European Journal of Clinical Nutrition
https://doi.org/10.1038/s41430-018-0144-8

BRIEF COMMUNICATION

Nutritional risk assessment at admission can predict subsequent muscle loss in critically ill patients

Amartya Mukhopadhyay[1] · Bee Choo Tai[2] · Deepa Remani[1] · Jeya Henry[3] · Yanika Kowitlawakul[4] · Zudin Amika Puthucheary[1,5]

Received: 21 August 2017 / Revised: 6 February 2018 / Accepted: 15 February 2018

Abstract

Muscle loss in critically ill patients may be related to nutrition. We study the association between modified NUTrition RIsk in the Critically ill (mNUTRIC) score obtained at admission to intensive care unit (ICU) and subsequent muscle loss. We measured rectus femoris cross-sectional area (RFCSA) by ultrasound on days 1, 3, 7, and 10 of ICU admission. We used linear mixed effects model following natural logarithmic transformation of the data. Forty-eight patients (median (IQR) age 66 (55–72.5) years, 71% male, APACHE II score 31 (25–34), BMI 24.2 (21.5–27.1) kg/m^2) were analyzed. The high mNUTRIC score (>5) cohort ($n = 35$) lost significantly more muscle as compared to the low (≤5) group ($n = 13$); the adjusted ratio (high versus low group) of the geometric mean RFCSA were (0.58, 95% CI 0.46–0.75) for right and (0.61, 95% CI 0.49–0.77) for left, both $p < 0.001$. mNUTRIC score obtained at admission to ICU can identify patients at risk of subsequent muscle loss.

Introduction

Increased inflammation plays major roles in both muscle loss and nutritional deterioration of critically ill patients. Puthucheary et al. [1] have shown a direct relationship between inflammatory markers and muscle loss, and the components of both acute and chronic inflammation were included in generating the NUTrition RIsk in the Critically ill (NUTRIC) score [2]. Heightened inflammation in the early phase followed by persistent inflammation of critical illness lead to muscle protein breakdown, often aggravated by poor nutritional status. Muscle loss prolongs the duration of mechanical ventilation (MV) and post-intensive care unit (ICU) length of stay (LOS), leading to poor functional status and difficulties in rehabilitation [3]. There have been limited attempts for early identification of critically ill patients at risk of muscle loss. We hypothesized that the modified NUTRIC score (mNUTRIC) [4] obtained at admission to the ICU would identify patients at risk of greater muscle loss.

Method

In a prospective observational cohort study conducted between August 2014 and September 2016, we screened critically ill patients with age ≥21 years, expected duration of MV and LOS in hospital of at least 72 h and 10 days, respectively. We excluded patients with amputation, surgery, neurological, or rheumatological problems involving the lower limbs. Rectus femoris cross-sectional area (RFCSA) of both sides were measured by a single ultrasonographer using B-mode ultrasonography with linear transducer placed perpendicular to the long axis of the thigh on its superior aspect, two-third of the distance from the

✉ Amartya Mukhopadhyay
amartya.mukherjee@gmail.com

1 Division of Respiratory and Critical Care Medicine, University Medicine Cluster, National University Health System and National University of Singapore, Singapore, Singapore

2 Saw Swee Hock School of Public Health, National University of Singapore and National University Health System, Singapore, Singapore

3 Clinical Nutrition Research Centre, Singapore Institute for Clinical Sciences, Singapore, Singapore

4 Alice Lee Centre for Nursing Studies, National University of Singapore and National University Health System, Singapore, Singapore

