

Greater Protein and Energy Intake May Be Associated With Improved Mortality in Higher Risk Critically Ill Patients: A Multicenter, Multinational Observational Study*

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Objectives: Controversy exists about the value of greater nutritional intake in critically ill patients, possibly due to varied patient nutritional risk. The objective of this study was to investigate whether clinical outcomes vary by protein or energy intake in patients with risk evaluated by the NUTrition Risk in the Critically Ill score.

Design: Prospective observational cohort.

Setting: A total of 202 ICUs.

Patients: A total of 2,853 mechanically ventilated patients in ICU greater than or equal to 4 days and a subset of 1,605 patients in ICU greater than or equal to 12 days.

Interventions: None.

Measurements and Main Results: In low-risk (NUTrition Risk in the Critically Ill, < 5) and high-risk (NUTrition Risk in the Critically Ill, ≥ 5) patients, mortality and time to discharge alive up to day 60 were assessed relative to nutritional intake over the first 12 days using logistic regression and Cox proportional hazard regression, respectively. In high-risk but not low-risk patients, mortality was lower with

greater protein (4-d sample: odds ratio, 0.93; 95% CI, 0.89–0.98; $p = 0.003$ and 12-d sample: odds ratio, 0.90; 95% CI, 0.84–0.96; $p = 0.003$) and energy (4-d sample: odds ratio, 0.93; 95% CI, 0.89–0.97; $p < 0.001$ and 12-d sample: odds ratio, 0.88; 95% CI, 0.83–0.94; $p < 0.001$) intake. In the 12-day sample, there was significant interaction among NUTrition Risk in the Critically Ill category, mortality, and protein and energy intake, whereas in the 4-day sample, the test for interaction was not significant. In high-risk but not low-risk patients, time to discharge alive was shorter with greater protein (4-d sample: hazard ratio, 1.05; 95% CI, 1.01–1.09; $p = 0.01$ and 12-d sample: hazard ratio, 1.09; 95% CI, 1.03–1.16; $p = 0.002$) and energy intake (4-d sample: hazard ratio, 1.05; 95% CI, 1.01–1.09; $p = 0.02$ and 12-d sample: hazard ratio, 1.09; 95% CI, 1.03–1.16; $p = 0.002$). In the 12-day sample, there was significant interaction among NUTrition Risk in the Critically Ill category, time to discharge alive, and protein and energy intake, whereas in the 4-day sample, the test for interaction was not significant.

Conclusions: Greater nutritional intake is associated with lower mortality and faster time to discharge alive in high-risk, longer stay patients but not significantly so in nutritionally low-risk patients. (*Crit Care Med* 2017; 45:156–163)

Key Words: energy; intensive care unit; mortality; protein; time to discharge alive

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Severe illness or injury results in ICU admission for more than 5 million people in the United States each year, with costs that represent 13% of total hospital costs (1). When the physiologic stress associated with critical illness is severe, muscle protein and energy depots may be limited to a point where survivability is threatened or rehabilitation care is needed (2).

A controversy has arisen over the risks versus benefits from enhanced delivery of protein (3, 4) and energy (5) in critically ill patients. Reports have suggested that increased protein (6, 7) or energy intake (8, 9) is harmful, whereas others find benefit in greater protein (10–13) or energy intake (12, 14–16) against various negative clinical outcomes, or no benefit (17).

One explanation for these widely divergent findings might be differences in the patient populations in terms of nutritional risk. The NUTrition Risk in the Critically Ill (NUTRIC) score was designed to identify critically ill patients who would have the greatest survival benefit relative to energy intake (18). A further analysis of data from a different dataset found greater benefit of energy intake in patients with higher NUTRIC scores (14). However, the NUTRIC score has not been evaluated in a large, diverse cohort or assessed relative to protein intake or time to discharge alive (TDA).

The purpose of this study was to determine whether intake of protein or energy interacts with high versus low NUTRIC score to impact 60-day mortality or TDA in the International Nutrition Survey 2013 database. We hypothesized that greater intake would be beneficial to survival and shorter TDA, particularly in patients with a higher NUTRIC score.

