## Mazuin Kamarul Zaman\*<sup>a</sup>, Mardhiah Mat Din<sup>a</sup>, Tah Pei Chien<sup>b</sup>, Mohd Shahnaz Hasan<sup>b</sup>

<sup>a</sup>Centre for Nutrition and Dietetics Studies, Faculty of Health Sciences, Universiti Teknologi MARA (UiTM) Selangor, Puncak Alam Campus, 42300 Bandar Puncak Alam, Selangor, Malaysia; <sup>b</sup>Department of Anesthesiology, Faculty of Medicine, University of Malaya, Malaysia.

#### Abstract:

\*Corresponding author

Mazuin Kamarul Zaman mazuin0233@uitm.edu.my

Medical advancements decrease mortality rate of critically ill patients over time. However, there are increasing number of patients discharged to nursing home and rehabilitation centers. Energy and protein deficit along with hypercatabolism during the period of critical illness may lead to malnutrition and poorer clinical outcomes. This study aims to investigate the association between energy and protein adequacy with and quality of life of Intensive Care Unit (ICU) survivors. Prospective observational study was conducted to follow ICU survivors from ICU admission day to a year post-admission. Convenience sampling was employed for study's enrollment. Energy and protein adequacy during critical illness were obtained from nutritional intake in ICU ward from admission day until patients were discharged of ICU or maximum of 14 days. Quality of life was measured using SF-12 and EuroQoL-5D-3L questionnaires through a phone interview. Of 189 patients followed, 105 patients were alive at 1-year post ICU admission. Only 26 ICU survivors with a median age of 52.3 (18-83) years old were able to be reached. Most of the critically patient received an adequate intake of energy (93%), protein (86.7%), and energy and protein (76.9%). 85% of ICU survivors reported poor quality of life. There was no association between energy adequacy (p=0.158), protein adequacy (p=0.921), energy and protein adequacy (p=0.921) and the quality of life. This study showed that most critically ill patients were adequately nourished during the ICU stay and there was no association between energy and protein adequacy and quality of life of 1-year ICU survivors.

Keywords: Quality of life, critically ill, energy adequacy, protein adequacy.

#### 1. INTRODUCTION

Advancement in medical care has driven increase in number of critically ill survivors worldwide [1]. Study reported increase in length of hospitalisation and complications among critically ill patients despite, the decrease of Intensive Care Unit (ICU) mortality [2]. On the other hand, the number of ICU patients discharged to nursing homes and rehabilitation centres tripled from the year 2000 to 2012[3]. Patients suffers from difficulties to move due to loss of strength during ICU stay. Patients who loss muscle mass would have limited joints movement. Skeletal muscle is the primary site of protein storage, and critical catabolic illness causes progressive reduction in muscle mass that leads to muscle atrophy [4, 5]. Consequently, ICU survivors faces difficulties to move, which leads to limited daily activities and poor quality of life due to the loss of lean body mass.

Lean body mass may preserved through optimization of nutrients intake during their stay in ICU [6]. American Society of Parenteral and Enteral Nutrition (ASPEN) and Society of Critical Medicine (SCCM) recommends energy requirement at 25 to 30 kcal/kg/day[7]. A systematic review concluded that protein requirement among critically ill patients between 2.0 to 2.5 g/kg/day is safe and optimal to most of ICU patients [8]. Studies have shown that adequate nutrition is necessary for optimal resolution of catabolism and the rehabilitation of quality of life after ICU stay [9-11]. Increase of 25% in nutrition adequacy resulted in a significant increase in physical functioning and role physical domains in the SF-36 score at three months followed up after ICU discharge. While there are numerous studies on quality of life among critically ill survivors, there are limited studies on the effect of nutrition therapy on Health-Related Quality of Life (HRQoL) in the developing countries [12]. This research aims to study the association between energy and protein adequacy and the quality of life at one-year post ICU discharge of local ICU survivors.

#### 2. MATERIALS AND METHODS

#### 2.1 Study design and patients

Prospective observational study was conducted in the general ICU of University Malaya Medical Centre (UMMC) Kuala Lumpur. This study was granted ethical clearance

#### © 2019 Faculty of Health Sciences, UiTM

from MARA University of Technology (UiTM) Research Ethics Committee: REC/234/18 and University Malaya Medical Centre (UMMC) Research Ethics Committee: 201868-6376. The inclusion criteria were patients aged 18 years, admitted to ICU within 48 hours of hospital admission, and expected to be mechanically ventilated in ICU for at least seven days. Informed consent was obtained from caretakers prior to data collection.

