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IMPACT OF NEGATIVE HYPOCALORIC FEEDING AND ENERGY BALANCE ON CLINICAL OUTCOME IN PATIENTS ADMITTED IN INTENSIVE CARE UNIT: AN OBSERVATION STUDY

Anaesthesiology

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ABSTRACT

Background: Hospitalized patients, especially intensive care unit (ICU) patients, have a high prevalence of malnutrition. Critically ill patients with complicated evolution are frequently hypermetabolic, catabolic, and at risk of underfeeding. **Aim:** The aim of this study was to assess the relationship between energy balance and outcome in critically ill patients in the intensive care unit. **Methods:** In this prospective, observational study a profile of 75 patients admitted in the intensive care unit SMHS hospital, Government Medical College Srinagar conducted from October 2019 to October 2020. Patients above 18 years with more than five days of admission were included. Demographic data, time to feeding, route, energy delivery, and outcome were recorded. Energy balance was calculated as energy delivery minus target. Data in means ±SD, linear regressions between energy balance and outcome variables were applied for consideration. **Results:** 75 patients aged above 18 years were investigated during the study period. Time to feeding was 2.16±1.31 days. Enteral nutrition was the most frequent route with 180±19 days. Mechanical ventilation lasted 9.2±3.4days, mean ICU stay was 13.5±9.8 days, and 30-days mortality was 26.66%. Mean daily energy delivery was 990±830 kcal. Mean energy balance was -188 kcal/day. Significant associations between death in the intensive care unit and the variables age and intensive care unit length of stay were observed, after removing the variables adequacy of energy intake, APACHE II, gender and age during the study period. **Conclusion:** Negative energy balances were correlated with increasing number of complications, particularly infections. Energy debt appears as a promising tool for nutritional follow-up, which should be further tested. Delaying initiation of nutritional support exposes the patients to energy deficits that cannot be compensated later on.

KEYWORDS

Enteral nutrition, Energy requirements, Permissive Underfeeding, Exposure, Risk or Outcome, Intensive Care Unit, Mortality.

INTRODUCTION:

Intensive care unit (ICU) patients can have issues such as metabolic stress, catabolism, prolonged immobilization and inappropriate nutrition intake, any of which may result in negative energy balance, meaning that the expended energy overcomes the intake. [1,2]

Hospitalized patients, especially intensive care unit (ICU) patients, have a high prevalence of malnutrition. It has been estimated that 40-50% of patients admitted to the ICU in Europe and USA present some degree of malnutrition,[3] a proportion that is not much different in Colombia.[4] There is strong evidence suggesting malnutrition is associated with increased rates of complications,[5] in the same way as obesity has been related to worse prognosis in critically ill patients.[6]

The optimal way to quantify malnutrition in the ICU is still a matter of debate, as the criteria are not unanimously accepted. Surgical scores, such as the prognostic nutritional index (PNI), have not been validated in ICU settings.[7] The actual weight is a source of confusion as is not reliable for nutritional assessment due to the enormous fluid shifts observed in critically ill patients. Indeed non nutritional factors such as fluid balance, and inflammatory status are more important determinants of body weight early on the clinical course, the actual body mass index (BMI) becomes unreliable. Protein indicators of malnutrition (plasma albumin <35 g/l, plasma transferrine <2 g/l), are altered by critical illness. Finally, anthropometric determinations such as the cutaneous skin-fold are rendered useless by edema. The patient's physical aspect, his nutritional history and the presence of acute disease on admission to the ICU appear as the best tool to assess nutritional status.[8] Such a clinical assessment should be part of routines, particularly in the sickest ICU patients.

Considering that early and adequate nutritional therapy (NT) in critically ill patients is an important factor for promoting health, decreasing physiological stress and maintaining immunity, assessing the suitability of this treatment is essential. The goals of NT include providing adequate nutritional support, preventing nutritional deficiencies, attenuating the loss of lean body mass, preventing complications and improving clinical outcomes. Enteral feeding using nasogastric tube is an important therapeutic modality because the patients being fed through nasogastric tube may be partially or totally unable to ingest food. So, in an observational study with adult patients hospitalized in intensive care unit having an exclusive enteral nutrition therapy for more than 72 hours, these patients received less enteral diet than prescribed. [9]

This present study aimed at testing the relationship between energy balance and clinical outcome in severely ill patients admitted in our surgical ICU with prolonged stay.

METHODS:

The study was designed as a prospective observational study conducted on patients staying for more than 5 days in the surgical ICU of the tertiary care unit SMHS Hospital, Government Medical College Srinagar. Data was collected daily through interviews, from medical records, from daily notes made by the nursing team and from the nutritional balance record of patients between October 2019 and October 2020. The patients were monitored to calculate the TEV and its adequacy, starting at the first day of hospitalization (T0).

