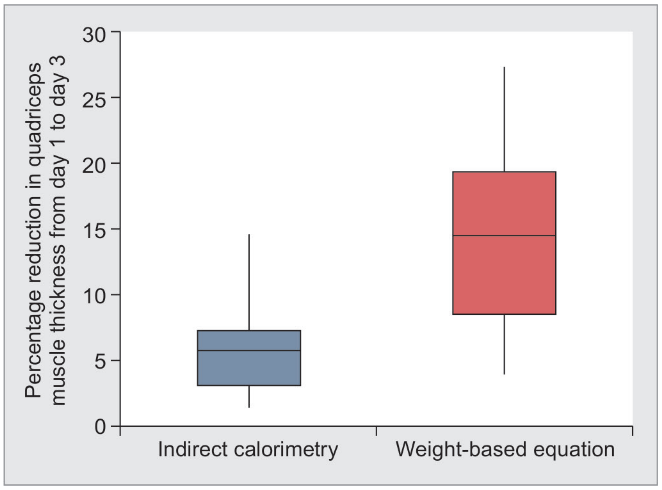

Fig. 6: Comparison of percentage reduction in quadriceps muscle thickness from day 1 to day 3 between indirect calorimetry and weight-based equation

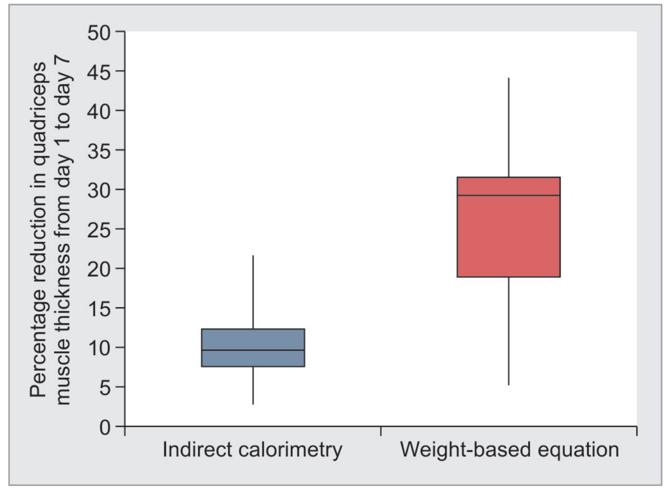

Fig. 8: Comparison of percentage reduction in quadriceps muscle thickness from day 1 to day 7 between indirect calorimetry and weight-based equation

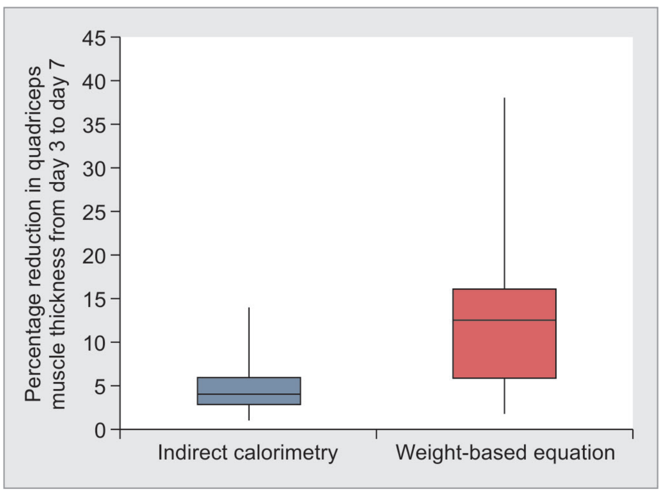

Fig. 7: Comparison of percentage reduction in quadriceps muscle thickness from day 3 to day 7 between indirect calorimetry and weight-based equation

organ failures exhibited by the SOFA score, that can influence the outcome were documented and analyzed between the two groups; and were found to be comparable.

