Association of Protein-Calorie Intake and Clinical Outcomes among Critically-ill COVID-19 Patients: A Retrospective Study

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Abstract

Background: Patients admitted due to severe COVID-19 pneumonia are at high risk for malnutrition and worsening of their clinical condition. Patients with type 2 diabetes admitted for COVID-19 pneumonia have an increased risk for poor clinical outcomes. Adequate nutrition is recommended to augment a strong immune response. The American Society of Parenteral and Enteral Nutrition (ASPEN), Philippine Society of Parenteral and Enteral Nutrition (PHILSPEN), European Society of Parenteral and Enteral Nutrition (ESPEN) recommend an energy intake goal of 15-20 kcal/kg actual body weight (ABW) per day or 70-80% of caloric requirements after the acute phase of critical illness, with recommended protein intake of 1.2-2.0 g/kg ABW per day. This study aims to provide an association between calorie and protein intake with negative clinical outcomes.

Methods: This is a retrospective cohort study of 55 mechanically ventilated SARS COV-2 RT-PCR positive patients admitted in the critical unit of Chinese General Hospital between April 1, 2020 to December 30, 2020. Clinical profile taken include: sex, age, height weight, BMI, comorbidities, and components of the modified SOFA score and APACHE II score. Calorie and protein intake from day 3 to day 7 of ICU admission were taken. Clinical outcome data were in-hospital mortality, number of days of ICU stay, hospital admission, vasopressor use and mechanical ventilation.

Results: Majority of the patients included in the study were male, elderly, overweight, and with comorbidities such as hypertension, diabetes, and chronic kidney disease. Majority of the patients were on mechanical ventilation and on vasopressors for more than 1 week. In-hospital mortality accounted for 65.5% of cases. For patients without diabetes, calorie intake was 16.9 kcal/kg/day and protein intake was 0.72 g/kg/day, while patients with diabetes had a calorie intake of 20.2 kcal/kg/day and protein intake of 0.86 g/kg/day. Based on the 70% cutoff, patients with diabetes were noted to have been provided with more adequate protein (P-value= 0.027). Higher caloric intake was inversely associated with in-hospital mortality among patients younger than 75 years old (P-value=0.026) and among patients with diabetes (P-value=0.003). Higher calorie intake was also significantly associated with decreased duration of pressors among patients with diabetes (P-value=0.021). Higher protein intake positively associated with the number of days admitted among patients with lower modified SOFA scores (P-value=0.041) and among patients with diabetes (P-value=0.021). All other associations did not display significant results (all P-values>0.05).

Conclusion: Based on this study, increased caloric intake was associated with increased survival among patients less than 75 years, but no association was found in patients 75 years and older. Among patients with lower mortality risk, increased protein intake was associated with longer duration of hospital stay, however patients with higher risk had higher in-hospital mortality regardless of protein and calorie intake. Among patients with diabetes, higher calorie intake was associated with increased survival and decreased duration of pressor requirement, while increased protein was associated with longer length of hospital stay. Treatment for COVID-19 pneumonia, however, was not established at this time and there was significant in-hospital mortality among these mechanically ventilated patients.

Keywords: *Protein-calorie intake, COVID-19, outcome, retrospective study, mechanically ventilated, critical care*

Introduction

COVID-19 pneumonia is a widespread disease that frequently necessitates mechanical ventilation and ICU admission. Progression of illness has been associated with hyperglycemia and medical malnutrition. The American Society of Parenteral and Enteral Nutrition (ASPEN), the European Society of Parenteral and Enteral

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Nutrition (ESPEN), and the Philippine Society of Parenteral and Enteral Nutrition (PHILSPEN) have released guidelines for the provision of adequate nutrition in COVID-19 pneumonia, however they are not based on direct evidence. This research aims to determine the association of calorie and protein intake with clinical outcomes, such as mortality, length of ICU stay, days on vasopressors, in patients with diabetes and without diabetes admitted for COVID-19 pneumonia.

The severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) is a worldwide phenomenon, affecting more than 180 million people worldwide, with more than 530,000 confirmed cases in the Philippines to date. The World Health Organization reports a worldwide case fatality rate of 2.1%, the highest of which are from the European region. In the Western Pacific region, the Philippines has the highest case fatality rate of 1.8%, with 0.1% of total cases being treated in an intensive care unit.[1] This pandemic is overwhelming critical care units worldwide because of the frequent progression to severe disease and respiratory failure. The cornerstone of management of severe disease is supportive therapy with adequate nutrition.