Data collection were conducted in two phases. Initial phase included acquisition of nutrition related data inclusive of energy and protein adequacy received by patients from day one to 14 of ICU stay or until ICU discharge. The adequacy of energy and protein intake was estimated by the ratio of energy prescribed and intake. Adequacy of energy and protein intake was determined with cut-off point of 60%. Energy and protein were divided into three categories which are underfeeding, adequate, and overfeeding with a cut-off point. Cut-off point underfeeding was below 60%, adequate 60% to 100%, and overfeeding over 100%. Latter phase of the study was conducted a year from the ICU admission whereby data on quality of life of ICU survivors were gathered through telephone interview. Quality of life was measured using two quality of life questionnaires: SF-12 and EuroQoL-5D-3L. The used of SF-12 along with EQ-5D questionnaires were validated, widely used in studies of ICU survivors, and suitable to be administrated through an interview via a telephone call or email [13]. EQ-5D consists of five dimensions, mobility, self-care, usual activities, pain/discomfort, and anxiety/depression. ICU survivors were called at least three times before being considered as lost to follow -up. The outcome of quality of life between the good and poor groups was defined based on a cut-off point value 47 using SF-12 questionnaire. The quality of life below 47 will be categorized into poor outcome group, and the ICU survivors with more than 47 quality of life score will be categorized into good outcome group.

#### 2.2 Statistical analysis

The data collected was analyzed using the Statistical Package for the Social Sciences IBM SPSS (Version 24.0, Chicago, IL, US). Kolmogorov–Smirnov was used to check the normality of the data. A p-value of <0.05 was taken to be considered statistically significant. Data between the two groups were analyzed using Student's T-test and reported as mean  $\pm$  SD or Mann-Whitney Test and reported as median  $\pm$  IQR. The Chi-square or Fisher's exact test was used to find associations between categorical variables.

### 3. RESULT AND DISCUSSION

## 3.1 Results

A total of 189 patient screened, met the inclusion and exclusion criteria of the study. Fifty-one and additional 33 critically ill patients died within 60 days and one year after the ICU admission. Of the 105 living ICU survivors, only 26 patients responded and completed quality of life follows up.

Mazuin et al

Table 1: Characteristics of the ICU survivor (N=26).

			,	/
Characteristics	Total (N=26)	Good QoL (N=4)	Poor QoL (N=22)	P value
		(14-4)		
Age <sup>b</sup>	52.3 (18-83)	48.5	$53.3 \pm 21.0$	0.255
		±19.0		
Sev <sup>c</sup>				0.086
Jen 1			10 (75.0)	0.080
Male	16 (61.5)	4 (25.0)	12 (75.0)	
Female	10 (38.5)	0 (0.0)	10 (100.0)	
Height, cm <sup>b</sup>	165.0	170.0	165.0 + 9.0	0.008
mengini, em	(151.0	+1.0	10010 = 210	0.000
	(151.0-	$\pm 1.0$		
	171.0)			
Weight, kg <sup>a</sup>	67.5 (43.0-	68.1	$67.4 \pm 13.0$	0.919
0 0	90.0	+15.0		
DMI Ira/m <sup>2</sup> a	24.4 (15.6	225 5 1	$245 \pm 41$	0 651
BMI kg/m <sup>-</sup>	24.4 (15.0-	23.3 ±3.1	$24.5 \pm 4.1$	0.651
	32.2)			
Admission				0.660
category <sup>c</sup>				
Caregory	0 (24 C)	1 (11 1)	0 (00 0)	
Surgical	9 (34.0)	1(11.1)	8 (88.9)	
Medical	17 (65.4)	3 (17.6)	14 (82.4)	
SAPS II Score <sup>a</sup>	48.38	52.75	47.49 ±	0.540
	$\pm 15.07$	+16.66	15 35	
GOEL G h	12.42 (0.10)	115.00	13.35	0.106
SOFA Score <sup>5</sup>	13.42 (9-19)	$14.5 \pm 4.0$	$12.0 \pm 4.0$	0.196
APACHE II Score <sup>a</sup>	$23.23 \pm 5.78$	26.75	22.59 ±	0.191
		+6.85	5.50	
Total of Co-Morbid				0.162
				0.102
Disease				
0	10 (38.5)	0 (0.0)	10 (100.0)	
1	3 (11.5)	1 (33.3)	2 (66.7)	
2	5 (19.2)	2(40.0)	3 (60 0)	
2	5(1).2)	2(+0.0)	5 (100.0)	
3	5 (19.2)	0 (0.0)	5 (100.0)	
4	3 (11.5)	1 (33.3)	2 (66.7)	
Infection <sup>c</sup>				0.044
Yes	12(462)	0(0,0)	12(100.0)	
105	12(+0.2)	4 (09. c)	12(100.0)	
INO A TOTA	14 (55.8)	4 (28.6)	10(/1.4)	
Length of ICU	$4.6 \pm 5.8$	$5.1 \pm 20.6$	$2.2 \pm 5.4$	0.943
mechanical				
ventilation <sup>b</sup>				
Length of ICU stavb	11 27 (2 42)	6 16	0.12	0.050
Length of ICU stay	11.27 (3-43)	$0 \pm 10$	$9 \pm 12$	0.858
Length of Hospital	33.19 (5-	$19 \pm 31$	$29.50 \pm 31$	0.337
stay <sup>b</sup>	160)			
No of	13 + 14	10 + 20	10 + 20	0.765
Hospitalization offer	1.5 ±1.7	1.0 ±2.0	1.0 ±2.0	0.105
nospitalization after				
the last admission <sup>b</sup>				
NUTRIC Score <sup>b</sup>	5.65 (2-9)	$5.0 \pm 2$	$6.0 \pm 2$	0.215
Albumin $(g/L)^a$	248 + 51	21.95	25 31 +5 2	0 234
(g, L)	$2.0 \pm 3.1$	+2.9	20.01 20.2	0.234
~~		±3.0		
C-Reactive protein	$12.47 \pm 6.3$	13.68	11.99 ±7.5	0.779
$(\alpha/\mathbf{I})^{a}$		+3 3		