We used ultrasound to measure QMT in our patients, as was recommended by Guerreiro et al., for assessment of anterior thigh.[13] They also concluded that QMT could predict re-hospitalization or death, even in patients without ambulatory ability. Pardo et al. concluded that nutrition-based interventions and consequent muscle wasting could be well evaluated using ultrasonographic QMT assessment in critically ill patients.[17] Hadda et al. also concluded that ultrasound has excellent inter- and intra-class reliability when used for QMT measurement.[18]

Parry et al. studied the QMT wasting in the first 10 days of ICU admission using ultrasound in 22 mechanically ventilated patients and concluded USG to be a useful modality for the same and that VI may be an important muscle to be assessed.[14] The mean age of the subjects involved in their study was 56 ± 18 (mean ± SD) representing a critically ill cohort with a mean APACHE II score of 23 which is more or less similar to the baseline characteristics in our study. They observed that VI thickness, RF thickness, and CSA were all reduced by 30% within 10 days of admission. There was an increase in muscle echogenicity score by +12.7% and +25.5% for the RF and VI muscles, in that order (indicating worsening of muscle quality). They reported 24.9% reduction in the RF thickness by day 7. In our study, we found an overall median 12.38% (IQR 9.05–29.116) reduction in QMT by day 7 which is different from what Parry et al. found. WBE group patients had a 29.21% reduction in QMT by day 7 as compared with 9.67% reduction in IC group in our study.[14] The results of WBE group in our study matches with that of results from Parry et al.[14] The baseline mean (+SD) RF and VI thickness were 2.44 ± 0.76 and 1.91 ± 0.73 cm, respectively, in their study while in our study baseline QMT was significantly less, 1.72 (±0.35) cm. This may be because of the body habitus variation between the study populations.

Puthucheary et al. determined muscle loss using serial ultrasound measurements of RF CSA on days 1, 3, 7, and 10 and concluded that in the first week of critical illness, muscle wasting happened fast and the severity was more in those patients who were having multi-organ failure.[12] A significant reduction in RF CSA was observed on day 10 [–17.7% (95% CI, –25.9–8.1%); $p < 0.001$]. The reduction in RF CSA by day 7 in patients with single organ failure was lesser (–3 0.0%; 95% CI, –5.3–2.1%) compared with those with multiorgan failure by day 7 (–15.7%; 95% CI, –27.7–11.4%) with a p-value < 0.001 and similar were the observations by day 3 even. To account for the effect of organ failures on muscle loss, we documented the SOFA scores on day 1, 3, and 7, whenever the ultrasound measurements were taken and we did not find a significant difference in the two groups. So, in our study, severity of organ failures did not contribute to the difference in loss of muscle mass between the two groups.

Katari et al. also found a significant decrease in RF and VI muscle mass in their study.[19]

The energy target in the IC group was significantly less than the WBE group in our study on all 3 measurement days. Sabatino et al. in their study also found that 25 kcal/kg/day equation overestimated EE in 67% of the estimates.[20] Tignanelli et al. in their study compared REE from IC and various other predictive equations and the 20, 25, and 30 kcal/kg/day using actual body weight, adjusted body weight, and ideal body weight.[21] They found that 25 kcal/kg/day actual body weight overestimated the EE and that 20 kcal/kg/day actual body weight underestimated it. In our study, we utilized the actual body weight in the WBE group and found overestimated EE values as compared with the IC group as in the above studies.

