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Original Article

Higher Energy and Protein Intake from Enteral Nutrition May Reduce Hospital Mortality in Mechanically Ventilated Critically Ill Elderly Patients☆

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S U M M A R Y

Background: The objective of this study was to investigate whether the nutrition intake from enteral nutrition (EN) and parenteral nutrition (PN) created a better clinical outcome than EN alone in high nutritional risk (HNR) mechanically ventilated critically ill elderly patients.
Methods: We included patients $\geq$ 65 years on mechanical ventilation $\geq$ 48 h and received EN. Nutritional status was evaluated by Modify NUTrition Risk in Critical ill score (mNUTRIC). We calculated the energy and protein requirements as Harris-Benedict equation $\times$ 1.0–1.3 and 1.0–2.0 gm/kg body weight respectively. Nutrition intake from EN and PN was recorded within 7 days. ICU and hospital mortalities in HNR elderly patients who could achieve more or less 80% prescribed nutrition were compared.
Result: Among 190 critically ill elderly patients, 173 (91.1%) HNR patients had mNUTRIC $\geq$ 5. HNR patients who achieved $\geq$80% prescribed calorie had lower ICU mortality (13.5% vs 25.8%; P = 0.04) and hospital mortality (23.4% vs 40.3%; P = 0.02) compared to those who achieved <80% prescription. For those who EN protein achieved $\geq$80% prescription had a lower hospital mortality (23.4% vs 40.3%; P = 0.02). For each point increase of mNUTRIC, ICU length of stay (LOS) increased 1.18 days, Days of Mechanical Ventilation (MVDs) increased 1.54 days, hospital LOS increased 1.52 days, the ICU mortality OR = 1.71 (1.22–2.39) and hospital mortality OR = 1.64 (1.24–2.15).
Conclusion: Very high percentage (91.1%) of medical intensive care (MICU) elderly patients were in HNR. Those who EN calorie achieved $\geq$80% prescription had lower ICU and hospital mortality. Increased EN protein intake only lowered hospital mortality.

1. Introduction

As the elderly population increases, Taiwan was predicted to enter an "aged society" by 2018, and becomes a "hyper-aged society" by 2026.[1] Poor chewing function, swallowing problem, gastrointestinal discomfort and loss of appetite increase the risk of malnutrition.[2] In Taiwan, the rate of frailty in elderly outpatient with chronic disease was 19%. Frail elderly had a higher rate of mobility disabilities, more chronic diseases, and polypharmacy.[3] Study has shown that age, first time 24 h' Acute Physiology and Chronic Health Evaluation II (APACHE II) score, and ICU LOS were significantly correlated with ICU readmission, and unplanned hospital readmission rate.[4,5]

Abbreviations: SOFA, Sequential Organ Failure Assessment; BMI, body mass index; Start EN, number of days after entering ICU to start EN; BW loss, body weight loss one month before admission to MICU; Poor intake, <2/3 of original food intake (one week before admission to MICU).

☆ This study was approved by the Institutional Review Board at Mackay Memorial Hospital, IRB No: 14MMHIS229 and Clinical Trials. gov. No: NCT02374203.

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Malnutrition Universal Screening Tool, Mini Nutritional Assessment, and Subjective Global Assessment are commonly used nutritional screening tools. These traditional nutritional screening tools were unable to evaluate the interaction between the patient's nutritional status and acute diseases.[6] Some researchers considered that these assessment tools are unable to predict postoperative complications and evaluate the severity of acute disease.[7–9] Since the NUTrition Risk in Critically ill (NUTRIC) score were designed to assess disease severity, it could more accurately screen critically ill patients at HNR.[9] Thus in 2016, the American Society for Parenteral and Enteral Nutrition (A.S.P.E.N) suggested using the NUTRIC score for assessing nutritional risk.[10]

