
Correlation between Sonographic Muscle Measurements of Vastus Intermedius and Rectus Femoris with Nitrogen Balance in Nutritional Assessment of Critically Ill Overweight and Obese Patients

Ma. Natalia Gómez-González¹, Oscar Olvera-Reyes², Pedro Luis González-Carrillo³

¹Master's degree in clinical research, Critical Care Medicine and Anesthesiologist Physician. Instituto Mexicano del Seguro Social, Unidad Médica de Alta Especialidad, Hospital de Especialidades No. 1, Centro Médico Nacional del Bajío, León Gto. México. Intensive Care Unit.

²Internist Medicine Physician. Instituto Mexicano del Seguro Social, Hospital General de Zona No. 3. Ciudad Mante, Tamaulipas. México.

³Critical Care Medicine and Internist Medicine Physician. Instituto Mexicano del Seguro Social, Unidad Médica de Alta Especialidad, Hospital de Especialidades No. 1, Centro Médico Nacional del Bajío, León Gto. México. Intensive Care Unit.

ABSTRACT

Introduction. Assessing nutritional status has become an essential practice in the critically ill patient, the tools available to the clinician such as anthropometric measurements are inaccurate in obese patients, so it has been necessary to look for other available options such as muscle ultrasound, which has become a novel way to the evaluation of nutritional status and muscle structure of critically ill patients regardless of their body mass index (BMI). Recent studies demonstrate a positive correlation between sonography and total nitrogen balance (TNB) for measuring nutritional status, both of which are considered to be able to assess the nutritional status of overweight and obese patients.

Objective. To correlate sonographic muscle measurements of the vastus intermedius (VI) and rectus femoris (RF) with the TNB in the nutritional assessment of critically ill overweight and obese patients.

Material and methods. A descriptive, prospective, analytical study in which 30 patients were included. Sonographic measurement of RF and VI muscle thickness was performed simultaneously with TNB on day zero (admission) and five (control). The population was divided into groups according to BMI (overweight, class I obesity, class II obesity, class III obesity). Sonographic measurements were correlated with the TNB measured in the patients.

Results. In the initial sonographic measurements, a moderate correlation was found with the TNB at admission. In the group comparison at five days, a strong correlation was demonstrated in the AP diameter of the VI muscle ($r=-0.609$, $p=0.001$.) In the initial and control cross-sectional area in cm^2 (CSA), a positive correlation was observed ($r=0.213$ and $r=0.258$, respectively).

Conclusion. There is an inverse correlation between sonographic measurements of RF and VI muscles with TNB in critically ill overweight and obese patients. A positive correlation between CSA of both muscles with the biochemical parameter is reported.

KEYWORDS: muscle sonography, nitrogen balance, obesity, muscle wasting.

ARTICLE DETAILS

Published On:
26 September 2022

Available on:
<https://ijmscr.org/>

I. INTRODUCTION

Critical illness could be defined as any acute medical condition requiring vital organ support, whether caused by sepsis, trauma or major surgery, among others and has been related to a state of hypercatabolism in response to such stress (1). This

hypercatabolic state generated during critical illness increases protein catabolism, extending to peripheral tissues (muscles, skin) causing accelerated protein degradation, this in conjunction with attenuated protein synthesis increases amino acid oxidation and nitrogen losses resulting in a negative

Correlation between Sonographic Muscle Measurements of Vastus Intermedius and Rectus Femoris with Nitrogen Balance in Nutritional Assessment of Critically Ill Overweight and Obese Patients

nitrogen balance and changes in body composition, predisposing to further loss of lean muscle mass (2). It has been reported that up to 80% of patients admitted to the ICU suffer muscle wasting and/or muscle weakness, which is driven by a set of factors, which may occur in isolation or together in the critically ill patient, including prolonged bed rest (immobility), reduced caloric and protein intake, a chronic proinflammatory state and anabolic and insulin resistance (3,4). This entity is associated with an increased susceptibility to infections, greater cognitive impairment and slow recovery, resulting in prolonged hospitalization and therefore increased mortality, depending on other factors such as the duration and intensity of the disease (5).

Nowadays the prevalence of obesity has tripled, currently reaching 13-40% of people with a BMI greater than 30 kg/m² worldwide (6), therefore increasing the admission of obese patients to intensive care units with a current prevalence of 20-25%, this has forced the development of new therapeutic and diagnostic strategies for the management of the critically ill patient with obesity (7). It is important to have adequate monitoring and constant evaluation of nutritional status during critical illness, since this is essential to control adequate caloric and protein intake, prevent muscle wasting and syndromes associated with nutrition such as overfeeding and underfeeding. (8) We usually use BMI [weight (kg) / height² (m)] or waist circumference and waist ratio measurement as tools to assess fat distribution and contribute to risk stratification, however, these two tools are inaccurate as a measure to define obesity, as they do not distinguish between fat and lean body mass therefore, they are a poor marker of excess body fat in patients with increased or decreased muscle mass, furthermore, they underestimate nutritional status; The poor estimation of body fat is a factor that has influenced the prognosis of obese patients, so new methods have been implemented for the estimation of body fat, mainly imaging studies, of which muscle ultrasound has been a milestone in the nutritional and muscular evaluation of patients with critical illness (9,10). Ultrasound provides quantitative and qualitative details about muscle disease and its structure, can identify those patients at increased risk of prolonged complications resulting from excess muscle catabolism, and allows rapid detection without exposing or mobilizing the patient, It has a sensitivity of up to 81% and a specificity of 96% for the detection of any alteration of the muscle tissue, although we must not forget that it is an operator-dependent tool, in spite of this, a low error rate has been seen in its use for the diagnosis and follow-up of muscle evaluation, being an effective nutritional marker (11,12). Muscle tissue is easy to distinguish in ultrasound, preferably using a transducer with frequencies ranging from 2 MHz to approximately 20 MHz. The most important factors contributing to muscle detection are the frequency of transducer selection and the field of view. The measurement can be performed in upper and lower extremity, the measures taken into account are the cross-sectional area (CSA), the penetration angle and echogenicity (13). Given the constant increase in the Mexican population with a BMI over 30