MATERIALS AND METHODS

This analysis was undertaken using the International Nutrition Survey 2013 database, a web-based multinational survey in patients admitted to ICUs (19, 20), under regulatory approval by both the University of Pennsylvania and Queens University, Ontario, Canada. In brief, prospective data collection for 4,040 patients in 202 ICUs began on May 15, 2013. Data from ICU admission with complete ascertainment of mortality, ICU, and hospital length of stay (LOS) were obtained for 20 consecutive patients in each ICU (excluding those in the ICU < 72 hr) for 60 days. Both goal intake and actual delivery of protein and energy from feedings and energy-containing medications for 12 consecutive days were included. Participating sites established goals for protein and energy intake based on local practice patterns. We evaluated protein and energy intake actually delivered to the patient as a percentage of these goals.

The current sample was restricted to those patients who remained in the ICU at least 4 days in order to obtain more uniform acuity by excluding patients with very short LOS or expectation of imminent demise ($n = 2,853$). Patients discharged before day 4 ($n = 1,097$) and those who died ($n = 116$) were excluded. A sensitivity analysis was conducted in the subset of patients who remained in the ICU at least 12 days ($n = 1,605$) and for whom 12 full days of data about protein and energy intake were available.

Because interleukin-6 was not available, the NUTRIC score ranged from 0 to 9, similar to that reported in the study by Rahman et al (14). Patients with NUTRIC scores greater than or equal to 5 were considered to be of high risk and those with less than 5 to be of low risk. Descriptive data were reported by the ICU sample (4/12 d) with continuous variables as mean \pm SD and categorical variables as frequency (%).

A binomial distribution (by NUTRIC category) comparing protein (or energy) intake on patient mortality was specified using generalized estimating equations controlled for ICU geographic region while accounting for clustering at the ICU unit level. To avoid collinearity, analyses were not adjusted for variables used to calculate the NUTRIC score (Acute Physiology and Chronic Health Evaluation [APACHE]

II [21], Sepsis-Related Organ Failure Assessment [SOFA] [22] at ICU admission, age, number of comorbid conditions, and days in the hospital prior to ICU admission [Supplementary Table 1, Supplemental Digital Content 1, <http://links.lww.com/CCM/C169>]). For the mortality analysis in the 4-day sample, an adjustment variable of nutrition evaluable days was used to account for the fact that patients who leave the ICU earlier will have had fewer days of feeding. An additional sensitivity analysis was done on the 4-day and 12-day samples excluding patients with a mean protein or energy intake of more than 100% to assess the potential influence of outliers. Logistic regression was used to evaluate the interaction between NUTRIC category and protein (or energy) intake on patient mortality. For each model, the R^2 and the C -statistic were used to assess goodness of fit (Supplementary Table 2, Supplemental Digital Content 1, <http://links.lww.com/CCM/C169>). A sensitivity analysis was done with adjustment for the type of hospital admission (Supplementary Table 3, Supplemental Digital Content 1, <http://links.lww.com/CCM/C169>).

To take into account the competing risk of death on TDA, for patients who died prior to 60 days and those remaining in the ICU at day 60, TDA was censored to 61 days. TDA was reported as hazard ratio (HR) where higher HR indicates shorter TDA. In the 4-day sample, TDA was not adjusted for nutrition evaluable days to avoid collinearity. The interaction between TDA, protein (or energy) intake, and NUTRIC group was evaluated by Cox proportional hazards while adjusting at the ICU unit level. We also did a sensitivity analysis of LOS among survivors.

RESULTS

Baseline descriptive characteristics of the population are shown in Table 1. The sample of 2,853 patients in the ICU greater than or equal to 4 days had a mean age of 61.2 years (59.7 for the 1,605 patients in the 12-d sample), and the majority were admitted to an ICU for medical (65%) or emergency surgery (27%) care (66% and 27%, respectively, for the 12-d sample). Mortality was 30% (25% for the 12-d subsample). Patients achieved only 59% of goal protein and 62% of goal energy intake (65% and 69%, respectively, for the 12-d subsample). Enteral nutrition (EN) was used in 75.5%, parenteral nutrition (PN) in 8.7%, both EN and PN in 13.8%, and neither in 2% of patients in the 4-day sample (76.9%, 6.5%, 16.1%, and 0.5%, respectively, in the 12-d sample). The mean NUTRIC score was 4.8 in both samples.

