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Energy target achievement and its determinants in critically ill COVID-19 patients in Indonesia

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Abstract

Introduction. Achievement of energy target in critically ill Covid-19 patients in Intensive Care Unit (ICU) is challenging. This study was aimed to depict the possibility of achieving energy target and its determinants in critically ill Covid-19 patients.

Methods. A cross sectional study was conducted in ICU of dr. Kariadi Hospital Semarang, Indonesia. Secondary data were obtained from Covid-19 patients who were in ICU for minimum 3 days, from March to December 2020. Data collected included age, sex, Body Mass Index (BMI), comorbidities, Modified Nutrition Risk in Critically Ill (mNUTRIC) score, energy intake, route of nutrition delivery (enteral or combination of enteral and parenteral nutrition), lactate status, ICU length of stay (LOS), duration of mechanical ventilator and mortality. Risk Prevalence calculations were conducted to measure risks. Variables with significant associations and p< 0.25 were included in multiple logistic regression.

Results. A total of 188 subjects were included in the analysis. Most patients were male (62.8%) and obese (61.8%). As much as 56.9% patients were able to achieve energy target of 20 kcal/kgBW on day 3 of ICU stay. Those with low risk mNUTRIC score and nutrition delivery was through enteral and parenteral route were more likely to achieve target energy of 20 kcal/kgBW in the first 3 days in the ICU.

Conclusions. Achieving energy target of 20 kcal on day 3 of ICU stay for critically ill Covid-19 patients is feasible. Low mNutric score and nutrition delivery through enteral and parenteral route were two determinants for the achievement.

Keywords energy target in ICU, mNutric score, early nutrition in ICU, Covid-19

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Introduction

Achievement of energy target during the first week of ICU stay is mandatory for better outcome. Several factors determine the achievement, putting unstable hemodynamic and gastrointestinal intolerance as pitfalls in reaching energy target. Factors associated with hemodynamic such as vasopressor dose, lactate level, the use of mechanical ventilator may affect energy intake. Other factors such as age, comorbidities may also contribute to failure of energy intake achievement. Nutritional screening tool for ICU patients, Nutric score, often shows association with ICU outcome.

Feeding patients with vasopressor is possible. Previous study reported in critically ill patients with vasopressor, enteral feeding can be started when the dose is low-medium or decreased by time.[1] High lactate level indicates the presence of splanchnic hypoperfusion and thus feeding intolerance.[2] The use of mechanical ventilator indicates perfusion problems and may lead to disruption of feeding.[3]

Route of nutrition administration determine the success of energy target achievement. In non-intubated critically ill Covid-19 patients, semi solid oral diet may be administered. Oral Nutrition Supplement (ONS) was advised for those who cannot obtain energy target due to shortness of breath. Patients with High Flow Nasal Canule (HFNC) need to be assessed and monitored closely for fulfillment of energy and nutrients target from oral intake. Tube feeding or ONS can be initiated for patients with HFNC when chewing foods caused dyspnea. Early enteral nutrition is also recommended for patients who proceed to mechanical ventilation. When all measures have been conducted and energy intake remains inadequate, early parenteral nutrition is acceptable for any critically ill covid-19 patients.[4]

The amount of enteral nutrition administered for critically ill covid-19 patients is of interest. Energy need in the ICU is suggested to be determined by using indirect calorimetry. In hospitals where indirect calorimetry is unavailable, prediction equation may be used. During early period, ESPEN recommended energy supply to start with 20 kcal/kg BW/day, increased to 50-70% in the following day and reached 80-100% predictive energy at fourth day of ICU stay.[4] A recent study measured REE in 22 intubated covid-19 patients reported that median REE of patients were 19 kcal/kg actual BW in first week of ICU stay. These numbers were slightly lower in obese patients either using actual or adjusted body weight measurement. [5] Another expert recommended a steeply increased energy prescription from 10 kcal/kgBW on the first day, 15 kcal/kgBW on the second day and 20 kcal/kgBW on the third day.[6]

Regardless the increasing number of available guidelines for ICU Covid-19 patients, there have been limited studies which depicted application of nutrition therapy for these patients. This study was aimed to measure risk factors for energy target achievement in critically ill Covid-19 patients in Indonesia.

Methods

Study design and subjects

A cross sectional study was conducted in the ICU dedicated for Covid-19 patients in dr. Kariadi General Hospital, Semarang, Indonesia. Inclusion criteria were all confirmed Covid-19 patients who were in ICU for 3 days or more from March to December 2020. Exclusion criteria were patients with unstable hemodynamic or massive upper gastrointestinal bleeding.