kg/m², new tools for nutritional evaluation have had to be implemented, and in view of the fact that conventional measures to evaluate it have their limitations in this population, it was decided to use muscle ultrasound, which has previously validated that sonographic measurements are useful in the nutritional evaluation of patients with a normal BMI. Recently, a positive relationship was found between conventional biochemical parameters and muscle sonography as part of nutritional monitoring in critically ill patients, especially and with greater relation to the nitrogen balance, so these tools will be used to assess the nutritional status in obese patients with critical illness (14).

II. MATERIAL AND METHODS

This is a prospective, longitudinal, descriptive, analytical study. Patients with critical illness admitted to the ICU, over 18 years of age, with any diagnosis were included. Patients categorized by BMI as overweight (25-29.9 kg/m²), class I obesity (30 to 34.9 kg/m²), class II obesity (35-39.9 kg/m²) and class III obesity (>40 kg/m²), who started feeding by any route within the first 24 to 48 hours of admission to the ICU and with a minimum protein intake of 0.8 g/kg/day. Patients with BMI less than 24.9 kg/m², patients with atrophy due to prostration (end-stage oncologic pathology, neuromuscular diseases, neurodegenerative diseases) of 2 months or more prior to hospitalization, patients who for any reason did not initiate diet early or did not reach the minimum protein intake of 0.8 g/kg/day, patients in whom the muscle area cannot be measured: either due to pathology of direct muscle involvement, deformity due to trauma or amputation of pelvic limbs, and pregnant patients. Patients with the presence of cellulitis in the anterior thigh region or any other severe infection located in that area, patients who cannot obtain an adequate diet or the minimum caloric-protein intake, either gastrointestinal intolerance or contraindication to feeding by any route or repeated forced suspension of enteral feeding due to multiple surgical procedures or who withdraw their consent to continue in the study were eliminated.

Using the correlation method based on the study published by Hernández P. and collaborators; "Relationship between sonographic measurements of the rectus femoris and vastus intermedius muscles and conventional biochemical parameters for assessing nutritional status in the intensive care unit", which reported a correlation of 0.77 between the total nitrogen balance in the intensive care unit and the reduction percentages of the rectus femoris and vastus intermedius, considering an alpha value of 0.05 and beta of 0.8, a sample size of 8 patients was calculated; however, in order to optimize the statistical calculations in accordance with the Principle of the Central Limit Theorem, this number was increased to 30 patients. A non-probabilistic sampling was performed due to the availability of cases.

The sample was collected from critically ill patients hospitalized in the ICU of the UMAE T1 HE CMN del Bajío who met the inclusion criteria. On admission, the patient's BMI

Correlation between Sonographic Muscle Measurements of Vastus Intermedius and Rectus Femoris with Nitrogen Balance in Nutritional Assessment of Critically Ill Overweight and Obese Patients

was calculated using the formula $[\text{weight (kg)} / \text{height}^2 \text{ (m)}]$, these parameters were measured using the electronic bed scale or the patient's weight was taken no less than three months prior to admission (in the case of not having an electronic bed scale) and the height was measured with a tape measure, according to the BMI the nutritional status was classified according to the WHO definition as follows: overweight (25 to 29.9 kg/m²); class I obesity (30 to 34.9 kg/m²); class II obesity (35-39.9 kg/m²) and class III obesity (>40 kg/m²). Subsequently, sonographic muscle measurement was performed using portable ultrasound (PHILIPS Affiniti 50G brand with 59 MHz and 74 MHz linear transducers), measurements were taken of the rectus femoris and vastus intermedius muscles in their anteroposterior diameter (AP); lateral-lateral diameter (LL); and the cross-sectional area (CSA) (calculated from the perimeter contour of the section of both muscles) on day 0 (24 hours after admission to the ICU or initial) and day 5 (control), we obtained a tracing prior to registration in both measurements, the measurement was performed in the middle third between the iliac crest and the proximal edge of the knee. We obtained the percentage of muscle wasting, which was obtained from the difference between the initial size of the muscle with the control muscle, for this we used the LL diameter of the RF muscle, the measurements were performed by a single operator. Simultaneously, urea was quantified during 24 h on the same days as the sonographic measurements and urea and nitrogen in urine were analyzed by means of "Slide" reflectance in a VITROS CREA equipment calibrated in the unit's laboratory, likewise the caloric intake was recorded to calculate the total nitrogen balance using the formula $(\text{Protein intake (g/day)} / 6.25) - (\text{Nitrogen (UUN g/day)} / 0.8) + 2.5 + 2.5$. The patients included in the study who died during hospitalization in the ICU were recorded, in addition to recording the APACHE II, SOFA and NUTRIC score which was taken on admission.