<code>aData</code> between the two groups were analysed by using Student's T-test and reported as mean  $\pm$  SD

<sup>b</sup>Data between the two groups were analysed by using Mann-Whitney Test and reported as median±IQR

<sup>c</sup>Data between the groups were analysed by using Chi-Square Test

#### 3.2 Characteristics of ICU survivor

The median age of the ICU survivors was 52.3, ranging from 18 until 89 years old. 61.5% were males, and 38.5% were females. Mean BMI was normal at 24.4 kg/m2. Most ICU survivors (65.4%) were admitted to ICU due to medical reasons as compared admission due to surgical, (34.6%). The mean of the SAPS II score and APACHE II score were 48.38  $\pm$  15.07 and 23.23  $\pm$  5.78 respectively, and the median of the SOFA score was 13.42. Thirty-nine percent survivors in this ICU had no underlying comorbidities. Total number of survivors that had infection was 12 (46.2%) and had no infection was 14 (53.8%). The median of the length of the ICU stay and hospital stay was 11 days, and 33 days of stay respectively. Patient were at high risk of malnutrition as the median value for NUTRIC score was 5.69.

Table 2: Nutritional outcomes of the ICU survivor (N=26).

Characteristics	Total	Good QoL	Poor QoL	Р
	(N=26)	(N=4)	(N=22)	value
Type of Nutrition				0.530
Support <sup>c</sup>				
Enteral	24 (92.3)	4 (16.7)	20 (83.3)	
Parenteral	0 (0)	0 (0.0)	0 (0.0)	
Combined	2 (7.7)	0 (0.0)	2 (100.0)	
Energy requirement <sup>a</sup>	1655.3	1723.3	1643.0	0.569
	$\pm 252.2$	$\pm 259.0$	$\pm 255.1$	
Protein requirement <sup>a</sup>	$75.6 \pm 10.3$	$81.5 \pm 12.6$	74.6 ±9.8	0.226
Energy intake <sup>a</sup>	1504.3	1561.3	1493.9	0.703
	±315.7	±406.3	$\pm 307.2$	
Protein intake <sup>b</sup>	$64.6 \pm 18.9$	$74.0 \pm 38.7$	$71.5 \pm 27.4$	0.477
Adequacy of energy <sup>a</sup>	$93.0 \pm 19.9$	$91.8 \pm 30.5$	$93.2 \pm 18.4$	0.896
Adequacy of protein <sup>b</sup>	$86.7 \pm 28.6$	$96.2 \pm 57.9$	94.3 ±38.3	0.887
Energy and protein				0.986
intake <sup>c</sup>				
Underfeeding below	6 (23.1)	1 (16.7)	5 (83.3)	
60%				
Adequate between	6 (23.1)	1 (16.7)	5 (83.3)	
60%-100%				
Overfeeding above	14 (53.8)	2 (14.3)	12 (85.7)	
100%				o .=o
Day start nutrition support <sup>c</sup>	$1.0 \pm 0.8$	$1.0 \pm 0.75$	$1.0 \pm 0.25$	0.670
TTT T				