Data collection and definitions

Data collected secondarily from e-medical record. Data obtained included characteristics of subjects such as age, sex, BMI, ICU length of stay (LOS) and mortality. Data for age and sex were obtained from patients' ID card. BMI (Quetelet index) of patients was calculated using formula Weight(kg)/height^2(m^2). ICU LOS was calculated from ICU admission until patients died or were allowed to be transferred to ward. Mortality was recorded as whether a patient transferred alive or died at the end of ICU stay. Other data collected for analysis were energy intake, route of intake, comorbidities, mNUTRIC score, dosage of vasopressor, the use of mechanical ventilator, lactate level.

Dependent variable was the achievement of energy target which was defined as whether a patient

achieved energy intake of 20 kcal on day 3 of ICU stay. This target based on a guideline for energy requirements of critically ill Covid-19 patient during early period in the ICU.[6]

Independent variables included route of intake, comorbidities, mNUTRIC score, dosage of vasopressor, the use of mechanical ventilator and lactate level. Route of intake was divided into enteral nutrition only and combination of enteral and parenteral nutrition. Comorbidities was defined as the presence of minimal 1 comorbidity at the time of admission, either reported by family or from previous medical record. mNUTRIC scores were calculated during the first 48 hours of ICU admission. Dosage of vasopressor was the maximum dose used during the period of ICU stay. It was categorized high when norepinephrine dose was more than 0.3mcg/kgBW or combination with other vasopressors such as dobutamine and vasopressin. Vasopressor dose was categorized as low if only norepinephrine was used and with dose 0.3mcg/kgBW or lower. [1] Use of mechanical ventilator was recorded as the number of days a patient was on mechanical ventilator during ICU stay. Lactate level that was measured in the first 3 day was used as variable in this study. It was categorized as more or less than 4 mg/L.

Statistical analysis

Data analysis was performed in SPSS 11 program. Nominal data were presented as frequencies while numeric data were presented as mean and standard deviation (SD) or median and interquartile range (IQR). Risk Prevalence was calculated for each independent variable. Further analyzed using multiple logistic regression to seek significant risk factors. Ethical Clearance has been obtained from Health Research Ethics Committee of RSUP dr.Kariadi Semarang no.531/EC/KEPK-RSDK/2020. Informed consent was not obtained as this was a retrospective study using secondary data from e-medical record.

Results

A total number of 188 eligible subjects out of 191 patients who were admitted to ICU from March to December 2020 were included in the analysis.

Table 1 depicted characteristics of our subjects, which showed that more than 30% subjects were elderly. Our patients were mostly male (62,8%) and obese (61.8%). A small number of subjects were undernourished based on BMI. Type 2 Diabetes Mellitus and hypertension were the two most frequent comorbidities observed in our subjects, followed by cardiovascular/ cerebrovascular diseases and chronic kidney disease. A small proportion of subject were pregnant women with hypertension and pre-eclampsia/eclampsia. According to mNutric score which was calculated in the first 24 hour of ICU admission, only 15% of our patients were admitted to ICU with high nutritional risk. Most of our patients were reported to have short period of symptoms before hospital admission and thus, a relatively fair condition at the point of admission.

More than 50% subjects were on mechanical ventilator and the rest were using HFNC. Few subjects wore non-rebreathing mask for a short period of time before putting on HFNC or being intubated. Most patients required mechanical ventilator in the first 5 days in the ICU, with the median of mechanical ventilator day length was 5 days (IQR 3 - 9). The longest duration of mechanical ventilator was 29 days. Median of ICU LOS was 8 days (IQR 4 - 11) with the maximum stay was 46 days. The mortality rate was as high as 53.7%, mostly those with mechanical ventilator (85.4%), elderly (60%) and undernourished based on BMI (100%).

In terms of energy target, more than 50% of subjects reached 20 kcal/kg BW/day during the first 3 days in the ICU. More than 80% of our subjects received enteral nutrition started on day 1 in the ICU and more that 90% received enteral nutrition during three days of ICU stay. About 60% of our subjects were prescribed supplemental parenteral nutrition in whom 50% of them received it during the first 3 days of their ICU stay.

Several factors associated with energy target achievement of 20 kcal on day 3 were observed and analyzed. Age, sex, the presence of comorbidities and dosage of vasopressor were not risk factors for achievement of energy target. Meanwhile, risk prevalence calculation suggested that patients who had low risk of malnutrition based on mNutric score, were not on mechanical ventilator, had lactate level

less than 4 mmol/L and had both enteral and parenteral nutrition as route of delivery were more likely to achieve energy target of 20 kcal on day 3 (**Table 2**).

Putting together, when a multiple logistic regression was performed, only mNUTRIC score group and route of nutrition administration became significant determinants (**Table 3**). Patients with low nutritional risk based on mNUTRIC score was 8.7 times more likely to achieved 20 kcal/kg BW at day 3. Similarly, patients receiving nutrition from both enteral and parenteral route, was 8.5 times more likely to reach 20 kcal/kgBW on day 3.