The normal or non-normal distribution of continuous quantitative variables was determined using the Shapiro-Wilk test. Continuous quantitative variables were expressed as means and standard deviations in case of normal distribution, medians and percentiles otherwise. Qualitative variables were expressed as frequencies and proportions.

For inferential analysis, data from day of admission or day 0 and day 5 or control were pooled. Comparison of groups for qualitative variables was performed using chi-square or Fisher's exact chi-square. Comparison between quantitative and qualitative variables was performed by t test for related samples or Wilcoxon test according to their distribution. Comparison of means of two or more groups was done by ANOVA (normal distribution) or the Kruskal-Wallis test otherwise.

Correlation of quantitative variables was performed with Pearson's correlation coefficient. For all inferential statistical analyses, a $p < 0.05$ was considered a significant value.

In this study, no dangerous actions or prohibited procedures were carried out that would have entailed an added risk to those inherent to the procedures used for the diagnosis or treatment of

her condition, such as cabinet studies (muscle ultrasound, X-rays, computerized tomography), 24-hour urine collection, laboratory samples, which were explained and subsequently authorized by the patient.

Once the protocol was authorized by the Hospital's research committee with registration number R-2020-1001-030, written authorization was requested for inclusion in the study, by means of the letter of informed consent to participate in the research protocol. The information obtained is confidential and the analysis of the data is exclusively performed by the investigators and the research committee. This protocol is in accordance with ethical standards, the regulations of the General Health Law on Health Research and the Helsinki Declaration of 1975 and its amendments, as well as the Nuremberg Code and current international standards for good practice in clinical research (the Belmont Report, the Code of Federal Regulations of the United States).

III. RESULTS

The patient registry was carried out in the ICU of the UMAE.HE1CMN Bajío in which the sample of 30 subjects who met the inclusion criteria was completed, most were men with 19 (63.3%) and 11 (36.7%) women. The mean age was 50.93 ± 18.4 years; classified according to their weight status obtained by BMI in 19 (63.3%) patients with overweight, 8 (26.7%) with class I obesity, 3 (10.0%) with Class II obesity, there were no patients with class III obesity, an average BMI of 29.19 ± 3.49 kg/m² was obtained. The most frequent diagnosis was traumatic origin 20 (66.7%), followed by surgical origin 6 (20.0%) and finally medical origin 4 (13.3%). The APACHE II and SOFA-3 prognostic severity scales were used, in addition to the NUTRIC score for the evaluation of nutritional risk, in which the APACHE II score at patient admission obtained a minimum of 10 points and a maximum of 25 points with a mean of 17.37 ± 4.71 points; SOFA score with a minimum of 2 and maximum of 13 points and a mean of 6.77 ± 2.75 points and NUTRIC score with a minimum of 1 and maximum of 5 points with a mean of 1.63 ± 0.85 . No significant difference was found between muscle wasting and SOFA ($p = 0.211$), but a significant difference was found between APACHE II and muscle wasting ($p = 0.001$). The route of administration of the diet was: 26 (86.7%) patients by enteral route with nasogastric tube, being this route the most frequent, 3 (10.0%) by parenteral route and 1 (3.3%) with mixed nutrition, during admission and control a protein intake above the minimum (0.8 g/kg/day) was maintained, with a mean of $1.27 \text{ g/kg/day} \pm .09 \text{ g/kg/day}$. In the mean difference analysis, the groups were compared according to their BMI and were divided into overweight ($n = 19$), class I obesity ($n = 8$), class II obesity ($n = 3$) and class III obesity was not recorded ($n = 0$), since no patients with this BMI were admitted; we found no significant difference in the comparison between groups, for muscle wasting ($p = 0.360$), mortality ($p = 0.217$) or catabolism at admission ($p = 0.762$) and at day 5 ($p = 0.807$). A total of 4 deaths

Correlation between Sonographic Muscle Measurements of Vastus Intermedius and Rectus Femoris with Nitrogen Balance in Nutritional Assessment of Critically Ill Overweight and Obese Patients

were recorded obtaining a mortality of 13.3% during ICU stay (Table 1).

Table 1. Demographic characteristics of the population according to the study groups (Overweight, Obesity class I and Obesity class II)

	Overweight (n=19)	Obesity grade I (n= 8)	Obesity grade II (n=3)	p
Age	49.42 ± 19.56	50.88 ± 18.56	60.67 ± 10.97	p=0.486 ^a
Gender				
Male, n (%)	13 (68.4%)	5 (62.5%)	1 (33.3%)	p=0.502 ^b
Female, n (%)	6 (31.6%)	3 (37.5%)	2 (66.7%)	
Diet route				p=0.23 ^a
Enteral	19 (100.0%)	5 (62.5%)	2 (66.7%)	
Parenteral	0 (0.0%)	2 (25.0%)	1 (33.3%)	
Mixed	0 (0.0%)	1 (12.5%)	0 (0.0%)	
Initial nitrogen balance	2.70 ± 5.50	6.13 ± 6.75	4.83 ± 7.16	p=0.393 ^a
Control nitrogen balance	-1.21 ± 6.61	2.42 ± 8.78	-0.33 ± 1.78	p=0.479 ^a
Protein intake	1.28 ± .11	1.28 ± .03	1.27 ± .04	p=0.479 ^a
Catabolism day 0				
Normal	18 (94.7%)	8 (100.0%)	3 (100.0%)	p=0.762 ^a
Mild	1 (5.3%)	0 (0.0%)	0 (0.0%)	
Moderate	0 (0.0%)	0 (0.0%)	0 (0.0%)	
Severe	0 (0.0%)	0 (0.0%)	0 (0.0%)	
Catabolism day 5				
Normal	16 (84.2%)	7 (87.5%)	3 (100.0%)	p=0.807 ^a
Mild	1 (5.3%)	0 (0.0%)	0 (0.0%)	
Moderate	1 (5.3%)	0 (0.0%)	0 (0.0%)	
Severe	1 (5.3%)	1 (12.5%)	0 (0.0%)	
Muscular wasting	11.42 ± 12.86	4.55 ± 3.05	9.42 ± 13.11	p=0.360 ^a
Mortality				
Survivors	18 (94.7%)	6 (75.0%)	2 (66.7%)	p=0.217 ^b
No survivors	1 (5.3%)	2 (25.0%)	1 (33.3%)	