<sup>a</sup>Data between the two groups were analysed by using Student's T-test and reported as mean  $\pm$  SD

<sup>b</sup>Data between the two groups were analysed by using Mann-Whitney Test and reported as median±IQR

°Data between the groups were analysed by using Chi-Square Test

#### 3.3 Nutrition intake during the ICU stay

Most ICU survivors received enteral nutrition as early as day one of admission. Energy and energy adequacy were high at  $93.0 \pm 19.9$  and  $86.7 \pm 28.6$  respectively. There was no significant difference in energy and protein adequacy between ICU survivors with good and poor quality of life during their ICU stay (Table 2).

#### 3.4 Quality of life among the ICU survivors

Finding from this study showed that ICU survivors reported poor quality of life (85%) at one-year post ICU hospitalization with median SF-12 score at 37.7 (6.8). There was a significant difference in the total score SF-12 between ICU survivors with good and poor quality of life (p=0.002). The median value of the total S-12 was significantly higher in the good quality of life group  $50.2 \pm 6.8$  compared to the poor quality of life group  $35.4 \pm 4.25$ . ICU survivors with good quality of life has significantly higher physical composite Score (p=0.027), Mental Composite Score (p=0.011), Physical Functioning (p=0.001) Role Physical (p=0.001) General Health (p=0.013) Vitality (p=0.002) Social Functioning (p=0.002) (Table 3).

Based on EQ-5D questionnaire, ICU survivors reported no problem in the domain of self-care and anxiety/depression at one-year post-ICU admission. However, they reported some problem in the domain of mobility, usual activity and pain/discomfort. An association was found between domain of usual activities in EQ-5D and quality of life (p=0.001). EQ-5D visual analog score were significantly higher in ICU survivors with good quality of life compared with poor quality of life (55.0  $\pm$  20.0 vs 30.0  $\pm$  22.5, p=0.001) (Table3).

Table 3: Quality of life outcome of the ICU survivor (N=26).