In critical illness, increased metabolic demands can lead to rapid and significant breakdown of lean body mass to provide precursor amino acids. This contributes to organ dysfunction and poor clinical outcomes. Adequate nutrition plays an important role in modulating inflammatory responses, maintaining immune function, slowing skeletal muscle catabolism, and promoting tissue repair. Studies have demonstrated that critically ill patients admitted at the ICU for more than 48 hours are at risk of underfeeding and malnutrition.[2,3] Additionally, malnutrition in hospitalized COVID-19 patients has been reported in chronic diseases, such as diabetes, chronic obstructive pulmonary disease, renal insufficiency, cardiovascular diseases or dementia, and has been associated with other risk factors such as socio-economic status or frailty.[4] Prolonged immobilization in the intensive care unit consequently results in muscle mass losses, prolonging recovery of patients.

Several observational studies have suggested the association of adequate calorie and protein intake with reduced mortality, hospital stay, time on mechanical ventilation, risk for infection, and length of ICU stay. Villet et al (2005) reported a strong association of cumulated energy deficit in the ICU stay with longer duration of hospital stay, antibiotics, mechanical ventilation, and infections.[5] Assis et al (2016) and Hsu et al (2018) associated a protein-calorie intake of more than 75% and 80% with clinical outcomes such as shorter hospital stay, decreased ICU mortality, and decreased risk for infection.[6,7] Compher et al (2017) and Jung et al (2018) showed that high risk or severely malnourished patients who had higher protein-calorie intake had lower mortality and decreased duration of hospital stay.[8]

In COVID-19, patients manifest with severe respiratory infections, which induce inflammation and hypercatabolism, with increased energy expenditure linked to ventilatory work, in turn increasing overall energy and protein requirements. Additionally, patients present with anorexia due to infection, dyspnea, dysosmia or dysgeusia, and are at high risk for malnutrition.[9] Physical immobility during the infection also leads to rapid muscle wasting and possibility of worsening malnutrition. A study conducted in Wuhan, China demonstrated a high prevalence of malnutrition among elderly patients with COVID-19 pneumonia.[10] The patients in the study were mostly male with a median age of 68 years old, median BMI was 24.8 kg/m^2, and majority presented with comorbidities such as diabetes and hypertension. Malnutrition was attributed to anorexia, nausea, vomiting, and diarrhea, hypoalbuminemia, and hypermetabolism.[10] Overfeeding is also harmful in critically ill patients since it can lead to increased levels of pCO_2, delayed respiratory of weaning, and the possibility of pulmonary edema and arrhythmias.[11]

Patients with diabetes have a two-fold risk of developing severe COVID-19 pneumonia, with increased risk of ICU admission.[12] The pathophysiologic process involves chronic hyperglycemia and insulin resistance, which influences immune response, fluid balance, inflammation, and portends to overall poor clinical outcomes. Additionally, long-term microvascular complications such as retinopathy, nephropathy, neuropathy, or macrovascular complications such as ischemic heart disease, stroke and peripheral vascular disease, ultimately contribute to a worse prognosis in these patients. A study by Bode et al (2020) reported diabetes and hyperglycemia without prior diabetes as strong predictors for mortality.[13]

In the critically ill mechanically ventilated patients, the recommendation is measurement of energy expenditure using indirect calorimetry. However, in the absence of indirect calorimetry, predictive weight-based equations of 20-25 kcal/kg/day in the critically ill, serve as the simplest and most practical option. The American Society of Parenteral and Enteral Nutrition (ASPEN) and the Philippine Society of Parenteral and Enteral Nutrition (PHILSPEN) released recommendations entailing nutrition timing and dose in the management of severely ill COVID-19 pneumonia patients. Due to the lack of direct evidence on patients with COVID-19, the recommendations were based on indirect evidence from critically ill patients with sepsis and ARDS.14 In the acute phase of illness, hypocaloric nutrition of less than 70% total energy expenditure is recommended. After which, the energy goal is 15-20 kcal/kg actual body weight (ABW) per day or 70-80% of caloric requirements, with recommended protein intake of 1.0-2.0 g/kg ABW per day.[14,15] The European Society of Parenteral and Enteral Nutrition (ESPEN) recommends achieving 80-100% of the goal caloric intake and similar protein requirements.[16] The provision of adequate protein intake is being recommended to overcome anabolic resistance in older age and critical illness. The ASPEN guidelines on critical illness nutrition recommends provision of >80% of estimated or calculated goal energy and protein within 48-72 hours of admission to achieve the clinical benefit of enteral nutrition over the first week of hospitalization.[2]

Survival was noted when protein intake of >1.3g/kg/day was administered, resulting in a gain of 1% survival for each 1g of protein.[13]

Significance of the Study. Results of this study may serve as direct evidence to support both local and international guidelines for the provision of adequate nutrition to critically ill COVID-19 pneumonia patients.