Protein Intake Versus Mortality and TDA

Mortality and TDA outcomes relative to protein intake and NUTRIC risk group are shown in Table 2. There was no significant interaction between NUTRIC category, protein intake, and mortality in the 4-day sample ($p = 0.560$). In the adjusted analysis for high-risk patients in the 4-day sample, the odds of death decreased significantly by 6.6% ($n = 1,636$; odds ratio [OR], 0.934; 95% CI, 0.894–0.975; $p = 0.003$) with each 10% increase in protein intake relative to goal (Fig. 1). In the adjusted analysis in low-risk patients, mortality was not

TABLE 1. Characteristics of Patients in ICU Four or More Days and in ICU Twelve or More Days

Characteristic	Sample in ICU ≥ 4 d	Subsample in ICU ≥ 12 d
No. of subjects	2,853	1,636
Age (yr)	61.2 (17.3)	59.7 (17.4)
Gender, <i>n</i> (%)		
Male	1,739 (60.9)	1,003 (62.5)
Female	1,114 (39.1)	602 (37.5)
Days in hospital prior to ICU admission	4.3 (14.3)	4.5 (16.0)
No. of comorbidities	2.0 (1.8)	2.0 (1.8)
Admission category, <i>n</i> (%)		
Medical	1,845 (64.7)	1,059 (66.0)
Surgical elective	241 (8.5)	121 (7.5)
Surgical emergency	767 (26.9)	425 (26.5)
Acute Physiology and Chronic Health Evaluation II	22.5 (8.5)	22.2 (7.9)
Sepsis-Related Organ Failure Assessment	8.9 (3.7)	9.0 (3.7)
NUTrition Risk in the Critically Ill score	4.8 (2.0)	4.8 (2.0)
Body mass index (kg/m ²)	27.0 (7.5)	27.5 (7.6)
60-d mortality, <i>n</i> (%)	879 (30.8)	402 (24.6)
Goal protein intake (g/kg/d)	1.2 (0.3)	1.2 (0.3)
Actual protein intake (g/d)	51.2 (25.8)	57.0 (24.0)
Actual protein intake (% goal/d)	58.9 (25.9)	64.5 (23.7)
Goal energy intake (kcal/kg/d)	24.1 (5.5)	24.0 (5.6)
Actual energy intake (kcal/d)	1,100.0 (409.0)	1,200.0 (500.0)
Actual energy intake (% goal/d)	62.4 (25.8)	68.5 (23.1)
Nutrition evaluable days (d)	9.93 (2.76)	12.0

Data as mean (sd) or *n* (%).

significantly different by the level of protein intake ($n = 1,217$; OR, 0.998; 95% CI, 0.936–1.064; $p = 0.944$).

There was a significant interaction in the 12-day sample between NUTRIC category, protein intake, and mortality ($p = 0.02$). In the adjusted analysis for high-risk patients in the 12-day sample, the odds of death decreased significantly by 10.1% ($n = 891$; OR, 0.899; 95% CI, 0.84–0.963; $p = 0.003$) with each 10% increase in protein intake relative to goal but not significantly in the low-risk patients ($n = 711$; OR, 1.052; 95% CI, 0.954–1.156; $p = 0.313$).

There was no significant interaction between NUTRIC category, protein intake, and TDA in the 4-day sample ($p = 0.155$). In the adjusted model, TDA was significantly shorter by 5.1% ($n = 1,636$; OR, 1.051; 95% CI, 1.012–1.091; $p = 0.01$) for each 10% increase in protein intake relative to goal in high-risk patients but not in low-risk patients ($n = 1,217$; OR, 1.013; 95% CI, 0.975–1.052; $p = 0.506$). Median (interquartile range [IQR]) LOS among survivors was 35.71 (19.75–61.00) days.

There was a significant interaction between NUTRIC category, protein intake, and TDA in the 12-day sample ($p = 0.039$). In the adjusted analysis in high-risk patients, TDA was significantly shorter by 9.2% ($n = 891$; HR, 1.092; 95% CI, 1.032–1.155; $p = 0.002$) for each 10% increase in protein intake relative to goal but not significantly in the low-risk patients ($n = 711$; HR, 0.99; 95% CI, 0.946–1.056; $p = 0.984$). Median (IQR) LOS among survivors was 51.81 (28.53–61.00) days.