Our findings, i.e., a statistically significant difference in the energy targets as well as the percentage reduction in QMT between the two groups, from day 1 to 3, 3 to 7, and 1–7 might be suggestive that overfeeding with a calorie excess might have caused greater degree of muscle loss in the WBE group. In a study conducted by Arabi et al. comparing permissive underfeeding (60–70% of the calculated EE) with standard of care target feeding among 240 ICU patients, they found a statistically significant reduction in hospital and 180 day mortality among patients who were permissively underfed.[22] They highlighted that this finding could have been because of a decreased metabolic rate and a lesser oxidative stress in the permissively underfed group.[22] Other factors like reduction in mitochondrial free radical generation, upregulation of plasma membrane redox system, and improvement in insulin sensitivity could have contributed to the reduction in mortality in the permissively underfed group.[23–25] Oxidative stress and impaired glycemic control with insulin resistance are important mechanisms in the pathogenesis of sarcopenia or muscle wasting in ICU too.[26] Similar mechanisms could explain the lesser muscle loss in the IC group in our study.

Understanding of the above concepts led us to the questions when and how much to feed. In the early part of acute critical illness, IC can be a safe target to aim for in order to circumvent the detrimental effects of overfeeding. Starvation leads to muscle wasting.[27,28] To choose a calorie target between the extremes of starvation and overfeeding, IC is the technology that is closest to accurate.

Our study had certain limitations. We did not take into account the post-randomization factors such as corticosteroid use and muscle relaxant use in the two groups which could have contributed to the difference in reduction of QMT. Also, we compared the energy targets in the two groups and ensured these targets were being met with the help of Dietetics Department in our hospital. Exactly, how many kcals were delivered to the patients were not documented by our study group, but the Dietetics Department of our hospital. In our study , a statistically significant difference in the QMT measured on day 1 with higher QMT was documented in the WBE group (Table 9) . The study done by Reid et al. substantiated a direct relationship between the muscle thickness on ICU admission and muscle wasting and said that patients with thicker muscles at the time of ICU admission suffered a more significant decrease in thickness.[29] This fact might have contributed to the higher percentage of muscle loss found in the WBE group.

Conclusion

In our study, we found a statistically significant difference between the reduction in QMT assessed by bedside ultrasonography. The IC group had been fed with lesser calories according to the IC REE target and also exhibited a significantly lower percentage reduction in QMT. Hence, we conclude that there is a reduction in sarcopenia in critically ill, mechanically ventilated medical ICU patients fed based on IC when compared with critically ill mechanically ventilated ICU patients fed based on WBE caloric targets(25 kcal/kg/day).

Ethical Approval

The study was started after approval from the Institute Ethics Committee, Medanta – The Medicity, Gurugram, Haryana (Ref. no.:1333/2021(DNB), CTRI registration- CTRI/2023/01/049119) and was carried out over a duration of 10 months.

Orcid

Aravind Chandrasekaran https://orcid.org/0009-0005-6075-1580
Divya Pal https://orcid.org/0000-0002-1607-3816
Rahul Harne https://orcid.org/0000-0002-0178-2628
Sweta J Patel https://orcid.org/0000-0003-2780-7691
Jagadeesh KN https://orcid.org/0000-0002-8396-9954
Anant V Pachisia https://orcid.org/0000-0003-1292-1141
Pooja Tyagi https://orcid.org/0009-0005-1247-4443
Keerti Brar https://orcid.org/0009-0005-5346-2457
Swagat Pattajoshi https://orcid.org/0009-0003-1644-2735
Parimal B Patel https://orcid.org/0000-0001-8410-0751
Ronak Zatakiya https://orcid.org/0009-0002-6938-3604
Deepak Govil https://orcid.org/0000-0002-4624-1614