^a one way ANOVA
^b Chi-square
^c p- significant value

Quantitative sonographic measurements of the rectus femoris and vastus intermedius muscles, which are part of the quadriceps muscle, were made in their antero-posterior (AP) diameters in cm, latero-lateral (LL) in cm and cross-sectional area (CSA) in cm² on the day of admission to the ICU or day 0 and day 5 or control, and the total nitrogen balance on the same days was also considered. In the comparison by groups, a significant difference was found between the sonographic measurement on day zero and day five in the LL diameters of the RF and VI muscles (p=0.001 and p=0.003, respectively); likewise, in the CSA measurement (p=0.001). Unlike the AP diameters of both muscles where no significant difference was found. Muscle wasting had a mean of 9.39 ± 11.22 % (Table 2).

Table 2. Sonographic measurements of the quadriceps muscle (rectus femoris and vastus intermedius) on day 0 and day 5

Sonographic measurements	Day 0	Day 5	p
Rectus femoris anteroposterior diameter (cm)	1.68 ± .55	1.57 ± .42	p= 0.11 ^a
Rectus femoris lateral diameter (cm)	1.66 ± .43	1.47 ± .37	p= 0.001 ^{a, b}
Vastus intermedius anteroposterior diameter (cm)	1.57 ± .81	1.46 ± .65	p= 0.58 ^a
Vastus intermedius lateral diameter (cm)	1.60 ± .77	1.49 ± .67	p= 0.003 ^{a, b}
Cross Sectional Area (cm ²)	8.5 ± 2.8	7.5 ± 2.6	p= 0.001 ^{a, b}
Muscle waisting (%)		9.39 ± 11.22	

^a t-test for related samples
^b p-significant value

As for the qualitative variables, the catabolic state of the patients was measured between day zero and day five, where we did not find a significant difference (p=0.984); on day zero we found that 27 (90.0%) of the patients had a normal catabolic state; 1 (3.3%) with mild catabolism; 2 (6.7%) with moderate and 0 (0.0%) with severe catabolism. By day five, 26 (86.7%) patients were reported in a normal catabolic state; 1 (3.3%) with mild catabolism, 1 (3.3%) with moderate catabolism and 2 (6.7%) with severe catabolism. In the report of the total nitrogen

balance we obtained a mean of 3.83 ± 5.98 (g/day) on day zero and on day five -0.15 ± 6.97 (g/day) with significant difference (p=0.002.) (Table 3).

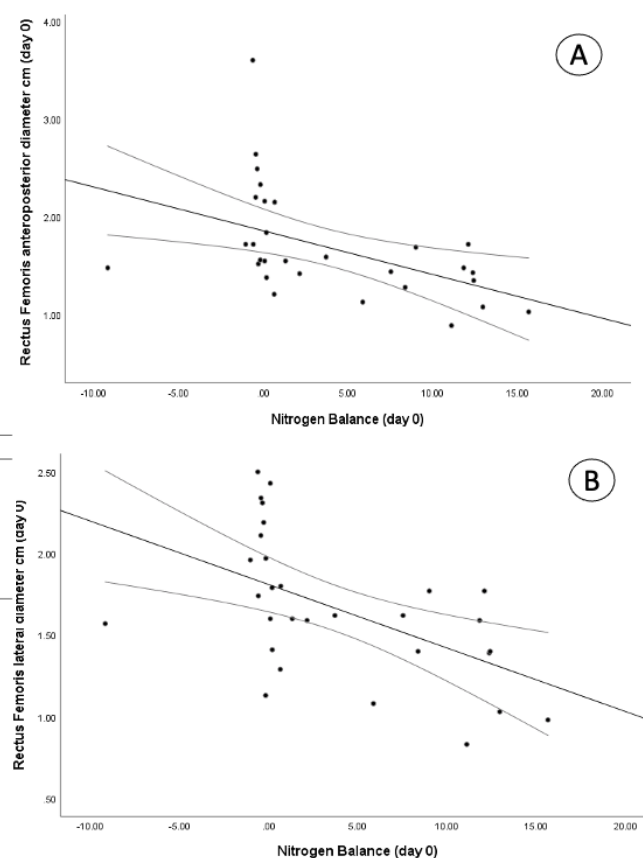
Table 3. Characteristics of catabolism and total nitrogen balance on day 0 and day 5