Objectives

General Objective

To determine association of protein-calorie intake and negative clinical outcomes among mechanically-ventilated patients with COVID-19 pneumonia

Specific Objectives

1. To describe the clinical profile and disease severity (APACHE II and modified SOFA score) of mechanically-ventilated patients admitted for COVID-19 pneumonia
2. To determine the mean calorie and protein intake and adequacy from enteral nutrition among patients with diabetes and patients without diabetes
3. To determine the association of caloric intake and protein intake with in-hospital mortality, length of ICU stay, length of hospital admission, days with vasopressor use, and length of mechanical ventilation

Methods

This is a single-center, retrospective cohort on mechanically-ventilated COVID-19 adult patients admitted in a critical care unit of Chinese General Hospital and Medical Center from April 2020 to December 2020. All consecutive admissions from April 1, 2020 to December 31, 2020, that satisfied the inclusion and exclusion criteria, were included in this study. Included in the study were all patients ages 18 years and above, diagnosed to have COVID-19 Pneumonia via RT-PCR, mechanically ventilated, admitted in the critical care unit in Chinese General Hospital and Medical Center, and started on enteral therapy within 48 hours of admission. There were no patients initiated on parenteral therapy within 48 hours of admission during the course of this study. Exclusion criteria were the following: end stage renal disease, feeding intolerance, active cancer, and prolonged NPO for more than 48 hours without initiation of parenteral therapy. Definition of terms can be found in the Appendix.

Data gathered include: sex, age, height weight, BMI, comorbidities, number of days from hospital to ICU admission. Actual body weight refers to the weight of the patient on admission, prior to IV hydration, in kilograms (kg). Ideal body weight was computed using the following formulas: (for males) 50kg +2.3 kg for each inch over 5 ft and (for females) 45.5kg +2.3 kg for each inch over 5ft. For obese patients, adjusted body weight was computed using the following formula: (actual body weight-ideal body weight) x 0.33 + ideal body weight. The recommended calorie intake of 25 kcal/kg ideal or adjusted body weight and recommended protein intake of 1 g/kg ideal or adjusted body weight was used.

All components of the modified SOFA score (spO2/FiO2, scleral icterus or jaundice, MAP or mean arterial pressure and vasopressor use, GCS score, Creatinine) and APACHE II score (temperature, MAP, heart rate, respiratory rate, oxygenation, arterial pH, Na, K, creatinine, hematocrit level, GCS) on the first day admission were obtained. Calorie intake (in kcal) and protein intake (in grams) via enteral route from day 3 to day 7 of ICU admission were recorded. Adequacy of calorie intake and protein intake was determined using a cut-off of 70% of the recommended intake. In-hospital mortality, length of ICU stay, length of hospital stay, days on vasopressor use were also be obtained on chart