			`	,
Tools	Total	Good QoL	Poor QoL	Р
10015	(N=26)	(N=4)	(N=22)	value
SF-12				
SF-12 score <sup>b</sup> *	37.7 ±6.8	50.2 ±4.95	35.4 ±4.25	0.002
SF-2	$31.0 \pm 7.6$	$51.8 \pm 0.0$	36.5 ±5.26	0.027
Physical				
Composite				
Score (PCS) <sup>b</sup>				
*				
SF-12 Mental	44.4 +8.8	45.4 +5.8	33.6 + 2.0	0.011
Composite Score				
(MCS) <sup>a</sup> *				
Physical	30 8 + 37 0	87 5 +25 0	0.0 + 50.0	0.001
Functioning (PF) <sup>b</sup> *	2010 22710	0/10010		0.001
Role Physical	14 1 +31 2	83 4 +45 8	$0.0 \pm 0.0$	0.001
(RP) <sup>b</sup> *	14.1 ±51.2	05.4 ±45.0	0.0 ±0.0	0.001
Rodily Pain (BP) <sup>b</sup> *	394+202	$50.0 \pm 50.0$	$25.0 \pm 25.0$	0 368
General Health	$55.4 \pm 20.2$	725+230	$61.0 \pm 9.0$	0.013
(GH) <sup>b</sup> *	55.0 ±10.5	12.5 ±25.0	01.0 ±9.0	0.015
Vitality (VT) <sup>b</sup> *	$75.4 \pm 19.0$	$40.0 \pm 15.0$	$80.0 \pm 5.0$	0.002
Social Eurotioning	53.8 ±25.2	$100.0 \pm 18.8$	$50.0 \pm 25.0$	0.002
(SE)b*	55.8 125.2	100.0 ±18.8	50.0 ±25.0	0.002
(SI')	$46.8 \pm 40.0$	100.0 ±25.0	$0.0 \pm 100.0$	0.057
	40.0 ±49.0	$100.0 \pm 23.0$	$0.0 \pm 100.0$	0.057
(KE) <sup>4</sup> Montol Hoolth	$70.0 \pm 10.6$	65.0 17.5	70.0 + 12.5	0.420
	$70.0 \pm 10.0$	$05.0 \pm 17.5$	70.0 ±12.5	0.450
(MH)**				
EQ-JD Malalitan				0.210
Modility <sup>2</sup>	5 (10.2)	2(40.0)	2((0,0))	0.219
No problem	5 (19.2)	2 (40.0)	3 (00.0)	
Some problem	19(73.1)	2 (10.5)	17 (89.5)	
Severe problem	2(7.7)	0 (0.0)	2 (100.0)	0.000
Self-Care	1		10 (7 ( 7)	0.286
No problem	17 (65.4)	4 (23.5)	13 (76.5)	
Some problem	8 (30.8)	0 (0.0)	8 (100.0)	
Severe problem	1 (3.8)	0 (0.0)	1 (100.0)	
Usual activities <sup>c</sup>				0.001
No problem	4 (15.4)	4 (100.0)	0 (0.0)	
Some problem	16 (61.5)	0 (0.0)	16 (100.0)	
Severe problem	6 (23.1)	0 (0.0)	6 (0.0)	
Pain/Discomfort <sup>c</sup>				0.504
No problem	3 (11.5)	1 (33.3)	2 (66.7)	
Some problem	19 (73.1)	2 (10.5)	17 (89.5)	
Severe problem	4 (15.4)	1 (25.0)	3 (75.0)	
Anxiety/Depression <sup>c</sup>				0.094
No problem	13 (50.0)	4 (30.8)	9 (69.2)	
Some problem	12 (46.2)	0 (0.0)	12 (100.0)	
Severe problem	1 (3.8)	0 (0.0)	1 (100.0)	
EQ-5D Visual	$54.2 \pm 16.0$	$55.0 \pm 20.0$	$30.0 \pm 22.5$	0.001
Analog score <sup>b</sup>				

<sup>a</sup>Data between the two groups were analysed by using Student's T-test and reported as mean±SD

<sup>b</sup>Data between the two groups were analysed by using Mann-Whitney Test and reported as median±IQR;

<sup>c</sup>Data between the groups were analysed by using Chi-Square Test

\* Score ranges from 0 to 100, with higher score indicating better quality of life.

# **3.5** Association between energy and protein adequacy with the quality of life.

This study found no significant difference in energy adequacy (p=0.158), protein adequacy (p=0.921), energy and protein adequacy (p=0.921), mNUTRIC score (p=0.921), type of nutrition support (p=0.530), energy and protein feeding categories (p=0.986) between ICU survivors with good and poor quality of life of the (Table 4).

Table 4: Association between energy and protein adequacy with the quality of life

		Good	OoI	Poor	OoI	
Variables	(N-4)	QUL	(N-22)	QUL	P value	
Energy adequacy	1	(11-4)		(1 - 22)		0.158
Vec	/	3 (12 5)		21 (87 5)		0.156
No		1(50.0)		$\frac{21}{(67.5)}$		
INU Dur talia a da mara se		1 (30.0)		1 (30.0)		0.021
Protein adequacy	/	2 (15 0)		17 (05 0)		0.921
Yes		3 (15.0)		17 (85.0)		
No		1 (16.7)		5 (83.3)		
Energy	Protein					0.921
adequacy						
Yes		3 (15.0)		17 (85.0)		
No		1 (16.7)		5 (83.3)		
mNUTRIC score	e					0.921
<5		1 (16.7)		5 (83.3)		
>5		3 (15.0)		17 (85.0)		
Nutrition Suppor	rt					0.530
Enteral		24 (92.3)		4 (16.7)		
Parenteral		0 (0)		0 (0.0)		
Combined		2 (7.7)		0 (0.0)		
Energy and Prote	ein					0.986
Underfeeding	below	6 (23.1)		1 (16.7)		
60%						
Adequate betwee	en 60%-	6 (23.1)		1 (16.7)		
100%						
Overfeeding	above	14 (53.8)		2 (14.3)		
100%		. /		. ,		
ND 1		1 11		<u> </u>		