The results for the sensitivity analyses excluding patients with mean protein intake greater than 100% goal were consistent with the analysis including all patients (data not shown). Thus, potential outliers did not have a significant effect on the results.

Energy Intake Versus Mortality and TDA

Mortality and TDA outcomes relative to energy intake and NUTRIC risk group are shown in Table 2. There was no significant interaction between NUTRIC category, energy intake, and mortality in the 4-day sample ($p = 0.341$). In the adjusted

TABLE 2. Protein and Energy Intake as Predictor of Mortality and Time to Discharge Alive Stratified by NUTRITION Risk in the Critically Ill Score

Sample in ICU ≥ 4 d				
Outcome	Protein Intake (per 10% of Goal)		Energy Intake (per 10% of Goal)	
	Low NUTRIC Score (n = 1,217)	High NUTRIC Score (n = 1,636)	Low NUTRIC Score (n = 1,217)	High NUTRIC Score (n = 1,636)
Mortality ^{a,b}	0.952 (0.895–1.011)	0.930 (0.892–0.969) ^c	0.962 (0.904–1.023)	0.927 (0.893–0.962) ^c
Adjusted ^d	0.998 (0.936–1.064)	0.934 (0.894–0.975) ^e	1.011 (0.946–1.079)	0.929 (0.893–0.966) ^e
TDA ^{f,g}	0.970 (0.936–1.006)	1.004 (0.967–1.043)	0.956 (0.921–0.992) ^e	0.995 (0.959–1.032) ^e
Adjusted ^d	1.013 (0.975–1.052)	1.051 (1.012–1.091) ^e	0.998 (0.958–1.039)	1.045 (1.007–1.085) ^e

Sample in ICU ≥ 12 d				
Outcome	Protein Intake (per 10% of Goal) ^h		Energy Intake (per 10% of Goal) ^h	
	Low NUTRIC Score (n = 711)	High NUTRIC Score (n = 891)	Low NUTRIC Score (n = 711)	High NUTRIC Score (n = 891)
Mortality ^{a,b}	1.059 (0.964–1.165)	0.913 (0.853–0.977) ^e	1.069 (0.975–1.173)	0.909 (0.854–0.967) ^e
Adjusted ^d	1.052 (0.954–1.156)	0.899 (0.84–0.963) ^e	1.067 (0.967–1.178)	0.884 (0.829–0.941) ^c
TDA ^{f,g}	0.963 (0.913–1.016)	1.062 (1.002–1.126) ^e	0.937 (0.888–0.989) ^e	1.048 (0.990–1.109)
Adjusted ^d	0.999 (0.946–1.056)	1.092 (1.032–1.155) ^e	0.981 (0.925–1.040)	1.091 (1.032–1.155) ^e

NUTRIC = NUTRITION Risk in the Critically Ill, TDA = time to discharge alive.

^aEvaluated by general estimating equation with outcome of mortality by day 60 after ICU admission.

^bInteraction between protein (or energy) intake, NUTRITION Risk in the Critically Ill (NUTRIC) group, and mortality evaluated by logistic regression.

^c*p* value significant at the 0.0001 level.

^dAdjusted for ICU geographic region. Sample in ICU ≥ 4 d also adjusted for nutrition evaluable days when outcome was mortality.

^e*p* value significant at the 0.05 level.

^fEvaluated by Cox proportion hazardous model with outcome of time to discharge alive (TDA) by day 60 after ICU admission.

^gInteraction between protein (or energy) intake, NUTRIC group, and TDA evaluated by Cox proportional hazards.

^hInteraction term *p* value significant at the 0.05 level.

analysis of patients in the 4-day sample, for high-risk patients, the odds of death significantly decreased 7.1% ($n = 1,636$; OR, 0.929; 95% CI, 0.893–0.966; $p < 0.001$) with each 10% increase in energy intake relative to goal (**Fig. 2**) but not in the low-risk patients ($n = 1,217$; OR, 1.011; 95% CI, 0.946–1.079; $p = 0.754$).

There was a significant interaction between NUTRIC category, energy intake, and mortality in the 12-day sample ($p = 0.010$). In the adjusted analysis for high-risk patients, the odds of death significantly decreased by 11.6% ($n = 891$; OR, 0.884; 95% CI, 0.829–0.941; $p < 0.001$) with each 10% increase in delivery of goal energy intake but not in the low-risk patients ($n = 711$; OR, 1.067; 95% CI, 0.967–1.178; $p = 0.194$).