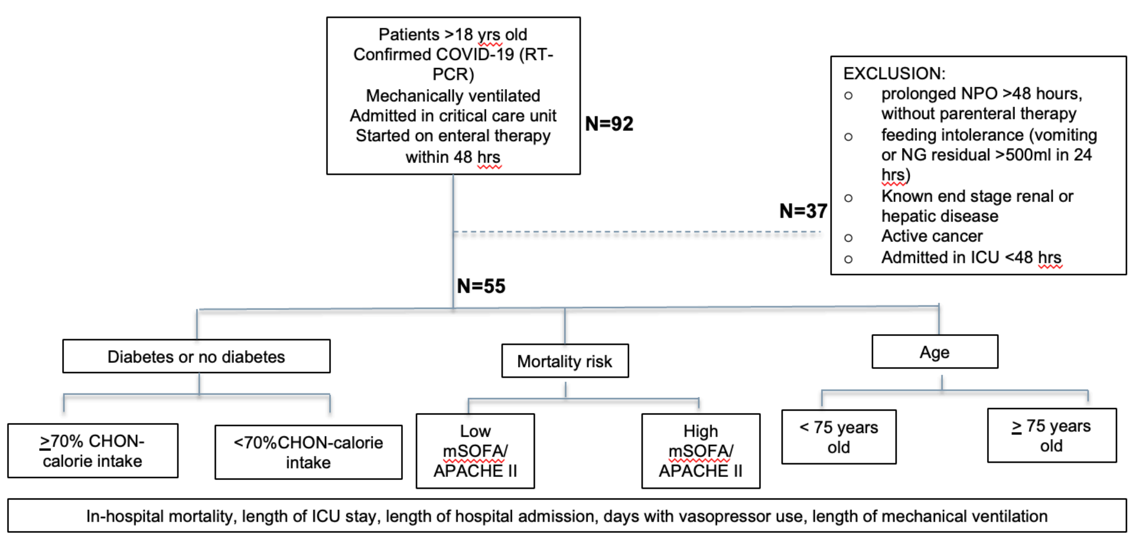

Figure 1. Illustration of Study Procedure

Table I. Demographic and clinical profile of patients.

Profile	N	Percentage	Median	Interquartile Range[1]
Number of patients	55	100.0		
Age (years)			69.0	61.0 - 75.0
Sex				
Female	15	27.3		
Male	40	72.7		
Length of hospital admission (days)			15.0	12.0 - 23.0
Length of ICU stay (days)			10.0	7.0 - 16.0
Height (cm)			170.0	158.0 - 170.0
Weight (kg)			70.0	63.0 - 70.0
Body mass index (kg/m2)			24.2	24.2 - 25.3
Ideal body weight (kg)			65.9	50.6 - 66.1
Adjusted body weight (kg)			67.2	56.6 - 67.4
Co-morbidities				
Diabetes	27	49.1		
Hypertension	36	65.5		
Heart disease	13	23.6		
Asthma	1	1.8		
Stroke	2	3.6		
Other	13	23.6		
Modified SOFA score			10.0	7.0 - 11.0
APACHE II score			16.0	14.0 - 20.0
Blood sugar			175.0	145.0 - 191.0
Length of vasopressor use (days)			7.0	4.0 - 15.0
Length of mechanical ventilation (days)			9.0	7.0 - 14.0
In-hospital mortality	36	65.5		

[1] Values in interquartile range (IQR) are 1st quartile and 3rd quartile.

Table II. Calorie and protein intake and adequacy among patients with and without diabetes.

Variable	All[a] (N=55)	Without diabetes[a] (N=28)	With diabetes[a] (N=27)	P-value
Caloric intake (kcal/kg/day)	17.8 (12.5 – 22.2)	16.9 (10.2 – 18.6)	20.2 (16.1 – 22.4)	0.412
Caloric adequacy >=70%		12 (21.8)	17 (30.9)	0.135
Protein intake (g/kg/day)	0.81 (0.62 – 0.98)	0.72 (0.49 – 0.81)	0.86 (0.79 – 1.06)	0.002*
Protein adequacy >=70%		15 (27.3)	22 (40.0)	0.027*

[a] Values are median (IQR). IQR is interquartile range with values 1st quartile and 3rd quartile.
[b] Values are n (%).
*Significant at p<0.05 level.

review. Patient names and identification numbers were not used. Confidentiality of the cases was maintained

Since data for baseline nutrition risk was not available, both the modified SOFA score and APACHE II were used as confounding variables during the analysis. Patients with mSOFA score less than or equal to 7 and APACHE II score less than or equal to 14 were grouped as having a lower risk of mortality, while those with mSOFA score more than 7 and APACHE II score more than 14 were grouped as having a higher risk of mortality. Data was also stratified by age group and analyzed to minimize bias.

Out of the total of 92 consecutive admissions that were SARS COV-2 RT-PCR positive, 37 patients were excluded and 55 patients were included in this study (Figure 1)

Data Analysis. Given the small sample size and the non-normality of the data, nonparametric statistical tools were utilized in the analysis. Descriptive statistics were used to summarize the general and clinical characteristics of the participants. Frequency and proportion were used for categorical variables whereas median and interquartile range (IQR) for continuous variables. Pearson Chi-square test were computed to determine differences between patients with diabetes and without diabetes among selected categorical variables and Mann-Whitney U test among continuous variables. Spearman's rank correlation was also computed to determine the association between calorie and protein intake and negative clinical outcomes (in-hospital mortality, length of ICU stay, length of hospital admission, days of vasopressor use, length of mechanical ventilation). Only valid data were included in the analysis. Missing values were neither replaced nor estimated. Null hypotheses were rejected at 0.05 α-level of significance. The analysis was aided with Stata version 16.0 (*StataCorp LP*, College Station, Texas, USA).