References

1. Compher C, Bingham AL, McCallM, Patel J, Rice TW, Braunschweig C, et al. Guidelines for the provision of nutrition support therapy in the adult critically ill patient: The American Society for Parenteral and Enteral Nutrition. JPEN J Parenter Enteral Nutr 2022;46(1):12–41. DOI: 10.1002/jpen.2267.
2. Singer P, Blaser AR, Berger MM, Alhazzani W, Calder PC, Casaer MP, et al. ESPEN guideline on clinical nutrition in the intensive care unit. Clin Nutr 2019;38(1):48–79. DOI: 10.1016/j.clnu.2018.08.037.
3. Arabi YM, Aldawood AS, Haddad SH, Al-Dorzi HM, Tamim HM, Jones G, et al. PermiT Trial Group. permissive underfeeding or standard enteral feeding in critically ill adults. N Engl J Med 2015;372(25):2398–2408. DOI: 10.1056/NEJMoa1502826.
4. Heyland DK, Lee Z-Y, Lew CCH, Ortiz LA, Patel J, Stoppe C. Nutritional prescription: Use of indirect calorimetry vs. predictive equations. Critical Care Nutrition: Systematic Reviews 2021. www.criticalcarenutrition.com.
5. Moisey LL, Mourtzakis M, Cotton BA, Premji T, Heyland DK, Wade CE, et al. Skeletal muscle predicts ventilator-free days, ICU-free days, and mortality in elderly ICU patients. Crit Care 2013;17(5):R206. DOI: 10.1186/cc12901.
6. Weijs PJ, Looijaard WG, Dekker IM, Stapel SN, Girbes AR, Oudemans-van Straaten HM, et al. Low skeletal muscle area is a risk factor for mortality in mechanically ventilated critically ill patients. Crit Care 2014;18(2):R12. DOI: 10.1186/cc13189.
7. Gariballa S, Alessa A. Sarcopenia: Prevalence and prognostic significance in hospitalized patients. Clin Nutr 2013;32(5):772–776. DOI: 10.1016/j.clnu.2013.01.010.
8. Heyland DK, Stapleton RD, Mourtzakis M, Hough CL, Morris P, Deutz NE, et al. Combining nutrition and exercise to optimize survival and recovery from critical illness: Conceptual and methodological issues. Clin Nutr 2016;35(5):1196–1206. DOI: 10.1016/j.clnu.2015.07.003.
9. Heidegger CP, Berger MM, Graf S, Zingg W, Darmon P, Costanza MC, et al. Optimisation of energy provision with supplemental parenteral nutrition in critically ill patients: A randomised controlled clinical trial. Lancet 2013;381(9864):385–393. DOI: 10.1016/S0140-6736(12)61351-8.
10. Petros S, Horbach M, Seidel F, Weidhase L. Hypocaloric vs normocaloric nutrition in critically ill patients: A prospective randomized pilot trial. J Parenter Enter Nutr 2016;40(2):242–249. DOI: 10.1177/0148607114528980.
11. Allingstrup MJ, Kondrup J, Wijs J, Claudius C, Pedersen UG, Hein-Rasmussen R, et al. Early goal-directed nutrition vs standard of care in adult intensive care patients: The single centre, randomised, outcome