There was no significant interaction between NUTRIC category, energy intake, and TDA in the 4-day sample ($p = 0.843$). In the adjusted model, TDA was significantly shorter by 4.5% ($n = 1,636$; HR, 1.045; 95% CI, 1.007–1.085; $p = 0.019$) for each 10% increase in energy intake relative to goal in high-risk patients but not in low-risk patients ($n = 1,217$; HR, 0.998; 95% CI, 0.958–1.039; $p = 0.914$).

There was a significant interaction between NUTRIC category, energy intake, and TDA in the 12-day sample ($p = 0.01$).

In the adjusted model, TDA was significantly shorter by 9.1% ($n = 891$; HR, 1.091; 95% CI, 1.032–1.155; $p = 0.002$) for each 10% increase in energy intake relative to goal in high-risk patients but not significantly in the low-risk patients ($n = 711$; HR, 0.981; 95% CI, 0.925–1.040; $p = 0.517$).

DISCUSSION

In a large, diverse sample of patients who stay in the ICU at least 12 days, lower mortality and shorter TDA are associated with greater protein and energy intake in the high NUTRIC group but not significantly in the low NUTRIC group patients. Lower mortality and shorter TDA were also associated with increased protein and energy intake in the 4-day sample in high-risk but not low-risk risk patients, but the test for interaction was not significant. This study suggests that more successful delivery of goal protein and energy intake is associated with the strongest improvement in clinical outcomes in longer stay, high-risk patients.

These findings about the benefit of greater energy intake on survival agree with a series of prior studies (14, 16, 18), even though the energy intake provided to patients was only 50% of goal (16), and the survival was observed over 28 (14, 18) and