Results and Discussion

A total of 55 mechanically-ventilated COVID-19 adult patients were included in the study (Table I). Majority of them were male (72.7%) and with median age of 69 years old. The median body mass index was 24.2 kg/m^2. They were admitted in the hospital for approximately 15 days and stayed in the ICU for 10 days. Most number of recorded co-morbidities were cases of hypertension (65.5%) and diabetes (49.1%). The median mSOFA score was 10 while the median APACHE II score was 16. These patients were mechanically ventilated for about 9 days and used vasopressor for approximately 7 days.

A significant finding in this study is the high mortality rate (65.5%) of the critically ill mechanically ventilated patients admitted for COVID-19 pneumonia. The clinical profile of the patients, however, are consistent with a meta-analysis that demonstrated a higher prevalence of comorbidities

Table III. Comparison of clinical outcomes between patients with diabetes and patients without diabetes

Clinical Outcome	Without diabetes[a] (N=28)	With diabetes[a] (N=27)	P-value
In-hospital mortality, n(%)	17 (60.7)	19 (70.4)	0.452
Length of ICU stay (days)	8.0 (0.0 - 13.5)	12.0 (9.0 - 19.0)	0.004*
Length of hospital admission	15.0 (11.0 - 20.5)	14.0 (12.0 - 28.0)	0.584
Length of vasopressor use	7.0 (3.0 - 13.5)	11.0 (5.0 - 16.0)	0.254
Length of mechanical ventilation	8.0 (5.5 - 13.0)	11.0 (8.0 - 15.0)	0.016*

[a] Values are n (%).
*Significant at 0.05 level.

Table IV. Association between calorie and protein intake and negative clinical outcomes among patients with low mSOFA score.

Clinical Outcome	Calorie Intake		Protein Intake	
	Correlation Coefficient	P-value	Correlation Coefficient	P-value
In-hospital mortality	-	-	-	-
Length of ICU stay (days)	0.083	0.778	0.411	0.145
Length of hospital admission	0.126	0.669	0.552	0.0406*
Length of vasopressor use	0.109	0.709	0.384	0.176
Length of mechanical ventilation	0.241	0.406	0.422	0.133

*Significant at $p<0.05$ level.

Table V. Association between calorie and protein intake and negative clinical outcomes among patients less than 75 years old

Clinical Outcome	Calorie Intake		Protein Intake	
	Correlation Coefficient	P-value	Correlation Coefficient	P-value
In-hospital mortality	-0.375	0.017*	-0.243	0.130
Length of ICU stay (days)	0.205	0.520	0.255	0.112
Length of hospital admission	0.089	0.583	0.135	0.405
Length of vasopressor use	-0.295	0.065	-0.008	0.963
Length of mechanical ventilation	-0.069	0.672	0.178	0.272

*Significant at $p<0.05$ level.

Table VI. Association between calorie and protein intake and negative clinical outcomes among patients 75 years old and above

Clinical Outcome	Calorie Intake		Protein Intake	
	Correlation Coefficient	P-value	Correlation Coefficient	P-value
In-hospital mortality	-0.114	0.687	-0.227	0.416
Length of ICU stay (days)	0.258	0.352	0.211	0.449
Length of hospital admission	0.300	0.277	0.244	0.380
Length of vasopressor use	0.127	0.653	0.155	0.581
Length of mechanical ventilation	0.285	0.303	0.175	0.532

*Significant at $p<0.05$ level.

in critical cases of COVID-19 pneumonia, with diabetes having a 4-fold risk and with hypertension having a 5-fold risk. The same study also reported a higher proportion of males and a higher mortality rate among patients older than 65 years.[20]