The NUTRIC score was developed by Heyland et al. (2011).[11,12] The score items include age, APACHE II, SOFA, number of co-morbidities, number of days between hospital admission and ICU admission, and IL-6. A total score of 6–10 indicates HNR and a score of 0–5 indicates LNR. Since IL-6 is not routinely measured, Rahman et al. (2016) suggested that NUTRIC score without IL-6 level (mNUTRIC) could be used, with a total score ≥5 indicating HNR and 0–4 indicating LNR.[13]

When critically ill patients were evaluated by the mNUTRIC score, approximately 15%–60% were found to be at HNR,[9,14,15] and patients with higher mNUTRIC scores increased probability of 28-day mortality and increased MVDs.[11,13,15] For patients at HNR, early enteral feeding and aggressive nutritional intervention lowered the probability of 28-day mortality.[11,13,15] Each 25% increase in prescribed calorie could lower 18% of 6-month mortality rate.[13] Therefore, our aims were to discover the prevalence of nutritional risk of critically ill elderly patients with mechanical ventilation in MICU by using the mNUTRIC score, and to investigate whether the nutrition intake from both EN and PN could have better clinical outcome than EN alone in HNR critically ill elderly patients.

2. Method

This study was conducted from Dec 2014 to June 2016 in the MICU of Taipei MacKay Memorial Hospital. Inclusion criteria were: age ≥65 years old, APACHE II ≥ 15, mechanical ventilation ≥48 h, and on nasogastric tube feeding. Patients who were on total parenteral nutrition, fasting >5 days, brain dead or terminally ill from cancer were excluded. This study was approved by the Institutional Review Board at MacKay Memorial Hospital, IRB No: 14MMHIS229 and Clinical Trials. gov. No: NCT02374203.

2.1. Data collection

Data were collected from the medical records included gender, height, and weight on admission to MICU, age, diagnosis, APACHE II, SOFA, co-morbidities, and days admitted from hospital to ICU. Patient's body weight change within one month, and food intake (no change, <2/3 of original food intake) were obtained from caregivers. When food intake <2/3 of original intake was defined as poor intake. We calculated the mNUTRIC score with a range from 0 to 9 without IL-6; a score of 0–4 was designated as LNR and 5–9 as HNR.

2.2. Nutrition intervention

Energy requirement was calculated by using Harris-Benedict equation × 1.0–1.3. Protein provision was set at 1.0–2.0 gm/kg BW. When patient was diagnosed chronic kidney disease with serum creatinine ≥2.0 mg/dL, protein prescription was set at below 1.0 gm/kg BW. We recorded and calculated energy and protein intake from EN and PN (energy containing medications) respectively within 7 days stay in the MICU (or until the day patient was transferred out or dead), MVDs, VAP, date of transferring out of ICU, date of discharge, and patients' survival.

2.3. Statistical analysis

We used SAS version 9.4 (SAS Institute Taiwan Ltd.) for statistical analysis. Statistically significance was set at P < 0.05. Continuous variables were reported as mean ± SD, and categorical values were presented as n (%). Student's t-test was used to compare MVDs, ICU and hospital LOS between HNR and LNR elderly patients. Chi-square test was used to compare ICU and hospital mortality between HNR and LNR. Multiple linear regression was used to analyze the association between mNUTRIC score and MVDs, ICU and hospital LOS. Logistic regression was used to analyze the effect of mNUTRIC score on the odds ratio of VAP, ICU and hospital mortality and associations between actual calorie and protein intakes and probability of 28-day mortality.