Discussion

Most of subjects were male and obese. This result is in accordance with other study in Indonesia which also observed a higher prevalence in these group of patients with Covid-19.[7] A meta-analysis of 75 worldwide studies reported that obese people have higher risks for being Covid-19 positive, hospitalization, ICU admission and mortality.[8] The prevalence of Covid-19 patients with BMI $\geq$ 30kg/m^2 in our study was lower compared to French studies which reported the range prevalence of 25% to 47%.[9, 10] Being obese put a person in higher susceptibility for some infectious disease such as influenza and nosocomial infection.[11] The link between obesity and Covid-19 infection may be explained through several mechanisms such as adipose inflammation, impaired immunity and comorbidities found in obese people such as hypertension and type 2 diabetes mellitus.[8]

Elderly patients comprised about one third of our subjects. This high proportion may be due to poor immunity states among older people. Higher prevalence of elderly with Covid-19 was also found in a study conducted in Indonesia's National General Hospital.[12] However, the prevalence of older people with Covid-19 in our study much higher compared to study conducted in Wuhan which reported the prevalence of 11.5%.[13]

Most prevalent comorbidities observed in our study were type 2 diabetes mellitus and hypertension. These findings were similar with study which were conducted in China[14] and Indonesia.[7] It suggested the role of ACE2 in the pathogenesis of Covid-19 infection.[15,16] These two comorbidities frequently occurs in obese people, suggesting metabolic dysfunction in these population.[8]

The prevalence of high mNUTRIC score was low in our study compared to other study findings. This may be due to different characteristics of study subjects across countries. Two studies in China reported thatqa mNUTRIC score was applicable to determine nutrition risk and mortality in critically ill Covid-19 patients.[17,18]

ICU LOS and VM length observed in our study were somewhat shorter compared to previous meta-analysis from 7 studies which reported duration of ICU stay and being ventilated of 7.8 and 10.1 days respectively.[19] These differences might be due to higher mortality in our study subjects in the ICU and those with MV compared to findings from the meta-analysis. Various mortality rates in critically ill Covid-19 have been widely published. Compared to our study, the ICU mortality rate of previous studies were similar, but, the proportion of deceased patients who were on mechanical ventilator in other studies were significantly lower.[20,21] Meanwhile, a meta-analysis from 28 studies from 7 countries found mortality rate of 28.3% and 43% of those who were in ICU and being in mechanical ventilator respectively. Mechanical ventilator usage was found to be the major predictor for mortality.[19]

Our study found that more than 80% of our patients tolerated small dose EN on day 1 in ICU (median 11.7 kcal/kg BW, IQR 8.4 – 15.1). A retrospective cohort study in critically ill Covid-19 patients reported that early enteral nutrition was feasible and safe for this group of patients during the first week of ICU stays.[22] Another retrospective study in critically ill Covid-19 patients receiving mechanical ventilator revealed that administration of EN in the first 24 hour of mechanical ventilation did no harm to the patients.[23] Our study also found that combining EN with PN made achievement of energy target of day 3 in ICU is possible. This was in concordance with a meta-analysis by Luo which reported that administration of combined PN and EN was reported to have no difference with EN only in terms of mortality, infection, nutrition related complication, ventilatory support or C-reactive protein (CRP).[24]

This study found that obtaining energy target of 20 kcal/kg BW in day 3 of ICU stay was possible. A

small retrospective study conducted in severe and critically ill Covid-19 patients in China reported that permissive under feeding is feasible in critically ill Covid-19 patients.[25] Interestingly, the LEEP Covid study reported that measured REE in critically ill Covid-19 patients were at the range of 15-20 kcal/kgBW during the first week, therefore, our study result was in line with LEEP Covid study.[5]

Bivariate analysis found that variables which significantly associated with energy target achievement of 20 kcal/kgBW were mNUTRIC score, the use of mechanical ventilator, lactate level and route of nutrition were. Risk prevalence for these variables indicated that in critically ill Covid-19 patients who had low mNutric score, were not on mechanical ventilator, had lactate level less than 4 mmol/L and received nutrition from both enteral and parenteral route were more likely reaching energy target of 20 kcal/kgBW on day 3. This may be explained that those patients were hemodynamically stable, less severe disease, and/or less complications, which may lead to disruption of nutrition delivery. Multiple logistic regression revealed that only mNUTRIC score group and route of nutrition administration became significant predictors. The plausible explanation for this finding was that low nutrition risk based on mNutric score indicated patients were in less severe ARDS and hemodynamically stable which made the delivery of nutrition was possible. The previous retrospective study in critically ill Covid-19 patients on mechanical ventilator also found that main reason for interruptions of enteral nutrition during the first week were hemodynamic instability and GI intolerance.[22] When an enteral route was used without any supplemental PN, it seemed that disruption of enteral feeding due to gastrointestinal intolerance/bleeding, unstable hemodynamic and fasting related procedure led to failure of energy target achievement at day 3. Adding supplemental parenteral nutrition seems feasible and safe for our subjects. A systematic review and meta-analysis comparing EN and combined EN with supplemental PN revealed that the later increasing energy intake without increasing ICU mortality and length of stay.[26]