All the patients were evaluated by a nutritionist based on 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 (A.S.P.E.N.), in which an estimate of 25-35kcal/kg/day is used to calculate a patient's energy requirements. [10]

Patient data:

Age, sex, pre-event weight, height, and BMI were recorded; nutritional status on admission was assessed as: malnourished if 2 of the 3 below criteria were present: weight loss >10% within the last 6 month, BMI <19, wasting disease, they were considered normal with BMI =20-29, and obese if BMI >30. Patients were weighted weekly during the stay when possible. Severity of disease was assessed using the simplified acute physiologic score (SAPS II) score during the first 24 h. [11] Organ failure was quantified by the SOFA score (sepsis-

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related organ failure assessment) [12] on admission, and on weekly basis: this score defines 6 organs/systems and attributes 0 (no failure) to 4 points (maximal failure) to each according to defined criteria of severity: stratification was 1–2 points for one organ =moderate failure, 3–4 points =severe failure. The cardiac SOFA score escalates from 1 = mean arterial pressure <70 mmHg, to 4 =continuous dopamine/ dobutamine 415 mg/kg or, epinephrine/ norepinephrine >0.1 mg/kg/min.

Feeding protocol:
Artificial nutritional support was considered in patients unable to resume oral feeding within 4–5 days.[13] Indications for early enteral nutritional support, i.e. within 48 h, were: multiple injury, major gastro- intestinal surgery for solid tumor, and pre-existing malnutrition.

SOFA score was measured at randomization (baseline) and then every 48 h. The primary endpoint for the study was change in SOFA score at 48 h (delta SOFA).

Secondary endpoints were: Change in SOFA score at 96 h, total SOFA score, insulin requirements, frequency of hyperglycemia or hypoglycemia, length of ICU stay, days on ventilator, and mortality.

Statistical analysis
The data were organized in Excel 2010 (Microsoft, USA) and analyzed using SPSS version 20.0 (SPSS Corp., Chicago, USA). A one-sided Student's *t*-test was used for the primary outcome, since its reduction was the primary hypothesis of our study; two-sided *t*-test was used for all other endpoints. All values were expressed as mean ± SD for continuous variables or proportions for categorical variables. We considered statistically significant a *P* value of 0.05 or less.

Conflict of interest: Nil
Funding: Nil

RESULTS:
Eighty five surgical ICU patients were enrolled out of 768 consecutive admissions (5.7%), 10 patients were excluded due to incomplete data, leaving 75 patients and 180 ICU days for analysis. Mean age of the study population was 58.5±11.12 years ranged from 18 to 90 years. The mortality rate was 26.66% among the study population. The patients' characteristics are reported in [Table 1].

Table 1: Study Population characteristics

Characteristics	Mean ±SD
Age (years)	58.5±11.12
Sex M/F	51/24
SOFA	3.5±1.8
Mechanical ventilation	9.2±3.4
Complications	19.28±8.28
Length of ICU stay	14.28±3.51
Mortality	20

The length of stay was variable with a mean length of stay of 13.5±3.5 days, 36% of patients stayed from 5 to 10 days fallowed by 24% from 10 to 15 days, 13.33% from 15 to 20 days [Table 2].

Table 2: Length of ICU stay

Length of ICU stay	Frequency	%
5-10 days	27	36
10-15 days	18	24
15-20 days	10	13.33
20-25 days	6	8
25-30 days	4	5.33
30-35 days	4	5.33
35-40 days	3	4
40-50 days	2	2.66
≥50 days	1	1.33

Mean percent adequacy between prescribed and calculated energy was 100.5% and between administered and prescribed energy, 78.2%. The mean administered/calculated energy ratio was 78.7%. This is reflected in the mean energy balance, which was slightly negative (less than 190 kcal/day) [Table 3].

Table 3: Energy values: calculated, prescribed, administered and energy balance (kcal/day)

Energy	Mean ±SD	Minimum	Maximum
Calculated	1487.6 (221.8)	580.0	1917.0
Prescribed	1592.5 (213.5)	570.0	1880.0
Administered	1306.9 (282.2)	524.9	2009.5
Energy balance	- 189.3 (209.3)	- 570.9	218.3

Nutritional support, feeding was started within 3.1±2.2 days after admission (Table 4).

Table 4: Time to feeding by diagnostic category

Diagnostic category	Frequency	Mean ±SD
General surgery	29	38.6
Neuro surgery	15	20
Trauma	11	14.6
Surgical GE	7	9.3
Sepsis	6	8
Respiratory failure	4	5.3
Others	3	4

Patients with a fatal outcome had significantly higher mean age and SOFA score than did survivors (p<0.001 and p=0.007, respectively). No statistically significant difference was found regarding gender, ICU time of stay, fasting time before ENT initiation and ENT days. When the study population was analyzed for the percentage of energy intake adequacy (<70%, 70-90%, >90%), no statistically significant difference was found for age (p=0.890), time of ICU stay (p=0.435) or SOFA score (p=0.567) [Fig 1].