3. Results

The distribution of the mNUTRIC score system variables were shown in Table 1. The mean mNUTRIC score of 190 critically ill elderly patients was 6.4 ± 1.4. The mean of MVDs and ICU LOS were 13.2 ± 9.9 days and 14.7 ± 9.6 days respectively (Table 2). The ICU mortality rate was 16.8%. The mean of hospital LOS was 26.4 ± 14.9 days, and the hospital mortality rate was 27.4% (Table 2). The rate of HNR patients was 91.1%. The HNR patients were older than low nutrition risk (LNR) patients (79.7 ± 7.0 years vs 72.7 ± 6.5 years; P = 0.0006), with higher mNUTRIC score (6.7 ± 1.2 vs 3.7 ± 0.4l; P < 0.0001), received EN later (1.4 ± 0.8 days vs 1.1 ± 0.3 days; P = 0.009), had longer MVDs (13.5 ± 10.2 days vs 9.8 ± 5.7 days; P = 0.03), longer hospital LOS (26.9 ± 15.3 days vs 21.5 ± 8.7 days; P = 0.03), higher hospital mortality rate (29.5% vs 5.9%; P = 0.04), less EN calorie intake (1111 ± 309 kcal/day vs 1267 ± 196 kcal/day; P = 0.007) and less EN protein intake (55.9 ± 19.2 gm/day vs 70.8 ± 15.5 gm/day; P = 0.002) (Table 2).

After 1 week of aggressive nutritional intervention, HNR elderly patients who could not achieve 80% prescribed nutrition had higher mNUTRIC score (Table 3). A total of 111 patients (64.2%) could achieve ≥80% of prescribed EN calorie and protein. These patients started NG tube feeding earlier (1.1 ± 0.3 days vs 2.0 ± 1.0 days; P < 0.0001), had lower ICU mortality rate (13.5% vs 25.8%; P = 0.04) and hospital mortality rate (23.4% vs 40.3%; P = 0.02). There was no difference in ventilator-associated pneumonia (VAP) occurrence, MVDs, ICU and hospital LOS (Table 3). HNR patients who consumed

Table 1
The mNUTRIC score variables distribution of critically ill elderly patients (n = 190).

mNUTRIC score Variables	Range	Points	n	(%)
Age	50~ < 75	1	52	(27.4)
	≥75	2	138	(72.6)
APACHE II	15~ < 20	1	27	(14.2)
	20~ <28	2	82	(43.2)
	≥28	3	81	(42.6)
SOFA	<6	0	51	(26.8)
	6~ < 10	1	83	(43.7)
	≥10	2	56	(29.5)
Number of Co-morbidities	0–1	0	14	(7.4)
	≥2	1	176	(92.6)
Days from hospital to ICU admission	<1	0	103	(54.2)
	≥1	1	87	(45.8)
Mean score ± SD			6.4	±1.4

Table 2
Characteristics of mechanically ventilated critically ill elderly patients.

Characteristics	All elderly patients	HNR	LNR	P value
	n = 190	mNUTRIC ≥5, n = 173	mNUTRIC <5, n = 17	
Age (years)	79.1 ± 7.2	79.7 ± 7.0	72.9 ± 6.5	0.0006
BMI (kg/m^2)	22.4 ± 4.7	22.3 ± 4.5	23.5 ± 6.4	0.45
mNUTRIC score	6.4 ± 1.4	6.7 ± 1.2	3.7 ± 0.4	<0.0001
Start EN (days)	1.4 ± 0.8	1.4 ± 0.8	1.1 ± 0.3	0.009
Male n (%)	108 (56.8)	99 (57.23)	9 (52.9)	0.73
BW loss n (%)	83 (43.7)	40 (43.9)	7 (41.2)	0.83
Poor intake n (%)	95 (50.0)	86 (49.7)	9 (52.9)	0.80
Diagnosis n (%)				
Diabetes	98 (51.6)	94 (49.5)	4 (23.5)	0.02
Renal disease	105 (55.3)	104 (60.1)	1 (5.9)	<0.0001
Lung disease	67 (35.3)	56 (32.4)	11 (64.7)	0.008
Sepsis	111 (58.4)	105 (60.7)	6 (36.3)	0.04
VAP n (%)	35 (18.4)	31 (17.9)	4 (23.5)	0.57
MVDs (days)	13.2 ± 9.9	13.5 ± 10.2	9.8 ± 5.7	0.03
ICU LOS (days)	14.7 ± 9.6	14.9 ± 9.8	12.5 ± 6.5	0.32
ICU mortality n (%)	32 (16.8)	31 (17.9)	1 (5.9)	0.21
hospital LOS (days)	26.4 ± 14.9	26.9 ± 15.3	21.5 ± 8.7	0.03
Hospital mortality n (%)	52 (27.4)	51 (29.5)	1 (5.9)	0.04
Calories goal (kcal)	1357 ± 157	1358 ± 156	1348 ± 170	0.81
PN calories (kcal/day)	63 ± 128	67.3 ± 132.9	16.1 ± 33.3	0.0002
EN calories (kcal/day)	1125 ± 304	1111 ± 309	1267 ± 196	0.007
Protein goal (gm)	69.3 ± 18.5	68.4 ± 18.6	78.5 ± 15.5	0.03
PN protein (gm/day)	1.8 ± 5.8	1.9 ± 6.1	0 ± 0	<0.0001
EN protein (gm/day)	57.2 ± 19.4	55.9 ± 19.2	70.8 ± 15.5	0.002