As to the calorie and protein intake and adequacy between COVID-19 patients with and without diabetes, Table II shows that calorie intake and adequacy was not significantly different between the two groups, at approximately 16-20 kcal/kg/day. Only 20-30% caloric adequacy was achieved in both groups, probably due to the limitation of free water intake to address pulmonary edema in Acute Respiratory Distress Syndrome (ARDS). Although increased inflammation and energy expenditure warrants increased caloric intake, the provision of increased carbohydrates may theoretically increase carbon dioxide production and adversely affect weaning off of mechanical ventilation. Studies have shown, however, that a higher proportion of calories and not carbohydrates was significantly associated with higher carbon dioxide production.[21] Table II also demonstrates that patients with diabetes were provided with more adequate protein and a significantly higher protein intake at 0.86 grams per kilogram per day (P-value=0.002). This may be due to the provision of diabetes-specific enteral formulas that are high in protein and low in calories, resulting in lower glycemic variability or mean glucose levels.[22,23] These formulas have been shown to have a positive clinical and economic impact on patients with diabetes.[24]

When clinical outcomes were compared between patients with diabetes and without diabetes (Table III), length of ICU stay was significantly longer among patients with diabetes with a median of 12 days. Length of mechanical ventilation was also noted to be significantly longer among patients with diabetes with a median of 11 days. This implies a more complicated hospital course for patients with diabetes due to chronic hyperglycemia and altered immune function.[12,13] However, there was no significant difference in in-hospital mortality, length of admission, and vasopressor use.

For the association of protein-calorie intake with negative clinical outcomes, all patients with lower risk of mortality as defined by the modified SOFA score, survived regardless of protein-calorie adequacy. However, the association of calorie and protein adequacy and negative clinical outcomes in patients with higher mortality risk was not significant. When intake instead of adequacy was used, a

Table VII. Correlation between caloric intake and protein intake and negative clinical outcomes among patients without diabetes.

Clinical Outcome	Caloric Intake		Protein intake	
	Correlation Coefficient	P-value	Correlation Coefficient	P-value
In-hospital mortality	-0.205	0.147	-0.276	0.077
Length of ICU stay (days)	0.066	0.369	0.163	0.204
Length of hospital admission	0.246	0.103	0.306	0.057
Length of vasopressor use	-0.041	0.417	-0.111	0.287
Length of mechanical ventilation	0.081	0.341	-0.039	0.422

Notes: *Significant at 0.05 level.

Table VIII. Correlation between caloric intake and protein intake and negative clinical outcomes among patients with diabetes

Clinical Outcome	Caloric Intake		Protein Intake	
	Correlation Coefficient	P-value	Correlation Coefficient	P-value
In-hospital mortality	-0.516	0.003*	-0.005	0.490
Length of ICU stay (days)	-0.083	0.341	0.220	0.134
Length of hospital admission	0.098	0.314	0.394	0.021*
Length of vasopressor use	-0.394	0.021*	0.019	0.462
Length of mechanical ventilation	-0.306	0.061	0.136	0.249

Notes: *Significant at 0.05 level.

significant association was seen with protein intake and number of hospital days in patients with lower risk for mortality (Table IV). This suggests that those patients who were admitted longer had higher protein consumption. Since the catabolic response in critical illness leads to reduced muscle mass, increased protein intake provides a more adequate source of amino acids for energy stores.[25] This is consistent with observational studies that have shown decreased morbidity and mortality with the provision of increased protein.[7,26,27] However, this study did not demonstrate an association of protein intake with mortality.

Among patients with higher modified SOFA and APACHE scores, there was no significant association of protein and calorie intake and negative clinical outcomes; however, overall survival was noted in only 10-16% of these patients.

Table V demonstrates that among patients less than 75 years old, calorie intake was significantly and inversely associated with in-hospital mortality (P-value=0.017). This implies that patients with higher consumption of calories more likely survived. In terms of nutrition, increased calorie intake is required to supply energy stores in the early catabolic phase of critical illness, characterized as increased energy expenditure, inflammation, and insulin resistance.[25] However, a progressive increase of intake is recommended to prevent overfeeding, which has also been associated with poorer clinical outcomes.[26] This association was not seen in patients 75 years and older (Table VI), however overall survival for these patients was noted to be only 13%. This is congruent with findings reported by Centers for Disease Control and Prevention (CDC) that increasing age corresponds to increased morbidity and mortality, citing a 9-fold increase in hospitalization rate and 230-fold increase in death rate among patients ages 75-85 years old relative to patients ages 18 to 29 years old.[28]