Wrapping up, most of our subjects are male and obese, with two third of them are elderly. The ICU mortality rate is quite high. Our study confirms that achieving energy target of 20 kcal/kgBW during the first 3 days of ICU stay for critically ill Covid 19 patients is possible. Two determinants for the achievement of energy target are mNUTRIC score and the route of nutrition delivery. Further study confirming other factors such as renal and liver functions which may influence the achievement energy target may be needed.

Table 1. Characteristics of subjects

Characteristics	Mean ± SD	n (%)
Age (years old)	53.7±12.67	
≥ 65		62 (33.0)
< 65		126 (67.0)
Sex		
Male		118 (62.8)
Female		70 (37.2)
Nutritional status (BMI, Asia Pacific Criteria)		
Underweight (<18.5 kg/m²)		4 (2.1)
Normoweight (18.5 – 22.9 kg/m²)		37 (19.6)
Overweight (23.0 – 24.9 kg/m²)		31 (16.5)
Obese Grade I (25.0 – 29.9 kg/m²)		84 (44.7)
Obese Grade II (30.0 – 34.9 kg/m²)		24 (12.8)
Obese Grade III/Morbid Obese (> 35 kg/m²)		8 (4.3)
Comorbidities (excluding obesity)		
DM without or with complication		66 (37.5)
Hypertension		61 (34.7)
Cardiovascular/cerebrovascular disease		35 (19.9)
Chronic kidney disease		26 (14.8)
No reported or observed comorbidities		60 (31.8)
mNUTRIC Score		
High risk		18 (15.5)
Low risk		98 (84.5)
Patients on VM		106 (56.4)
VM length (days)	6,8 ± 5.46	
ICU LOS (days)	8.8 ± 6.83	
ICU discharge status		
Deceased		101 (53.7)
Alive		87 (46.3)
Achieved 20 kcal/kg BW at day 3		
Yes		107 (56.9)
No		81 (43.1)
Proportion of subjects received EN for the first 3 days in ICU		178 (96.7)
Proportion of subject received PN for the first 3 days in ICU		60 (51.7)

Table 2. Risk factors for achievement of energy target

Achievement of 20 kcal at day 3		No	Yes	RP (95% CI)
		n (%)	n(%)	
Age (year)	≥ 65	12 (16.2)	22 (21.6)	0.74 (0.33-1.53)
	< 65	62 (83.8)	80 (78.4)	
Sex	Male	49 (59.8)	70 (64.8)	0.93 (0.51-1.74)
	Female	33 (40.2)	38 (35.2)	
Comorbidity	Yes	57 (69.5)	70 (64.8)	1.06 (0.56-2.02)
	No	25 (30.5)	38 (35.2)	
Vasopressor	High	8 (22.2)	6 (26.1)	0.71 (0.21-2.46)
	Low-medium	28 (77.8)	17(73.9)	
m-NUTRIC score	High risk	13 (28.9)	5 (7.0)	5.03 (1.63-15.54)
	Low risk	32 (71.7)	66 (93.0)	
Mechanical Ventilator	Yes	66 (61.1)	42 (38.9)	6.70 (3.27-13.74)
	No	16 (19.5)	66 (61.1)	
Lactate level	> 4	20 (48.8)	11 (22.4)	3.18 (1.26-8.09)
	≤ 4	21 (51.2)	38 (77.6)	
Route	EN	55 (77.5)	62 (62.0)	2.11 (1.06-4.19)
	EN+PN	16 (22.5)	38 (38.0)	

EN: enteral nutrition; PN: parenteral nutrition; RP: risk prevalence

Table 3. Multiple logistic regression models for variables with p<0.05

	B	p	Risk (95%CI)
m-NUTRIC score	2.162	0.013*	8.7 (1.19-32.08)
Mechanical ventilator	0.872	0.271	2.4(0.47-10.6)
Lactate group	0.979	0.168	2.7 (0.70-11.65)
Nutrition route	2.140	0.005*	8.5 (2.15-30.23)

Conflict of Interest

Authors declared no conflict of interest regarding this article.

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