Chi-square test used to compare the differences in each categorical variable.
Student's t-test used to compare the differences in each continuous variable.
P < 0.05 as significance level for statistical tests.

≥80% EN protein prescription had lower hospital mortality rate (23.4% vs 40.3%; P = 0.02), but no difference in ICU mortality, VAP occurrence, MVDs, ICU and hospital LOS (Table 3).

Fig. 1a and Fig. 1b were the association between caloric intake from EN plus PN or EN alone and the probability of 28-day mortality of HNR and LNR groups. HNR elderly had a higher predicted probability of 28-day mortality. As calorie intake increased, 28-day mortality rate decreased. A more obvious trend was found in patients who received EN calories alone (Fig. 1b). Increasing in protein intake (PN plus EN) was not associated with this benefit (Fig. 2a). However, when EN protein intake increased, the 28-day mortality also tended to decrease (Fig. 2b).

When gender, body mass index (BMI), BW loss, and poor intake was adjusted, each point mNUTRIC increased, the MVDs, ICU LOS, and hospital LOS increased by 1.54 days (P = 0.006), 1.18 days (P = 0.028), and 1.52 days (P = 0.046) respectively (Table 4). The OR of ICU and hospital mortality increased when mNUTRIC score increased (ICU mortality OR: 1.71 (1.22–2.39; P = 0.002); hospital mortality OR: 1.64 (1.24–2.15; P < 0.001)) (Table 5).

4. Discussion

The 2016 A.S.P.E.N guidelines for nutritional care in critically ill patients suggested that ICU patients be evaluated for nutritional risk using the NUTRIC score.[10] In previous research on mNUTRIC score in critically ill patients, finding an average mNUTRIC score of 4.4–5.5.[16–20] Our study subjects were MICU mechanically ventilated elderly patients with APACHE II ≥ 15. Only 14 (7.4%) individuals had co-morbidity ≦1. Therefore, the average mNUTRIC score (6.4 ± 1.4) in our study was higher than previous studies with mixed ICU patients aged ≥18 years,[9,14,16,19–24] and the HNR rate was as high as 91.1%.

A previous research indicated that 36% of ICU critically ill patients could achieve ≥80% of prescribed nutrition.[14] Average calorie and protein intake of HNR patients could only reach about 30%–60% of prescription.[16,25] In our study, the results showed that 64% of HNR critically ill elderly patients were able to achieve ≥80% of prescribed calories and protein.