On further analysis, patients without diabetes did not demonstrate a significant association between protein-calorie intake and negative clinical outcomes (Table VII). While among patients with diabetes (Table VIII), increased caloric intake was significantly and inversely associated with in-hospital mortality and vasopressor use, implying increased survival and decreased pressor requirement with increased caloric intake. Additionally, increased protein intake among patients with diabetes was associated with increased length of hospital admission. These results suggest the importance of the provision of protein and calories in the critically ill COVID-19 patient to overcome the inflammatory process resulting from hyperglycemia and insulin resistance. Factors that could have led to the variability of results include age, severity of disease, and the presence of concomitant chronic kidney disease among patients with diabetes, since increased protein intake could cause further kidney injury and lead to a poorer prognosis.

The results of this study demonstrated significant associations only among younger patients with lower mortality risk, and in patients with diabetes. This emphasizes the need for baseline nutritional evaluation, which could influence protein-calorie requirements. There are several evaluation tools for the assessment of nutritional status, such as the Subjective Global Assessment (SGA) and the NUTRIC score, however this was not applied in this study due to lack of data.

It is also important to note that the results of this study demonstrate significant associations of calorie and protein intake and not adequacy, with negative clinical outcomes. This suggests a lower cut-off in terms of protein and calorie adequacy for critically ill COVID-19 Filipino patients. This may be due to lower BMI and lean body mass of the population. An observational study in Japan noted a lower calorie intake of 7-15 kcal per kilogram per day and lower protein intake of 0.4 grams per kilogram per day in patients admitted in the ICU, owing to the lower BMI of the Japanese population and the influence of physical and regional characteristics and available nutritional formulas.[29] Another study conducted in Malaysia also demonstrated decreased calorie and protein intake in ICU patients, with an increased 60-day mortality among those who were given more than 60% of the prescribed energy (25mg/kg/day) and protein intake (1.2g/kg/day).[30]

The results of this study may contribute to local data on the nutrition of severely ill mechanically ventilated COVID-19 pneumonia patients. Due to increased mortality in these patients, provision of adequate nutrition is recommended to enhance immune response and to prevent further morbidity.

Conclusion

This study demonstrated that increased caloric intake was associated with increased survival among patients less than 75 years old and among patients with diabetes. Increased protein intake was associated with longer hospital stay among patients with lower mortality risk and among patients with diabetes. However, treatment for COVID-19 pneumonia was not established at this time and there was significant in-hospital mortality among these mechanically ventilated patients.

Limitations

Limitations of this study include its retrospective nature, having used only chart review in a single center for data collection, hence causing selection bias. Potential confounding factors were not observed firsthand. Although consecutive admissions were included in the study, the total number of mechanically ventilated COVID-19 patients did not meet the projected sample size, partly because of excluded subjects from chart review, which could have decreased the statistical power of the study. Additionally, COVID-19 pneumonia treatment was not established in the duration of this study, therefore the different modes of management affected the outcome of the patients. Care should thus be taken in generalizing results.

Further studies should be done in a prospective design, with a larger sample size. Patients who are not mechanically ventilated can be included, to analyze nutritional intake in different disease severities of COVID-19 pneumonia. Baseline nutritional status should be taken using the NUTRIC score or Subjective Global Assessment (SGA) and should be the basis in determining calorie and protein requirements for each patient. Future investigators may also aim to determine more adequate cut-offs for protein and calorie intake of critically ill COVID-19 patients in the local setting.