5 Intensive Care Department, Royal Free Hospital NHS Trust, Hampstead, United Kingdom

Published online: 26 March 2018

Table 1 Patient characteristics in low and high mNUTRIC score group

	All patients	mNUTRIC Score		
	N=48	Low (*N*=13)	High (*N*=35)	*p*
Demographics				
Age, median (IQR), years	66 (55–72.5)	54 (49–61)	68 (62–75)	0.004
Gender, male, *N* (%)	34 (71)	12 (92)	22 (63)	0.050
BMI, median (IQR), kg/m^2	24.2 (21.5–27.1)	28.2 (25.2–31)	22.3 (20.9–26.4)	<0.001
Scores				
APACHE II, median (IQR)	31 (25–34)	22 (18–25)	32 (29–36)	<0.001
Charlson comorbidity index, median (IQR)	4 (1.5–6)	1 (0–3)	5 (2–7)	0.007
Treatment and investigations				
Renal replacement treatment, *N* (%)	12 (25)	0	12 (34)	0.020
Fluid balance, median (IQR), mls				
Day 1	3002 (1154–4488)	2977 (1421–3660)	3027 (785–4662)	0.900
Day 3	3634 (1968–5415)	3605 (1879–5589)	3643 (1968–5415)	0.900
Day 7 (*N*=16)	6377 (2278–7969)	10135 (6245–14025)	5731 (976–7827)	0.400
Hemoglobin, median (IQR), gm/dL	10.2 (9.2–13.3)	13.3 (9.9–16.2)	9.9 (8.8–12.7)	0.009
Albumin, median (IQR), gm/dL	32.5 (26.5–39)	37 (30–41)	31 (23–37)	0.090
Bicarbonate, median (IQR), mmol/L	21.6 (18.8–24.9)	22.2 (21.2–24.6)	21.3 (16.1–24.9)	0.300
pH, median (IQR)	7.36 (7.23–7.42)	7.37 (7.36–7.39)	7.34 (7.21–7.43)	0.400
Base excess, median (IQR)	−3.1 (−7.6–0.1)	−2.8 (−4.4–0.2)	−4 (−10.9–(−)0.1)	0.300
PF ratio, median (IQR)	139 (109–267)	131(108–306)	142 (109–267)	0.900
Calorie adequacy during MV, (%)	47.4 (19–63.7)	23 (8–52)	51 (32–64)	0.050
Protein adequacy during MV, (%)	44.6 (12.8–63.9)	22 (0–45)	50 (26–71)	0.020
Outcomes				
Length of stay in the ICU, median (IQR), days	5.75 (3–-9.5)	4 (3–5)	7 (3–11)	0.030
Length of stay in the hospital, median (IQR), days	15 (9.5–25.5)	8.5 (8–10)	19 (11–44)	<0.001
28-Day mortality, *N* (%)	11 (23)	1 (7.7)	10 (28.6)	0.120
Duration of MV, median (IQR), days	4.5 (3–7.5)	3 (2–4)	5 (3–9)	0.020

Continuous variables are presented in terms of median (IQR) and categorical variables in terms of *N* (%)

IQR interquartile range, *BMI* body mass index, *APACHE* Acute Physiology and Chronic Health Evaluation, *PF* PaO2/FiO2, *MV* mechanical ventilation

anterior superior iliac spine to the superior patellar border [5] on days 1, 3, 7, and 10 of ICU admission. Ultrasound measurements of lower limb muscle area have been validated against CT and MRI measurements [6] as well as histological and biochemical gold standard measures in critically ill patients with excellent inter-rater and intra-rater reliability [1].

We collected demographics, ICU scores, MV, fluid balance, renal replacement treatment, investigations, calorie and protein adequacies, and outcomes from the computerized clinical information system (IntelliSpace Critical Care and Anesthesia, Philips Healthcare). mNUTRIC scores (0–9) consisting of five variables (age, Acute Physiology And Chronic Health Evaluation (APACHE) II, Sequential Organ Failure Assessment (SOFA), comorbidities, days from hospital to ICU admission) were recorded. The cohort was divided into low (≤5, $n = 13$) and high (>5, $n = 35$) groups.

Statistical analysis

Differences in demographic and clinical characteristics between the two groups were compared using the χ^2 and Wilcoxon rank sum test for categorical and continuous variables, respectively. As the RFCSA measures were skewed, natural logarithmic transformation was applied to normalize the data. The linear mixed effects model was used to identify the individual component of mNUTRIC score for predicting muscle loss (defined by changes in RFCSA over time) taking into account possible intra-subject correlation between repeated measures. The effect of each mNUTRIC component on muscle loss was

Table 2 Association between individual components of NUTRIC score and muscle loss