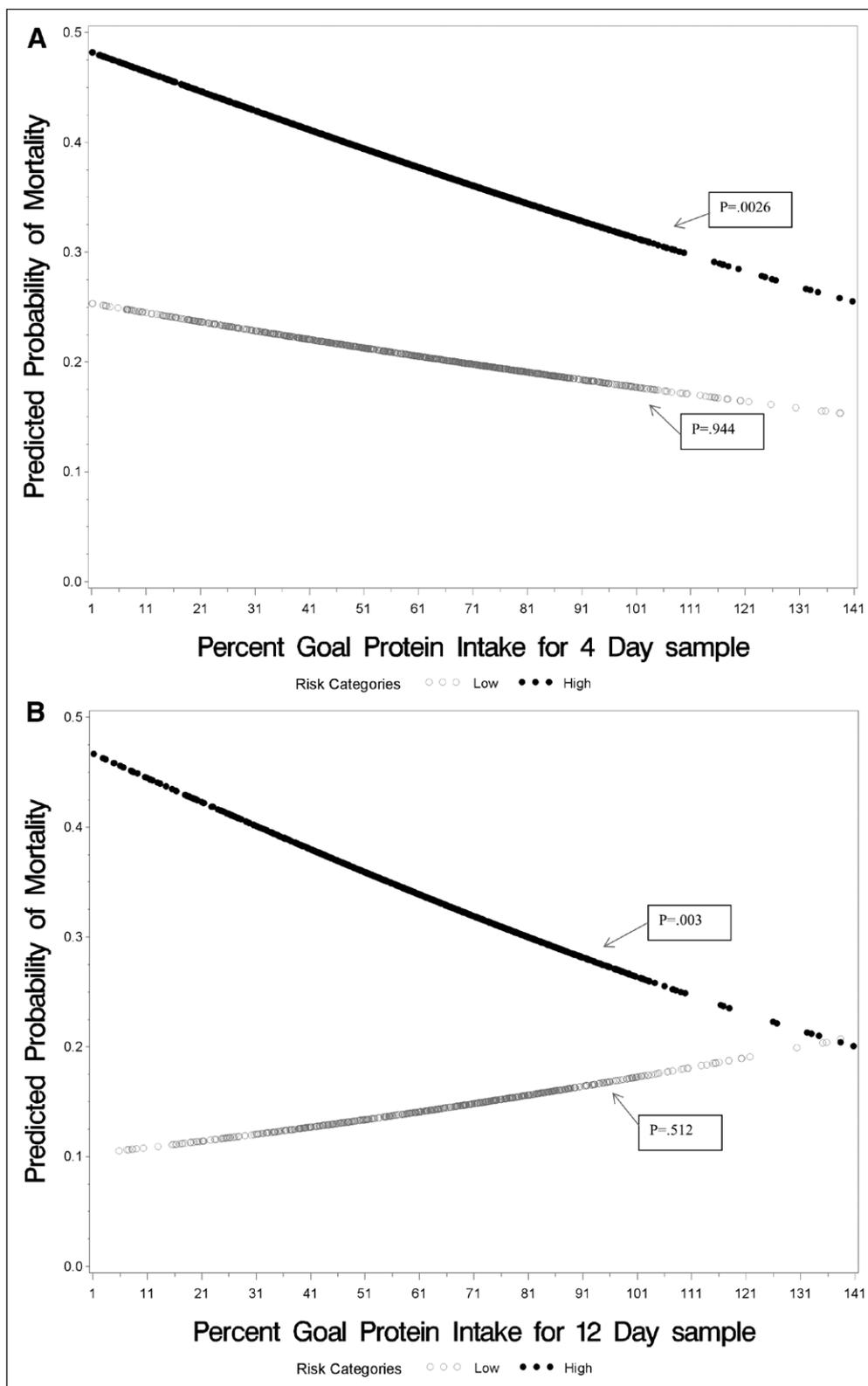


Figure 1. Sixty-day mortality, odds ratio (95% CI) for achieving percentage of goal protein intake by low versus high NUTRITION Risk in the Critically Ill score.

180 days (14, 16). Greater benefit from adequate energy intake in higher NUTRIC score patients was also observed by Rahman et al (14). This current study expands the finding by Rahman et al (14) with outcomes of 60-day mortality and TDA associated with

als were considerably beyond that delivered to patients in the current study.

A consensus is building about the beneficial impact of protein rather than full energy intake in ICU patients (3, 4). In a

benefit from greater protein (and energy) intake in high-risk but not low-risk patients, particularly in the 12-day sample. In fact, the observation of differences in high-risk but not low-risk patients from a much larger, more diverse population from 202 ICUs in varied international locations enhances the generalizability of the NUTRIC score and this study's findings.

Some investigators have suggested that greater energy intake is harmful. The Early Parenteral Nutrition Completing Enteral Nutrition in Adult Critically Ill Patients trial randomized 4,630 patients to day 3 versus day 8 initiation of PN (23). Mortality was not different but the early PN group had more infections and longer ICU stay (though the ICU LOS of 3–4 and 2 d of mechanical ventilation suggest a low-risk population). The late PN group received ~ 10 kcal/kg/d largely from EN, whereas the early PN group had ~ 30 kcal/kg/d (7). The Intensive Nutrition in Acute Lung Injury (INTACT) trial randomized 78 patients to a target of 30 kcal/kg/d during the entire hospital admission, and achieved intake of 25 kcal/kg/d in the intervention group versus 16.7 kcal/kg/d in the control group (9). In the INTACT trial, more aggressive feeding resulted in early study termination due to greater mortality in the intervention group. However, this trial was criticized for excessive energy intake and for the possibility that early mortality may have been due to some unmeasured process, such as refeeding syndrome (24). Regardless, the levels of intake in these tri-