Catabolism	Day 0	Day 5	p
Normal	29 (96.7%)	26 (86.7%)	
Mild	1 (3.3%)	1 (3.3%)	p= 0.984 ^b
Moderate	0 (0.0%)	1 (3.3%)	
Severe	0 (0.0%)	2 (6.7%)	
Nitrogen balance	3.83 ± 5.98 (g/day)	-1.15 ± 6.97 (g/day)	p= 0.002 ^{a, c}

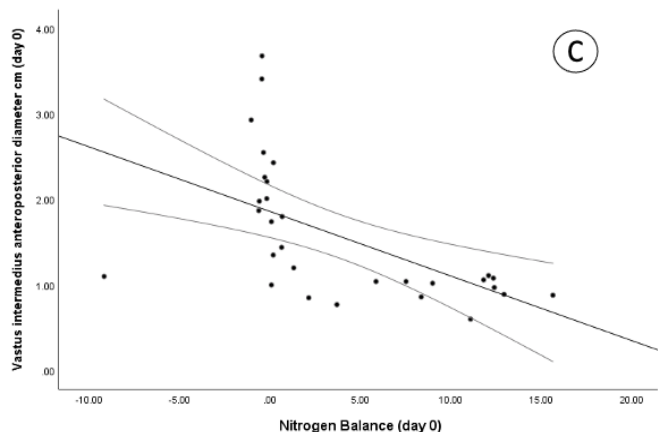
^a t-test for related samples
^b Chi-square
^c p-significant value

The correlation analysis used the total nitrogen balance at day zero and five and the sonographic measurements of the AP and LL diameters and the CSA of the rectus femoris and vastus intermedius muscles. In the correlation between initial sonographic measurements and initial TNB, a negative correlation with moderate strength of association was found in the LL diameters of the RF muscle and in the AP and LL diameters of the VI muscle (r=-0.533, p=0.002; r=-0.558, p=0.001 and r= -0.530, p=0.03, respectively) (Figure 1).

Figure 1. Correlation between initial nitrogen balance (g/day) and initial sonographic measurements of rectus femoris and vastus intermedius

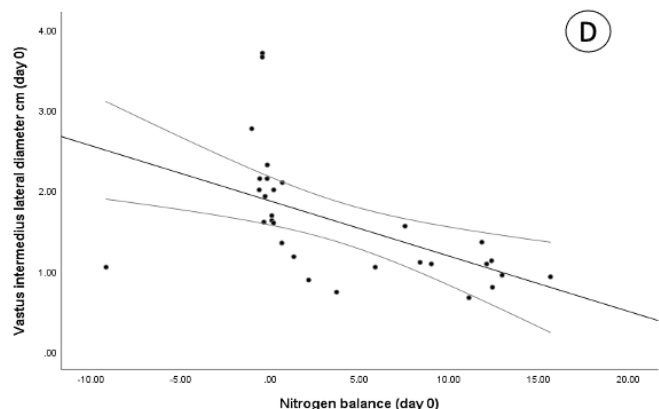
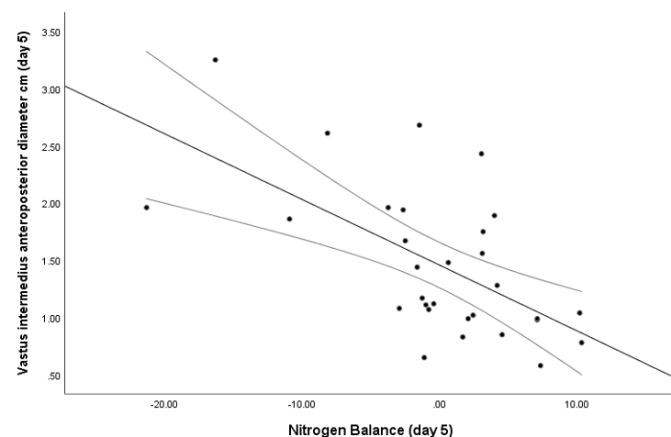


Correlation between Sonographic Muscle Measurements of Vastus Intermedius and Rectus Femoris with Nitrogen Balance in Nutritional Assessment of Critically Ill Overweight and Obese Patients



In the association between the control sonographic measurements and the control TNB, negative correlations were also found with a higher value obtained between the AP diameter of the VI muscle and the control TNB ($r=-0.609$, $p=0.001$) (Figure 2), in the rest of the control diameters, mostly weak negative correlations were observed: between nitrogen balance and control RF AP diameter $r= -0.409$, $p= 0.025$ and between nitrogen balance and control VI LL diameter $r= -0.457$, $p= 0.011$.

Figure 2. Correlation between control nitrogen balance (g/day) and control measurement of vastus intermedius anteroposterior diameter (cm)



On the contrary, between CSA at day zero and at day five with the respective TNB a weak correlation was obtained, however, in this case it was positive ($r=0.213$, $p=0.258$ and $r=0.297$, $p=0.111$, respectively). Finally, we obtained that between muscle wasting and control TNB there is a negative correlation ($r= -0.369$, $p=0.45$).