\*Data between groups were analysed by using Chi-Square

#### 4. DISCUSSION

This study found that most of the ICU survivors have a poor quality of life a year after the ICU admission. Similar result reported reduced quality of life after a year of ICU admission in 61% of the ICU survivors [14]. In this study, it was found that there was a significant reduction of physical composite score  $36.5 \pm 5.26$  and mental composite score  $33.6 \pm 2.0$  in SF-12 as compared to the normative values 47 to 53[15]. Other study also reported that the physical composite score had a relevant reduction  $39.3 \pm 10.9$ , and a minor reduction in the mental composite score  $47.7 \pm 10.9$  as compared to the normative values  $50.0 \pm 10.0$  at 3 months of ICU survival [16]. However, after 1 year, the mean value of the physical composite score increased to  $43.4 \pm 12.0$ , meanwhile the mental composite score normalized at  $49.3 \pm 10.3$ .

The reduction in physical composite score may resulted from the critical ill condition, the increase of energy requirement, the risk for malnutrition, and nutrition interruption that leads to muscle wasting, and slow muscle mass recovery after discharge from the ICU. It was also found that ICU-acquired muscle weakness could be one of the factors for the poor physical composite score. ICU-acquired muscle weakness is an involuntary consequences of long-term bed rest and inactivity among ICU patients [17]. Prolonged ICU-acquired muscle weakness will lead to short- and long-term morbidity, and physical impairment [18].

The reduction in mental composite score occurs possibly due to some psychological alteration due to the experiences of disease, and the ICU admission. In our study, half of the ICU survivors reported having some or severe problems with anxiety or depression. A study in outpatient clinic of the post-ICU survivors reported that half of the patients (45.2%) were having depression, anxiety, and post-traumatic stress disorder. Most patients claimed for having the memory of the events in the ICU, which include the recall memories of the real events, illusion memories, nightmare, and hallucination [19]. In contrast, the study of quality of life among critically ill patient in a developing country, by using the SF-36 found that after the hospital discharged, the survivors' quality of life has positively improved, significantly at the role physical domain[12]. The researchers claimed that the socioeconomic status and health care systems in the different countries may affect the quality of life of ICU survivors.

The median of adequacy of energy and protein intake in relation to requirement was 93.0% and 86.7% respectively. ASPEN 2009 guideline of the optimum energy and protein intake had a cut-off point above 60% [20]. Most of the ICU survivors achieved the energy and protein adequacy during the ICU stay through optimizing of feeding and limiting feeding interruptions in ICU. The results from this study found no association between energy /protein adequacy and quality of life of ICU survivors one-year after ICU discharge. A similar finding was reported elsewhere [24]. However, another study suggested that the higher protein adequacy is associated with the improvement of bodily pain (BP) domain in SF-36 [21]. In a multicentre randomized controlled trial suggested that energy adequacy in the first 8 days of ICU stay was associated with the improved progression functional aspects of health-related quality of life among survivors at 3 months followed up [11].

The strength of this study is the use of more than one tool to measure the quality of life outcome: SF-12, and EQ-5D and the long chronic assessment of quality of life at one-year post ICU hospitalization. Limitations of our study includes the method of sampling used, convenience sampling which are not random and may not be representing the ICU survivors population. The high rate to follow up, 75% resulted in the small sample size (n=26) and responds from non-respondents may significantly affect the findings from this study. The long study period which was a 1-year follow-up of the ICU survivors through the phone interview limited the respondents' rate possibly due to the lack of updated contact information.

#### **5. CONCLUSION**

In conclusion, ICU survivors has poor quality of life at one-year after ICU admission. Energy and protein adequacy were high in ICU. However, there was no association found between energy/protein, and quality of life outcome among ICU survivors at one-year post-ICU admission.

## ACKNOWLEDGEMENTS

We thank the patients for their participations in the study as well as intensivists and ICU nurses for their assistance throughout data collection period.

## **REFERENCES:**

- [1] Mogensen, Kris M., et al. "Malnutrition, critical illness survivors, and postdischarge outcomes: a cohort study." *Journal of Parenteral and Enteral Nutrition* 42.3 (2018): 557-565.
- [2] Singer, Pierre, et al. "The tight calorie control study (TICACOS): a prospective, randomized, controlled pilot study of nutritional support in critically ill patients." *Intensive care medicine* 37.4 (2011): 601-609.