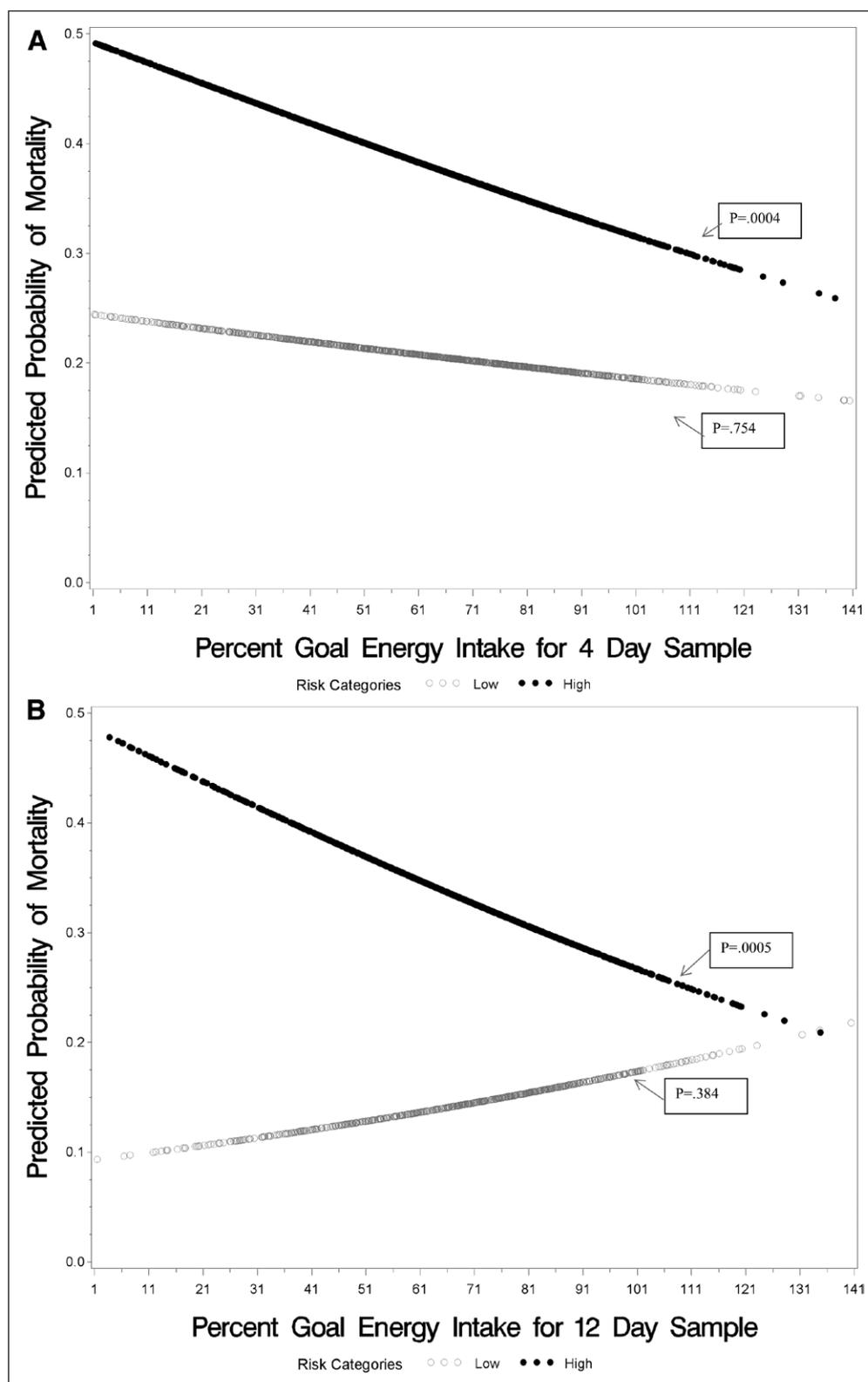


Figure 2. Sixty-day mortality, odds ratio (95% CI) for achieving percentage of goal energy intake by low versus high NUTrition Risk in the Critically Ill score.

cohort of 113 patients, Allingstrup et al (11) reported lower 28-day mortality per gram of protein intake (HR, 0.98; 95% CI, 0.97–0.99) though greater energy intake did not provide significant benefit. In a cohort of 726 nonseptic ICU patients, mortality was lower with greater protein intake (OR, 0.80; 95% CI,

0.67–0.95) but increased with energy overfeeding (OR, 1.89; 95% CI, 1.19–3.02) (13). Nicolo et al (10) observed that delivery of more than or equal to 80% of goal protein intake was associated with a 40% reduction in mortality, whereas energy delivery was not. This current study agrees about the importance of protein intake to mortality outcomes but also found improved energy intake to be beneficial in high-risk patients.