IV. DISCUSSION

Assessing nutritional status has become an essential practice in the critically ill patient, since it is essential to control adequate caloric and protein intake, prevent muscle wasting, nutrition-related syndromes such as overfeeding and underfeeding, and in-hospital malnutrition, which are deleterious and increase mortality (8). The tools used in nutritional assessment are inaccurate in obese and malnourished patients, as they do not distinguish between fat and lean body mass, therefore, they are a poor marker of excess body fat in patients with increased or decreased muscle mass, and they underestimate nutritional status. Several studies revealed that the use of muscle ultrasound has a good correlation with lean body mass measured by computed tomography ($r = 0.77$), dual energy X-ray absorptiometry ($r = 0.80$) and magnetic resonance imaging ($r= 0.87$) (15,17). Given the constant increase in the Mexican population with a BMI above 30 kg/m^2 and therefore an increase in the admission of obese patients to intensive care, new tools have had to be implemented for the nutritional evaluation of this population, in view of the fact that the conventional measures for evaluation have their limitations in this population, it was decided to use muscle ultrasound and thigh muscle measurements for the nutritional evaluation of critically ill overweight and obese patients (18,19).

In the present study it was observed a higher proportion of patients classified by BMI as overweight ($n=19$), followed by those with class I ($n=8$) and class II obesity ($n=3$) respectively, when comparing the groups we found that patients had on admission mostly positive nitrogen balances $3.83 \pm 5.98 \text{ (g/24 h)}$ which reflects a normal catabolism, in comparison with the control samples where more neutral and negative balances were seen ($-0.15 \pm 6.97 \text{ g/ 24h}$), even so, only 13.3 % presented a hypercatabolic state, mostly in the overweight patients, not finding a significant difference. The patient with critical illness is highly catabolic, losing large amounts of protein and muscle, secondary to an increase in proteolysis and gluconeogenesis, ubiquitination is triggered which causes muscle destruction and by a proinflammatory phenomenon that increases IL-6 and C-reactive protein (CRP), thus increasing amino acid oxidation and nitrogen losses resulting in a negative nitrogen balance and changes in body composition, predisposing to a greater loss of lean muscle mass (20). We must remember that this study focused on obese population, and that recently it was found that obesity has a positive association with increased survival of serious diseases and some chronic diseases known as the "obesity paradox", which has generated several theories including protection for muscle wasting and protein loss,

Correlation between Sonographic Muscle Measurements of Vastus Intermedius and Rectus Femoris with Nitrogen Balance in Nutritional Assessment of Critically Ill Overweight and Obese Patients

however, studies are still controversial (21). The variation found in catabolism with the entry and control TNB may be due to the fact that most of the patients in the study had a mean age between 50.93 years \pm 18.4, which reflects that a large part of the population were young patients and therefore, without a previous history of chronic degenerative disease. The days of difference between sample collection could explain the variation between the catabolism of admission and control, since the significant loss of proteins begins around the fifth to seventh days, another factor is the severity and reason for admission of patients, which in our case were mostly of traumatic origin and were found with a moderate severity and risk of mortality according to the APACHE II, SOFA score (17.37 points \pm 4.71 and 6.77 \pm 2.75 points), a previous study demonstrated a higher protein loss in abdominal post-surgical patients also demonstrating the importance of TNB measurement (22).

In the comparison between sonographic measurements on day zero and day five, a decrease was observed in all diameters and measurements, with a significant difference in the LL diameters of the RF and VI muscle, as well as in the CSA, also finding a mean of 9.39 \pm 11.22% in muscle wasting, the loss being greater in overweight patients, followed by obese class II and class I patients respectively, this had been previously attempted to demonstrate in the study performed by Segaran et al, which compared muscle loss between obese and non-obese patients, finding no difference between the two groups ($p > 0.05$). The relationship found in our study is important since the protective effect of obesity on muscle wasting is still under study, this has been studied by Goossens and his group in one of their studies found a better preservation of muscle mass and myofibril size in obese mice than in normal or low weight mice ($p < 0.001$) which partially explains the inverse correlation between muscle diameters and muscle wasting with TNB reported in this study (24). During the course of the study the patients received diet mostly by enteral route and at all times a protein intake greater than 0.8 g/kg/d was maintained, with a mean of 1.28 \pm .11 g/kg/d. It has been suggested that high protein administration (2 g / kg / d and more) together with hypocaloric regimens could be useful to improve outcome in obese patients, however, the evidence behind these recommendations is not strong. (25,26) Current ESPEN recommendations do not distinguish between obese and non-obese patients: 1.3g/kg/d (27).

Mortality was mostly recorded within the group of patients with class II obesity, with a low average risk of warranting aggressive nutrition by NUTRIC score. In contrast to what we found, in the study conducted by Gutierrez (28) et al. a correlation was observed between the presence of muscle wasting in the critically ill patient and the delay in reaching nutrition goals and an inverse correlation between the SOFA score value and the percentage of muscle loss ($r = 0.31$ and $r = -0.48$). We note that sonographic measurements of RF and VI muscles in their AP and LL diameters have moderate correlation with TNB at admission ($r = -0.478$, $r = -0.533$, $r = -0.558$ and $r =$