Conflict of Interest: None

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APPENDIX

DEFINITION OF TERMS

Diabetes[17]	Patients on anti-hyperglycemic medications, on regular follow up for Diabetes; or Fasting blood sugar ≥ 126 mg/dL or 2-h post prandial glucose ≥ 200mg/dL or A1C ≥ 6.5% or RBS ≥ 200 mg/dL with polydipsia, polyuria, polyphagia or hyperglycemic crisis		
Modified SOFA (mSOFA) score[18]	spO2/FiO2	>400	0
		>315 to ≤400	1
		>235 to ≤315	2
		>150 to ≤235	3
		≤150	4
	Scleral icterus or jaundice	No	0
		Yes	3
	Hypotension	No hypotension	0
		MAP < 70 mmHg	1
		Dopamine ≤ 5 mcg/kg/min or Dobutamine at any dose	2
		Dopamine >5 mcg/kg/min, epinephrine ≤ 0.1 mcg/kg/min, or norepinephrine ≤ 0.1 mcg/kg/min	3
		Dopamine >15 mcg/kg/min, epinephrine >0.1 mcg/kg/min, or norepinephrine >0.1 mcg/kg/min	4
	Glasgow Coma Scale (GCS)	15	0
		13-14	1
		10-12	2
		6-9	3
		<6	4
	Creatinine (mg/dL)	<1.2	0
		1.2-1.9	1
		2.0-3.4	2
		3.5-4.9	3
		≥5.0	4
	HIGH MORTALITY RISK	mSOFA score > 7	
	LOWER MORTALITY RISK	mSOFA score ≤ 7	
APACHE II score[19]	Age	≤44 0 points, 45-54 +2 points, 55-64 +3 points, 65-74 +5 points, >74 +6 points	
	History of severe organ insufficiency or immunocompromised	Yes, and nonoperative or emergency postoperative patient +5 points, Yes and elective postoperative patient +2. No 0 points	
	Temperature, °C	≥ 41 +4 points, 39-41 +3 points, 38.5- <39 +1 point, 36-38.5 0 points, 34-<36 +1 point, 32-<34 +2 points, 30-<32 +3 points, <30 +4 points	
	Mean arterial pressure, mmHg	>159 +4 points, >129-159 +3 points, >109-129 +2 points, >69-109 0 points, >49-69 +2 points, ≤49 +4 points	
	Hear rate, beats per minute	≥180 +4 points, 140 to 179 +3 points, 110 to 139 +2 points, 70-109 0 points, 55 to 69 +2 points, 40 to 52 +3 points, <40 +4 points	
	Respiratory rate, breaths per minute	≥50 +4 points, 35 to 49 +3 points, 25 to 34 +1 point, 12-24 0 points, 10 to 11 +1 point, 6 to 9 +2 points, <6 +4 points	
	Oxygenation, A-a gradient or PaO2 if FiO2<50%	>499 +4 points, 350-499 +3 points, 200-349 +2 points, <200 0 points, paO2 61-70 +1 point, paO2 55-60 +3 points, paO2 <55 +4 points	
	Arterial pH	≥7.7 +4 points, 7.6 to 7.7 +3 points, 7.5to 7.59 +1 point, 7.33 to 7.49 0 points, 7.25 to 7.32 +2 points, 7.15 to 7.24 +3 points, <7.15 +4 points	
	Serum sodium, mmol/L	≥180 +4 points, 160 to 170 +3 points, 155 to 159 +2 points, 150 to 154 +1 point, 130 to 149 0 points, 120 to 129 +2 points, 111 to 119 +3 points, <111 +4 points	
	Serum potassium, mmol/L	≥7 +4 points, 6 to 6.9 +3 points, 5.5 to 5.9 +1 point, 3.5 to 5.4 0 points, 3.0-3.4 +1 point, 2.5 to 2.9 +2 points, <2.5 +4 points	
	Serum creatinine, mg/100mL	≥3.5 and acute renal failure +8 points, 2 to 3.4 and acute renal failure +6 points, ≥3.5 and chronic renal failure +4 points, 1.5 to 1.9 and acute renal failure +4 points, 2 to 3.4 and chronic renal failure +3 points, 1.5 to 1.9 and chronic renal failure +2 points, 0.6 to 1.5 0 points, <0.6 +2 points	
	Hematocrit, %	≥60 +4 points, 50 to <60 +2 points, 46 to <50 +1 point, 30 to <46 0 points, 20 to <30 +2 points, <20 +4 points	
	White blood count, total/cubic mm in 1000's	≥40 +4 points, 20 to <40 +2 points, 15 to <20 +1 point, 3 to <15 0 points, 1 to <3 +2 points, <1 +4 points	
	Glasgow Coma Scale (GCS)	15-GCS score	
	HIGH MORTALITY RISK	APACHE II score >14	
	LOWER MORTALITY RISK	APACHE II score ≤ 14	
Calorie intake	The average total calorie intake per day received in kcal via enteral route from day 3 to day 7 of ICU admission		
Caloric adequacy	(Total calorie intake from day 3 to day 7 ÷ Total calorie requirement for 5 days) x 100		
Protein intake	The average total protein intake per day received in grams via enteral route from day 3 to day 7 of ICU admission		
Protein adequacy	(Total protein intake from day 3 to day 7 ÷ Total protein requirement for 5 days) x 100		