Several studies have suggested that lower energy intake was not important to outcome. In the Permissive Underfeeding versus Target Enteral Feeding in Adult Critically Ill Patients trial with 894 patients randomized to delivery of 40–46% versus 70–100% of energy goal (is-nitrogenous feeding) using EN, mortality was not different (17). The Early versus Delayed Enteral Nutrition trial randomized 1,000 patients with acute lung injury to trophic versus full feedings (400 vs 1,300 kcal/d), with no difference in mortality, pneumonia, or infections over 6 days (25). While not designed to test the impact of a specific level of feeding, no difference in 60-day mortality was noted with early PN providing 1,500 kcal and 55 grams of protein daily versus lower intake levels by standard care (26). However, the ICU LOS trended lower and the quality of life was significantly better in the group with greater intake. In a randomized controlled trial (RCT) of 305 patients comparing supplemental PN versus EN, the 28-day occurrence rate of nosocomial infections was lower in the supplemental PN group that received 28 kcal/kg/d (103% goal) than the EN group with 20 kcal/kg/d (77% goal) (27). In a second RCT comparing EN versus PN in 2,388 ICU patients, with delivery of 15–18 kcal/kg/d and protein 0.6 g/kg/d, there was no difference in 30-day mortality (28). What is missing in the analysis of these RCTs of various feeding strategies is an

explication of the nutrition risk of included patients and how the treatment effect may have varied based on nutrition risk. In our analysis of a much larger, more diverse observational study, lower mortality was associated with greater protein and energy intake, particularly in the longer stay, higher NUTRIC score patients.

This analysis has several strengths. The sample size is large, and all data collection were prospective. Patients in the ICU 12 days had daily collection of protein and energy intake from all sources. We do not know exactly how the protein and energy goals were determined, as they were not based on a fixed, study-directed protocol. This feature is an important characteristic of this study as it reflects real-world nutrition support practice in today's ICUs, making the findings more generalizable. All patients had complete ascertainment of ICU LOS and mortality through day 60. Conservative statistical approaches reduced the risk of bias. Confirmation of the findings in the 4-day sample with the sensitivity analysis of the subgroup that remained in the ICU 12 or more days, with generally stronger relationships, is an important strength. Sensitivity analyses also confirmed the TDA findings and the lack of influence of outliers.

One limitation of this sample is the limited success in achievement of goal protein and energy intake, with less than two out of three of goal levels achieved in either sample. Achieving goal intake using EN can be challenging in more severely ill or injured patients who may experience ileus, multiple intra-abdominal procedures, or intolerance at greater rates than in other patients. However, in this study, similar to Rahman et al (14), the difference in intake between high and low NUTRIC groups was very small (2–3% difference, data not shown), suggesting that the dynamic of intolerance did not play a powerful role in limiting protein/energy intake. Even though the levels of intake reported here are similar to many other studies, this study does not provide enough information on outcomes of patients with higher levels of protein and energy intake. In fact, the maximum intake was 150% of goal, and few patients received either protein or energy greater than 100% of goal. However, a sensitivity analysis suggested that high intake outliers did not influence the findings. Finally, while we observe significant associations with increased nutritional intake and mortality in the 4-day sample in the nutritionally high-risk group but not in the low-risk group, the lack of a significant interaction term weakens the inferences we can make about this association.

We recognize the inherent risk in this survey that data submitted by volunteers at study ICUs may not be fully accurate. There may also be other variables important to predicting mortality or TDA that were not available in this survey. Mortality was greater in the 4-day (30.8%) than the 12-day (24.6%) sample, though the NUTRIC, APACHE II, and SOFA scores were not different. Though APACHE II and SOFA describe severity of disease, they may not describe mortality risk adequately in such a diverse ICU sample where differences in nutrition support practice and ICU management patterns also play a critical role. Nevertheless, since prediction about LOS at ICU admission is difficult, efforts to optimize nutritional intake should be made in all patients mechanically ventilated more than 4 days

with the understanding that the patients who stay the longest will derive the greatest benefit.

CONCLUSION

In conclusion, this study, in a large, diverse, real-world ICU sample suggests that patients who have higher NUTRIC scores at ICU admission may benefit most significantly from greater protein and energy intake, especially during longer ICU stays, whereas those with lower NUTRIC scores do not have worse mortality or TDA with greater intake. Since it is not possible to predict which patients will remain in the ICU longer, the best policy may be to attempt to feed all patients optimally with an understanding that low-risk and short-stay patients are less likely to benefit significantly from near-goal protein or energy intake. Future clinical trials should determine the most optimal levels of protein and energy intake in high- versus low-risk ICU patients.

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