-0.530 , respectively) and at five days between sonographic measurements and TNB a strong correlation was demonstrated in the AP diameter of the VI muscle ($r = -0.609$, $p = 0.001$.) On the other hand, between the initial and control CSA with the respective TNB a positive correlation was found ($r = 0.213$ and $r = 0.258$, respectively), however, the correlation between the initial and control CSA and the respective TNB was positive ($r = 0.213$ and $r = 0.258$, respectively), however with a weak association, and finally a moderate correlation was observed between muscle wasting and control TNB ($p = -0.369$). The above tells us that a greater muscle diameter is proportional to a more negative nitrogen balance in obstructed patients in the AP and LL diameters of the RF and VI muscles; in the AST it was observed that a greater diameter is proportional to more positive nitrogen balances. Despite these results, the use of AP and LL diameters in isolation is not recommended for assessing nutritional status in obese patients. In previous studies a strong correlation was found between qualitative and quantitative sonographic measurements with biochemical parameters, specifically nitrogen balance ($r = 0.77$ and $r = 0.76$, respectively), however, in this study more biochemical parameters of nutritional assessment were used and it was in a mostly non-obese population, reasons that differentiate it from the present study (15). This study shows that CSA (thickness of both RF and VI muscles) can be useful for measuring nutritional status in obese patients, CSA is determined by the number and size of individual fibers of a muscle, it is divided into an anatomical and a physiological area, it has been used to measure muscle structure and strength, therefore, muscle mass can be measured by CSA, whose variation depends on age, sex and muscle group (29). Most lower limb ultrasound investigations consider muscle layer thickness and CSA. Greening et al (30). demonstrated a smaller quadriceps muscle size measured by CSA, and thus it was shown to be an independent risk factor for increased mortality and readmission. CSA has also been evaluated in selected critically ill populations, such as trauma and obese patients. In particular, a 3-week follow-up analysis of CSA and muscle diameter followed in ICU trauma patients demonstrated that 100% of them had severe muscle mass loss (31). Another study compared muscle depth as a measure of muscle atrophy between obese, overweight and normal weight patients using a muscle ultrasound technique, compared to a previous study using similar methodology, muscle depth loss was comparable and not statistically different between groups at each of the time points interrogated (23). Subsequently, several studies focused on investigating the muscle thickness of different muscle groups, and the main results in most of them indicated that it was significantly reduced, the rectus femoris muscle has proved to be an important marker and that the rest of the muscle thickness measurements significantly underestimate the loss of muscle mass in the ICU (32). However, recent studies have attempted to assess muscle wasting at the molecular level, in order to determine whether adipose tissue acts to prevent muscle wasting and to implement new strategies in the nutrition of critically ill

Correlation between Sonographic Muscle Measurements of Vastus Intermedius and Rectus Femoris with Nitrogen Balance in Nutritional Assessment of Critically Ill Overweight and Obese Patients

patients (33,34). Thus, there is still much room for further study in the obese and critically ill population.

V. CONCLUSIONS

The study revealed an inverse association between muscle sonographic measurements of rectus femoris and vastus intermedius in their AP and LL diameters with total nitrogen balance, as well as an association between cross-sectional area and total nitrogen balance in the nutritional assessment of critically ill overweight and obese patients. The above evidences the importance of the use of muscle sonography as a tool for the nutritional assessment of the critically ill obese patient, mainly the joint measurement of both muscle thicknesses. The present study can be a gateway for future studies in the field of nutritional assessment of the critically ill patient, as well as for implementing new nutritional and therapeutic strategies in the critically ill obese patient, due to the fact that patients with a BMI > 30 kg/m² are admitted to the ICU more frequently every day, taking into account that ultrasound and nitrogen balance will continue to be used as methods for nutritional assessment of the critically ill patient.

Sponsorship:

The authors declare not having received support from any sponsor or resources outside those granted by the medical institution

Conflicts of interest:

The authors declare that they have no conflicts of interest.

REFERENCES

- I. Vanhorebeek I, Langouche L, Berghe G, et al; "Endocrine aspects of acute and prolonged critical illness." *Nat Clin Pract Endocrinol Metab* 2006; Vol. 2:20–31.
- II. Cretoi M, Zugravu A; Nutritional Considerations in Preventing Muscle Atrophy. *Muscle Atrophy* 2018; 23:497–528.
- III. Jolley S, Bunnell A, Hough C. Intensive care unit acquired weakness. *Chest* 2016; 150 (5): 1129–1140.
- IV. Fantuzzi G; Adipose tissue, adipokines, and inflammation. *J Allergy Clin Immunol* 2005; 115:911–919.
- V. Fletcher S, Kennedy D, Ghosh I, et al. Persistent neuromuscular and neurophysiologic abnormalities in long-term survivors of prolonged critical illness. *Crit Care Med* 2003; 31:1012–1016.
- VI. Piche M, Poirier P, Lemieux I, et. al. Overview of epidemiology and contribution of obesity and body fat distribution to cardiovascular disease: an update. *Prog Cardiovasc Dis* 2018; 61:103–113.
- VII. DeJong A, Verzilli D, Sebbane M, et. al. Medical versus surgical ICU obese patient outcome: a propensity-matched analysis to resolve clinical trial controversies. *Crit Care Med* 2018; 46:e294–e301
- VIII. Ndahimana D, Eun-Kyung K. Energy Requirements in Critically Ill Patients. *Clin Nutr Res* 2020; 7(2): 81-90.
- IX. McClave S, Taylor B, Martindale R, et al. Guidelines for the provision and assessment of nutrition support therapy in the adult critically ill patient: society of critical care medicine (SCCM) and American Society for Parenteral and Enteral Nutrition (A.S.P.E.N.). *JPEN J Parenter Enteral Nutr* 2016; 40:159–211.
- X. Schetz M, DeJong A, Deane A, et al. "Obesity in the critically ill: a narrative review"; *Intensive Care Med* 2019.
- XI. Peetrons P. Ultrasound of muscles. *Eur Radiol* 2002; 12:35–43.
- XII. Formenti P, Umbrello M, Coppola S; et al. Clinical review: peripheral muscular ultrasound in the ICU. *Annals of Intensive Care* 2019; 9:57.
- XIII. Strasser M, Draskovits T, Praschak M, et al. Association between ultrasound measurements of muscle thickness, pennation angle, echogenicity and skeletal muscle strength in the elderly. *Age Dordr* 2013; 35:2377–88.
- XIV. Hernández E, Gómez N, Soriano R, et al. "Relación entre la medición sonográfica de los músculos recto femoral y vasto intermedio y los parámetros bioquímicos convencionales para valorar el estado nutricional en la unidad de cuidados intensivos."; *Med Crit* 2018; 32(6):351-358.
- XV. Paris M, Mourtzakis M, Day A, et al. Validation of bedside ultrasound of muscle layer thickness of the quadriceps in Perspective 1501 the critically ill patient (VALIDUM Study): a prospective multicenter study. *JPEN J Parenter Enteral Nutr* 2017; 41:171–180.
- XVI. Berger J, Bunout D, Barrera G, et al. Rectus femoris (RF) ultrasound for the assessment of muscle mass in older people. *Arch Gerontol Geriatr.* 2015;61(1):33-38. 14.
- XVII. Miyatani M, Kanehisa H, Ito M, et al. The accuracy of volume estimates using ultrasound muscle thickness measurements in different muscle groups. *Eur J Appl Physiol.* 2004;91(2-3):264-272.
- XVIII. Connolly B, MacBean V, Crowley C, et al. Ultrasound for the Assessment of Peripheral Skeletal Muscle Architecture in Critical Illness. *Critical Care Medicine* 2015; 43(4): 897–905.