Researches also pointed out that increasing nutrient intake in HNR patients could lower mortality, earlier discharge alive and increased survival.[11,13,15,17,18] Every 1000 kcal/day increase could decrease the 60-day mortality[26] and 2.2 days of LOS.[15] Arabi et al. (2017) compared the patients who achieved 40–60% and 70–100% of prescribed calorie with full protein (from EN plus PN), but found no differences in ICU and hospital mortality, MVDs, VAP, ICU and hospital LOS.[24] Our study showed that HNR critically ill elderly patients who achieved ≥80% EN calorie prescription, had lower ICU and hospital mortality. But who could achieve ≥80% EN protein prescription, had only lower hospital mortality. There were no differences in MVDs, VAP, and ICU and hospital LOS for groups who achieved ≥80% prescribed nutrition or not. These results adhere to what McClave et al. suggested that patients at highest nutrition risk may require advancement to goal feeds as soon as possible when patients could well tolerate EN.[27]

Researches pointed out that increase calorie intake only can lower HNR patients' 28-day mortality but not LNR patients'.[11,13,15] However, Nicolo et al. (2016) showed that it is protein intake not calorie intake (PN plus EN) achieved ≥80% of prescription, can lower mortality rate.[18] Another study outcome indicated that patients received ≥2/3 of prescribed energy and protein (PN plus EN) were associated with a trend of increased 60-day mortality.[23] In our critically ill elderly patients, as calorie intake increased, the 28-day mortality decreased, and a more obvious trend showed in EN group only (Fig. 1b). And only EN protein intake increased, the 28-day mortality decreased (Fig. 2b). Possible reason was our research

Table 3
Comparison of HNR (mNUTRIC score ≥5) critically ill elderly with EN ≥ 80% and <80% of prescribed nutrition.

Characteristics	Percentage of calorie prescription			Percentage of protein prescription		
	≥80% n = 111	<80% n = 62	P value	≥80% n = 111	<80% n = 62	P value
mNUTRIC score	6.5 ± 1.2	7.1 ±1 .1	0.001	6.5 ± 1.2	7.0 ± 1.1	0.02
Start EN (days)	1.1 ± 0.3	2.0 ± 1.0	<0.0001	1.1 ± 0.4	1.9 ± 1.0	<0.0001
VAP n (%)	19 (17.1)	12 (19.4)	0.71	16 (14.4)	15 (24.2)	0.11
MVDs (days)	13.5 ± 11.1	13.6 ± 8.3	0.95	13.0 ± 10.5	14.4 ± 9.6	0.38
ICU LOS (days)	15.2 ± 10.5	14.5 ± 8.5	0.65	14.7 ± 10.0	15.3 ± 9.5	0.73
hospital LOS (days)	26.5 ± 14.6	27.7 ± 16.6	0.61	25.7 ± 14.6	29.1 ± 16.5	0.16
ICU mortality (%)	12 (13.5)	16 (25.8)	0.04	17 (15.3)	14 (22.6)	0.23
Hospital mortality (%)	26 (23.4)	25 (40.3)	0.02	26 (23.4)	25 (40.3)	0.02

Student's t-test used to compare the differences in each continuous variable.
Chi-square test used to compare the differences in each categorical variable.
P < 0.05 as significance level for statistical tests.