Components	Right			Left		
	Ratio of geometric mean (95% CI)		*p*-Value[a]	Ratio of geometric mean (95% CI)		*p*-Value[a]
	Unadjusted	Adjusted[a]		Unadjusted	Adjusted[a]	
mNUTRIC score						
Low	1	1		1	1	
High	0.58 (0.45–0.74)	0.58 (0.46–0.75)	< 0.001	0.61 (0.49–0.77)	0.62 (0.49–0.77)	< 0.001
Age score			0.209			0.081
0	1	1	—	1	1	—
1	0.87 (0.60–1.26)	0.87 (0.60–1.25)	0.449	0.93 (0.67–1.29)	0.93 (0.67–1.29)	0.660
2	0.71 (0.47–1.07)	0.71 (0.47–1.07)	0.100	0.70 (0.48–1.02)	0.70 (0.4–1.02)	0.061
APACHE II score			<0.001			<0.001
0	1	1	—	1	1	—
1	1.08 (0.50–2.35)	1.09 (0.50–2.36)	0.834	0.93 (0.42–2.03)	0.93 (0.42–2.04)	0.859
2	0.45 (0.22–0.91)	0.45 (0.23–0.91)	0.027	0.48 (0.24–0.98)	0.49 (0.24–0.99)	0.046
3	0.41 (0.21–0.81)	0.41 (0.21–0.82)	0.011	0.41 (0.20–0.81)	0.41 (0.21–0.82)	0.011
SOFA score			0.374			0.262
0	1	1	—	1	1	—
1	0.71 (0.42–1.19)	0.71 (0.42–1.19)	0.196	0.68 (0.41–1.11)	0.68 (0.41–1.12)	0.127
2	0.69 (0.42–1.15)	0.69 (0.42–1.16)	0.163	0.66 (0.41–1.08)	0.67 (0.41–1.09)	0.104
Days from hospital to ICU admission score	1.12 (0.87–1.45)	1.12 (0.87–1.46)	0.374	1.19 (0.93–1.52)	1.20 (0.94–1.53)	0.148
Comorbidity score	0.73 (0.54–0.98)	0.73 (0.54–0.98)	0.037	0.77 (0.58–1.03)	0.77 (0.58–1.02)	0.072

Overall, NUTRIC score is significantly associated with RFCSA (both left and right), and the association seems to be driven mainly by the APACHE score although comorbidity score also showed marginal association with right RFCSA.

[a]Adjusted for the main effect of time

quantified based on the ratio of geometric mean and its 95% confidence interval (CI). Separate adjustment for adequacy of protein and calorie intakes were also considered in the linear mixed models. Statistical evaluations were made using STATA v14 (StataCorp LP, College Station, TX, USA), assuming a two-sided test at the conventional 5% level of significance.

The study was approved by the ethics board (National Healthcare Group DSRB reference no. 2014/00327) and all patients or their representative consented to the study.

Results

The characteristics of the 48 patients (median (IQR) age 66 (55–72.5) years, 71% male) are described in Table 1 according to mNUTRIC score. Patients with high mNUTRIC group had significantly lower body mass index, higher Charlson comorbidity index, and stayed longer in the ICU and hospital. Table 2 shows that patients with high mNUTRIC score had significantly lost more muscle; the adjusted ratio (high versus low group) of the geometric mean of the right and left muscles were 0.58 (95% CI 0.46–0.75) and 0.61 (95% CI 0.49–0.77), respectively, both $p < 0.001$. The effect of mNUTRIC score and APACHE II remained significant even after adjusting for the adequacies of protein and calorie intake in the respective models (results not shown).

Discussion

High nutritional risk patients identified by mNUTRIC score on the day of admission lost significantly more muscle than those at low risk. Of the variables included in the mNUTRIC score, APACHE II score was most significantly associated with muscle loss.

mNUTRIC score has been used for the nutritional risk assessment of critically ill patients and in the prediction of short- and long-term mortality [4, 7]. Heyland et al. [2] found that energy adequacy was significantly associated with the 28-day mortality in high NUTRIC group. Significant association between mNUTRIC score and important morbidity such as muscle loss was demonstrated in the current study for the first time. Possible reason(s) for this association may include higher inflammation, longer period of immobilization, and nutritional factors, which were not investigated in this study. In contrast to our study,

Puthucheary et al. [1] found that higher organ failure as assessed by SOFA score calculated at least 3 days after admission was associated with muscle loss.