- [3] K Kaukonen, Kirsi-Maija, et al. "Mortality related to severe sepsis and septic shock among critically ill patients in Australia and New Zealand, 2000-2012." *Jama* 311.13 (2014): 1308-1316.
- [4] Morris, Peter E. "Moving our critically ill patients: mobility barriers and benefits." *Critical care clinics* 23.1 (2007): 1-20.
- [5] John, Hoffer L., and Bruce R. Bistrian. "Nutrition in critical illness: a current conundrum." *F1000Research* 5 (2016).
- [6] Wade, Charles E., et al. "Evaluation of nutrition deficits in adult and elderly trauma patients." *Journal of Parenteral and Enteral Nutrition* 39.4 (2015): 449-455.
- [7] McClave, Stephen A., et al. "Guidelines for the provision and assessment of nutrition support therapy in the adult critically ill patient: Society of Critical Care Medicine (SCCM) and American Society for Parenteral and Enteral Nutrition (ASPEN)." *Journal of Parenteral and Enteral Nutrition* 33.3 (2009): 277-316.
- [8] Hoffer, L. John, and Bruce R. Bistrian. "Appropriate protein provision in critical illness: a systematic and narrative review." *The American journal of clinical nutrition* 96.3 (2012): 591-600.
- [9] Singer, Pierre, et al. "Pragmatic approach to nutrition in the ICU: expert opinion regarding which calorie protein target." *Clinical nutrition* 33.2 (2014): 246-251.
- [10] Hiesmayr, Michael. "Nutrition risk assessment in the ICU." Current Opinion in Clinical Nutrition & Metabolic Care 15.2 (2012): 174-180.
- [11] Wei, Xuejiao, et al. "The association between nutritional adequacy and long-term outcomes in critically ill patients requiring prolonged mechanical ventilation: a multicenter cohort study." *Critical care medicine* 43.8 (2015): 1569-1579.
- [12] da Silva, Janete Maria, et al. "Quality of life of critically ill patients in a developing country: a prospective longitudinal study." *Journal of physical therapy science* 28.10 (2016): 2915-2920.
- [13] Cuthbertson, Brian H., et al. "Quality of life in the five years after intensive care: a cohort study." *Critical care* 14.1 (2010): R6.
- [14] Quispe-Laime, A. M., et al. "Lung diffusion capacity and quality of life 6 months after discharge from the ICU among survivors of acute respiratory distress syndrome due to influenza A H1N1." *Medicina Intensiva (English Edition)* 36.1 (2012): 15-23.
- [15] Gamrin-Gripenberg, Lena, et al. "An attenuated rate of leg muscle protein depletion and leg free amino acid efflux over time is seen in ICU long-stayers." *Critical Care* 22.1 (2018): 13.
- [16] Langerud, Anne Kathrine, et al. "Health-related quality of life in intensive care survivors: Associations with social support, comorbidity, and pain interference." *PloS one* 13.6 (2018): e0199656.
- [17] Stevens, Robert D., et al. "Neuromuscular dysfunction acquired in critical illness: a systematic review." *Intensive care medicine* 33.11 (2007): 1876-1891.
- [18] Hermans, Greet, et al. "Interventions for preventing critical illness polyneuropathy and critical illness myopathy." *Cochrane database of systematic reviews* 1 (2014).
- [19] Duarte, Péricles AD, et al. "Characteristics and Outcomes of Intensive Care Unit Survivors: Experience of a Multidisciplinary Outpatient Clinic in a Teaching Hospital." *Clinics* 72.12 (2017): 764-772.
- [20] Peterson, Sarah J., et al. "Adequacy of oral intake in critically ill patients 1 week after extubation." *Journal of the American Dietetic Association* 110.3 (2010): 427-433.

- [21] Tah, P. C., et al. "Association between energy and protein adequacy with quality of life in mechanically ventilated critically III patients: A preliminary result." *Clinical Nutrition* 37 (2018): S300-S301.
- [22] Cuthbertson, Brian H., et al. "Mortality and quality of life in the five years after severe sepsis." *Critical Care* 17.2 (2013): R70.
- [23] Ylipalosaari, Pekka, et al. "Intensive care unit acquired infection has no impact on long-term survival or quality of life: a prospective cohort study." *Critical Care* 11.2 (2007): R35.
- [24] Needham, Dale M., et al. "One year outcomes in patients with acute lung injury randomised to initial trophic or full enteral feeding: prospective follow-up of EDEN randomised trial." *Bmj*346 (2013): f1532.