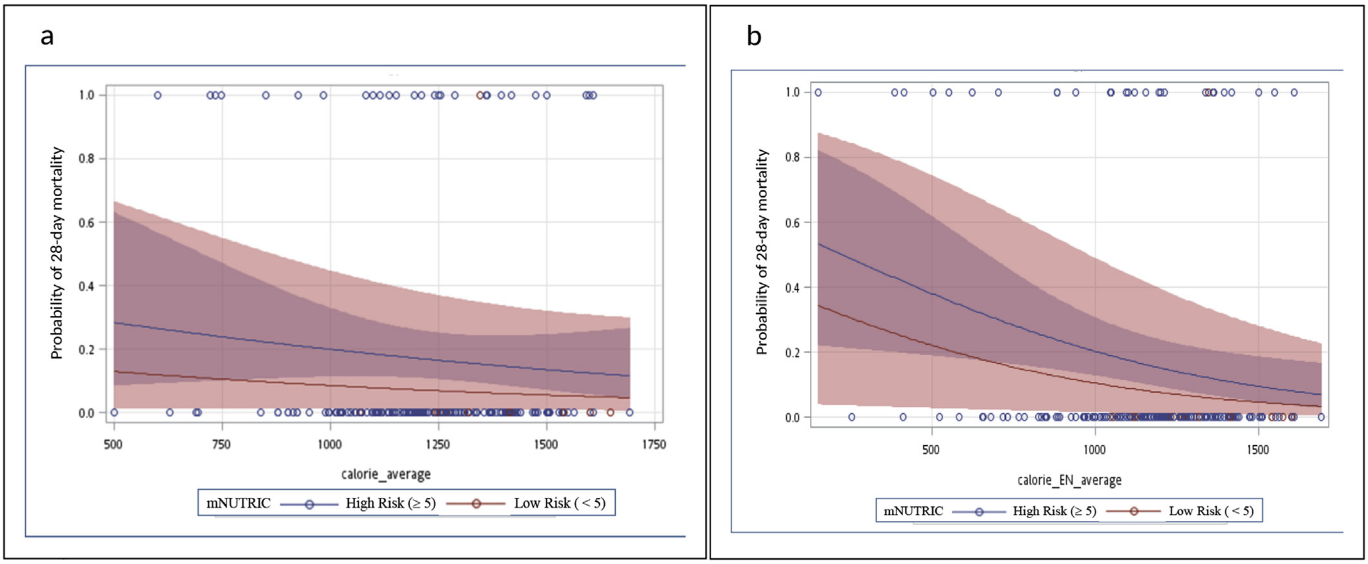

Fig. 1. Predicted probability of 28-day mortality by average calorie intake from PN plus EN (1a) or EN only (1b).

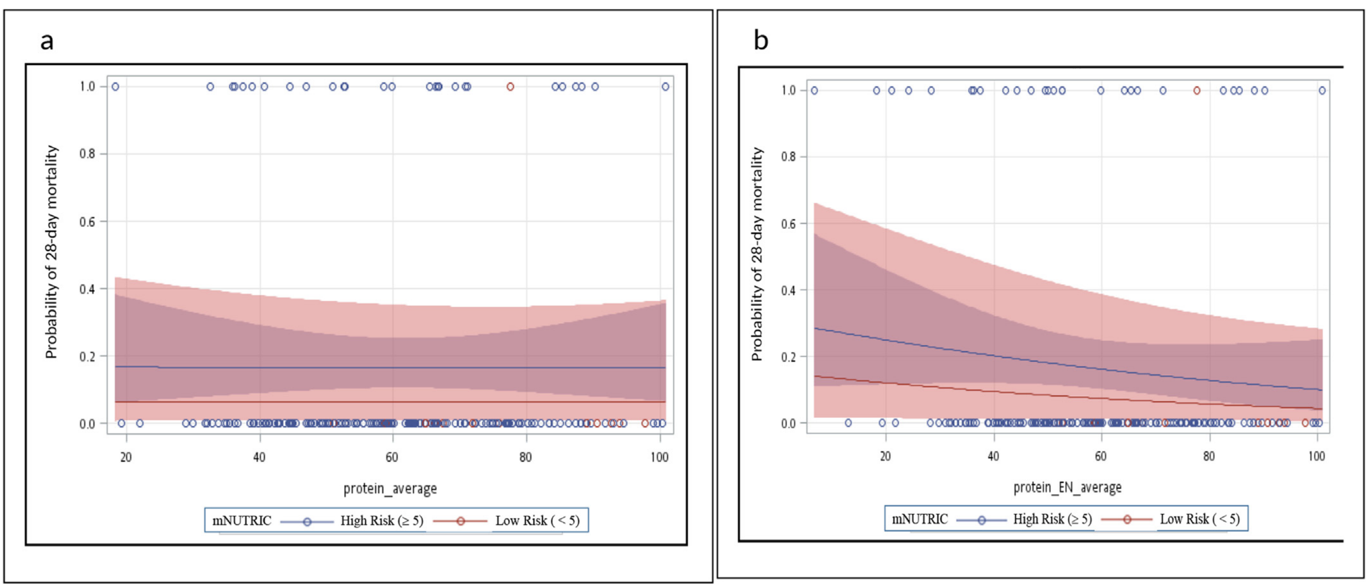

Fig. 2. Predicted probability of 28-day mortality by average protein intake from PN plus EN (2a) or EN only (2b).