assessor-blinded EATICU trial. Intensive Care Med 2017;43(11): 1637–1647. DOI: 10.1007/s00134-017-4880-3.
12. Puthucheary ZA, Rawal J, McPhail M, Connolly B, Ratnayake G, Chan P, et al. Acute skeletal muscle wasting in critical illness. JAMA 2013;310(15):1591–1600. DOI: 10.1001/jama.2013.278481.
13. Guerreiro AC, Tonelli AC, Orzechowski R, Dalla Corte RR, Moriguchi EH, de Mello RB. Bedside ultrasound of quadriceps to predict rehospitalization and functional decline in hospitalized elders. Front Med (Lausanne) 2017;4:122. DOI: 10.3389/fmed.2017.00122.
14. Parry SM, El-Ansary D, Cartwright MS, Sarwal A, Berney S, Koopman R, 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–e14. DOI: 10.1016/j.jcrc.2015.05.024.
15. Osler SW. The principles and practice of medicine: Designed for the use of practitioners and students of medicine. 1st ed. Edinburgh: Young J. Putland; 1892.
16. De Jonghe B, Sharshar T, Lefaucheur J, Authier FJ, Durand-Zaleski I, Boussarsar M, et al. Paresis acquired in the intensive care unit: A prospective multicenter study. JAMA 2002;288(22):2859–2867. DOI: 10.1001/jama.288.22.2859.
17. Pardo E, El Behi H, Boizeau P, Verdonk F, Alberti C, Lescot T. Reliability of ultrasound measurements of quadriceps muscle thickness in critically ill patients. BMC Anesthesiol 2018;18(1):205. DOI: 10.1186/s12871-018-0647-9.
18. Hadda V, Khilnani GC, Kumar R, Dhunguna A, Mittal S, Khan MA, et al. Intra- and inter-observer reliability of quadriceps muscle thickness measured with bedside ultrasonography by critical care physicians. Indian J Crit Care Med 2017;21(7):448–452. DOI: 10.4103/ijccm.IJCCM_426_16.
19. Katari Y, Srinivasan R, Arvind P, Hiremathada S. Point-of-care ultrasound to evaluate thickness of rectus femoris, vastus intermedius muscle, and fat as an indicator of muscle and fat wasting in critically ill patients in a multidisciplinary intensive care unit. Indian J Crit Care Med 2018;22(11):781–788. DOI: 10.4103/ijccm.IJCCM_394_18.
20. Sabatino A, Theilla M, Hellerman M, Singer P, Maggiore U, Barbagallo M, et al. Energy and protein in critically ill patients with AKI: A prospective, multicenter observational study using indirect calorimetry and protein catabolic rate. Nutrients 2017;9(8):802. DOI: 10.3390/nu9080802.
21. Tignanelli CJ, Andrews AG, Sieloff KM, Pleva MR, Reichert HA, Wooley JA, et al. Are predictive energy expenditure equations in ventilated surgery patients accurate? J Intensive Care Med 2019;34(5):426–431. DOI: 10.1177/0885066617702077.
22. Arabi YM, Tamim HM, Dhar GS, Al-Dawood A, Al-Sultan M, Sakkijha MH, et al. Permissive underfeeding and intensive insulin therapy in critically ill patients: A randomized controlled trial. Am J Clin Nutr 2011;93(3):569–577. DOI: 10.3945/ajcn.110.005074.
23. Dandona P, Mohanty P, Ghanim H, Aljada A, Browne R, Hamouda W, et al. The suppressive effect of dietary restriction and weight loss in the obese on the generation of reactive oxygen species by leukocytes, lipid peroxidation, and protein carbonylation. J Clin Endocrinol Metab 2001;86(1):355–362. DOI: 10.1210/jcem.86.1.7150.
24. Gredilla R, Sanz A, Lopez-Torres M, Barja G. Caloric restriction decreases mitochondrial free radical generation at complex I and lowers oxidative damage to mitochondrial DNA in the rat heart. FASEB J 2001;15(9):1589–1591. DOI: 10.1096/fj.00-0764fje.
25. Hyun DH, Emerson SS, Jo DG, Mattson MP, de Cabo R. Calorie restriction up-regulates the plasma membrane redox system in brain cells and suppresses oxidative stress during aging. Proc Natl Acad Sci USA 2006;103(52):19908–19912. DOI: 10.1073/pnas.0608008103.
26. Bloch S, Polkey MI, Griffiths M, Kemp P. Molecular mechanisms of intensive care unit-acquired weakness. Eur Respir J 2012;39(4): 1000–1011. DOI: 10.1183/09031936.00090011.
27. Cahill GF. Starvation in man. N Engl J Med 1970;282(12):668–675. DOI: 10.1056/NEJM197003192821209.
28. Dulloo AG, Jacquet J. The control of partitioning between protein and fat during human starvation: Its internal determinants and biological significance. Br J Nutr 1999;82(5):339–356. DOI: 10.1017/s0007114599001580.
29. Reid CL, Campbell IT, Little RA. Muscle wasting and energy balance in critical illness. Clin Nutr 2004;23(2):273–280. DOI: 10.1016/S0261-5614(03)00129-8.