Due to the observational nature of our study, protein adequacy was higher in patients with high mNUTRIC score. The association between muscle loss and protein intake in critically ill patient is unclear. Studies suggesting protein supplementation to be associated with greater muscle loss are limited by methodological problems [1, 8]. However, a randomized trial had shown that early protein supplementation by parenteral nutrition decreased muscle wasting by subjective assessment [9].

mNUTRIC score calculated on ICU admission identifies high-risk group who will benefit from adequate nutritional supplementation. LOS in the ICU and hospital were longer in the high score group who were deficient in energy supplementation [2, 7] speculating that greater muscle loss and functional deterioration in these vulnerable patients as possible contributors. Wei et al. [10] had shown that patients with improved nutritional adequacy in ICU had better physical functioning at 3 months. It is conceivable that preserved muscle mass with higher nutritional adequacy may lead to improved physical wellbeing.

Conclusion

Poor nutritional status described by mNUTRIC score at admission to the ICU can identify patients at risk of greater muscle loss subsequently. Early identification of patients at risk of higher muscle loss will be useful for future intervention.

Funding The study was supported with National University Health System Clinician Grant 2013.

Compliance with ethical standards

Conflict of interest The authors declare that they have no conflict of interest.

References

1. Puthucheary ZA, Rawal J, McPhail M, Connolly B, Ratnayake G, Chan P, et al. Acute skeletal muscle wasting in critical illness. JAMA. 2013;310:1591–600. https://doi.org/10.1001/jama.2013.278481.
2. Heyland DK, Dhaliwal R, Jiang X, Day AG. Identifying critically ill patients who benefit the most from nutrition therapy: the development and initial validation of a novel risk assessment tool. Crit Care. 2011;15:R268 https://doi.org/10.1186/cc10546.
3. De Jonghe B, Bastuji-Garin S, Durand MC, Malissin I, Rodrigues P, Cerf C, et al. Respiratory weakness is associated with limb weakness and delayed weaning in critical illness. Crit Care Med. 2007;35:2007–15.
4. Rahman A, Hasan RM, Agarwala R, Martin C, Day AG, Heyland DK. Identifying critically-ill patients who will benefit most from nutritional therapy: further validation of the "modified NUTRIC" nutritional risk assessment tool. Clin Nutr. 2016;35:158–62. https://doi.org/10.1016/j.clnu.2015.01.015.
5. Seymour JM, Ward K, Sidhu PS, Puthucheary Z, Steier J, Jolley CJ, et al. Ultrasound measurement of rectus femoris cross-sectional area and the relationship with quadriceps strength in COPD. Thorax. 2009;64:418–23. https://doi.org/10.1136/thx.2008.103986.
6. Walton JM, Roberts N, Whitehouse GH. Measurement of the quadriceps femoris muscle using magnetic resonance and ultrasound imaging. Br J Sports Med. 1997;3:59–64.
7. Mukhopadhyay A, Henry J, Ong V, Leong CS, Teh AL, van Dam RM, et al. Association of modified NUTRIC score with 28-day mortality in critically ill patients. Clin Nutr. 2017;36:1143–8. https://doi.org/10.1016/j.clnu.2016.08.004.
8. Casaer MP, Langouche L, Coudyzer W, Vanbeckevoort D, De Dobbelaer B, Guiza FG, et al. Impact of early parenteral nutrition on muscle and adipose tissue compartments during critical illness. Crit Care Med. 2013;41:2298–309. https://doi.org/10.1097/CCM.0b013e31828cef02.
9. Doig GS, Simpson F, Sweetman EA, Finfer SR, Cooper DJ, Heighes PT, et al. Early parenteral nutrition in critically ill patients with short-term relative contraindications to early enteral nutrition: a randomized controlled trial. JAMA. 2013;309:2130–8. https://doi.org/10.1001/jama.2013.5124.
10. Wei X, Day AG, Ouellette-Kuntz H, Heyland DK. The association between nutritional adequacy and long-term outcomes in critically ill patients requiring prolonged mechanical ventilation: a multicenter cohort study. Crit Care Med. 2015;43:1569–79. https://doi.org/10.1097/CCM.0000000000001000.