Correlation between Sonographic Muscle Measurements of Vastus Intermedius and Rectus Femoris with Nitrogen Balance in Nutritional Assessment of Critically Ill Overweight and Obese Patients

- XIX. World Health Organization. Obesity and overweight: World Health Organization; 2015. [Internet] [Cited 4 June, 2015] Available from: <http://www.who.int/mediacentre/factsheets/fs311/en/>.
- XX. Weijs PJM. Fundamental determinants of protein requirements in the ICU. *Curr Opin Clin Nutr Metab Care* 2014;17:183e9.
- XXI. Horwich T, Fonarow G, Hamilton M, et al. The relationship between obesity and mortality in patients with heart failure. *J Am Coll Cardiol* 2001; 38(3):789-95.
- XXII. Cheatham M, Safcsak K, Brzezinski S, et al; Nitrogen balance, protein loss, and the open abdomen. *Crit Care Med*. 2007; 35(1):127-131.
- XXIII. Segaran E, Wandrag L, Stotz M, et al. Does body mass index impact on muscle wasting and recovery following critical illness? A pilot feasibility observational study. *J Hum Nutr Diet* 2017; 30:227–35
- XXIV. Goossens C, Marques MB, Derde S, Et al. “Premorbid obesity, but not nutrition, prevents critical illness-induced muscle wasting and weakness.” *Journal of Cachexia, Sarcopenia and Muscle* 2016; 13:1-13
- XXV. Dickerson RN, Patel JJ, McClain CJ. Protein and calorie requirements associated with the presence of obesity. *Nutr Clin Pract* 2017;32:86Se93S.
- XXVI. Pan Janice, Shaffer R, Sinno Z, et al. The obesity paradox in ICU patients. *Conf Proc IEEE Eng Med Biol Soc* 2017:3360e4.
- XXVII. Singer P, Reintam AB, Berger MM, Et al. “ESPEN guideline on clinical nutrition in the intensive care unit”. *Clinical Nutrition*, 2019; 38:48-79.
- XXVIII. Gutierrez D, Rosas K, Cerón U, et al. “Ultrasonografía del musculoesquelético como valoración nutricional en el paciente crítico”. *Med Crit* 2017;31(3):122-127.
- XXIX. Ikai M, Fukunaga T. Calculation of muscle strength per unit cross-sectional area of human muscle by means of ultrasonic measurement. *Int Z Angew Physiol*. 1968; 26:26–32.
- XXX. Greening N, Harvey-Dunstan T, Chaplin E, et al. Bedside assessment of quadriceps muscle by ultrasound after admission for acute exacerbations of chronic respiratory disease. *Am J Respir Crit Care Med* 2015; 192:810–6.
- XXXI. Annetta MG, Pittiruti M, Silvestri D, et al. Ultrasound assessment of rectus femoris and anterior tibialis muscles in young trauma patients. *Ann Intensive Care*. 2017; 7:104.
- XXXII. Puthuchery Z, McNelly A, Rawal J, et al. Rectus femoris cross-sectional area and muscle layer thickness: comparative markers of muscle wasting and weakness. *Am J Respir Crit Care Med* 2017; 195:136–8.
- XXXIII. Goossens C, Vander S, Vanden-Berghe G, et al. Proliferation and differentiation of adipose tissue in prolonged lean and obese critically ill patients. *Intensive Care Medicine Experimental* 2017; 5:1-16.
- XXXIV. Goossens C, Weckx R, Derde S, et al. Adipose tissue protects against sepsis-induced muscle weakness in mice: from lipolysis to ketones. *Crit Care* 2020; 23(1): 236