Table 4
Prediction of MVDs, ICU and hospital LOS by mNUTRIC score.

outcome	Model 1		Model 2		Model 3	
	β	P-value	β	P-value	β	P-value
MVDs	1.61	0.003	1.59	0.003	1.54	0.006
ICU LOS	1.26	0.016	1.25	0.017	1.18	0.028
Hospital LOS	1.36	0.062	1.35	0.065	1.52	0.046

Multiple Linear Regression was used to predict the effect of mNUTRIC score.
Model 1: adjusted by gender.
Model 2: adjusted by gender, BMI.
Model 3: adjusted by gender, BMI. BW loss, poor intake.

Table 5
The effects of mNUTRIC score on VAP, ICU and hospital mortality.

Outcome	Model 1		Model 2		Model 3	
	OR	95% CI	OR	95% CI	OR	95% CI
VAP	1.11	0.86–1.45	1.12	0.86–1.45	1.14	0.87–1.50
ICU mortality	1.68	1.22–2.32	1.68	1.22–2.32	1.71	1.22–2.39
Hospital mortality	1.59	1.23–2.07	1.60	1.23–2.08	1.64	1.24–2.15

Logistic Regression was used to analyze OR of VAP, ICU and hospital mortality.
Model 1: adjusted by gender.
Model 2: adjusted by gender, BMI.
Model 3: adjusted by gender, BMI. BW loss, poor intake.

only had 17 (8.9%) elderly patients at LNR and our patients had a mean EN intake of 1125 ± 304 kcal and 57.2 ± 19.4 gm proteins per day within 7 ICU days, both achieved ≥80% of prescribed nutrition.

Higher NUTRIC or mNUTRIC score increased 28-day mortality,[11,13,15,19] MVDs,[11,19] delayed in starting EN,[14] increased ICU and hospital LOS[9,19,22] and higher 60-day and 6-month mortality.[13,16] The results of our study showed that for every point increment of the mNUTRIC score, MVDs, ICU and hospital LOS increases by 1.54 days, 1.18 days and 1.52 days, respectively. The average MVDs was 13.2 ± 9.9 days, which was higher than the finding of Moretti (2014) and Arabi (2017) of 8.5–9.0 days.[21,24] The ICU LOS (14.7 ± 9.6 days) and hospital LOS (26.4 ± 14.9 days) were also longer than the results from Mukhopadhyay (2016) and Mendes (2017).[15,19] However the ICU mortality of 16.8% and hospital mortality of 27.4% were lower than results in other studies.[18,21–24] The reasons for these results may be due to our elderly patients could achieve ≥80% of the prescribed calories intake within one week's stay in the MICU. And our patients began to receive NG tube feeding 1.4 ± 0.8 days earlier since admitted to ICU.

4.1. Limitation

The results cannot be extended to all ICU elderly patients due to only MICU elderly patients were included. Adjusted protein and energy prescription for high percentage of renal and diabetic patients caused large standard deviation of actual EN calorie and protein intakes in HNR patient. The number of days of calculation actual PN and EN intakes was 7 days which accounts only half of ICU LOS of study subjects.

5. Conclusion

The rate of HNR was high (91.1%) in the mechanical ventilated critically ill elderly patients assessed by the mNUTRIC. For each point increment of the mNUTRIC, ICU LOS, MVDs, and hospital LOS increase by 1.18 days, 1.54 days, and 1.52 days, respectively. Also the OR of ICU and hospital mortality were 1.71 and 1.64. Critical elderly patients who could achieve ≥80% EN calorie prescription could lower ICU and hospital mortality, and those who achieved ≥80% EN protein prescription could only lower hospital mortality.

Conflicts of interest

The authors have no conflicts of interest relevant to this article.

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