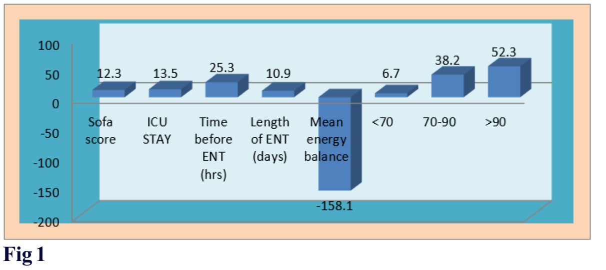

Fig 1
Routes of feeding and energy delivery during the whole stay days of feeding among the study population [Fig 1].

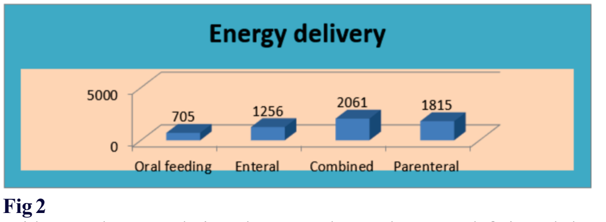

Fig 2
With regard to correlations between the total energy deficit and the total number of complications during the ICU stay. The correlations were strong with the length of mechanical ventilation, the total number of complications, the infectious complications, the antibiotic days, and the length of ICU stay. Energy deficit was not correlated with mortality [Fig 3].

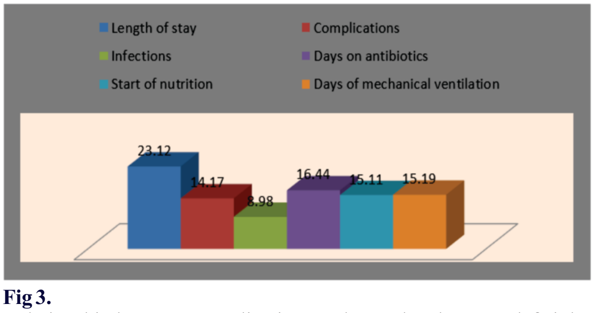

Fig 3.
Relationship between complications and cumulated energy deficit by regression analysis.

DISCUSSION:
The hypermetabolic state and accelerated proteolysis of skeletal muscle in critically-ill patients, particularly if combined with pre-existing malnutrition, leads to marked immunosuppression, muscle weakness and increased risk of nosocomial infection. Artificial

nutritional support is unquestionably indicated in these patients. However, is it necessary or desirable to achieve positive energy balance, at least in the early flow phase of illness. Evidences suggest that nutritional support actually influences clinically-important outcomes is difficult to obtain (Heyland, 1998).[14] It cannot be assumed that providing energy intake to match energy expenditure is optimal for the management of critically-ill patients (Zaloga & Roberts, 1994). [15]

In the present study, our results suggest that negative feeding nutrition is associated with high risk of multiple organ failure. The loss of lean body mass during acute illness is well-known and has been associated with poor clinical outcomes;[16] the functional recovery after ICU discharge depends on the residual lean body mass. The objectives of nutritional support therapy are to overcome the acute catabolic phase, and to ameliorate the loss of body nitrogen, preserving rather than increasing the lean body mass. No precise method in clinical practice is available to determine the maximum acceptable loss of lean body mass, and to evaluate, in real time, the direct effect of nutritional therapy. In our usual practice, we estimate macronutrients using percentages of the total caloric amount, but in the critically ill patient population this approach is not appropriate. There is still controversy regarding the accurate nutritional therapy for critically ill patients, specially the amount of calories and the types of nutrients required. [17-19]

The hypothesis that persistent hypocaloric feeding and negative energy balances are associated with poor outcome in the sickest critically ill patients was verified. This study investigated the nutritional support over 180 ICU days in 75 very sick patients with prolonged ICU stay. It confirms the difficulty to keep a positive energy balance using the enteral route. Only 26 patients (34.66%) were in positive balance at the end of their stay, while 49 (65.33) were in negative balance throughout. These results were observed in an ICU, which has been applying feeding protocols for a prolonged period of time.[20]

Infections are a classical complication of malnutrition and underfeeding: a recent study including 138 medical ICU patients, [21] showed that hypocaloric feeding was associated with increasing blood stream infections. Another study including 200 medical ICU patients, observed a reduction in length of mechanical ventilation associated with improved nutritional support. [22] The negative energy balance was strongly correlated with complications, and particularly with the infectious complications. The multiple regression analysis showed that energy balance at the end of the first week, and the cumulated energy balance of the ICU stay were the strongest predictors of prolonged ICU stay. Correlation does still not mean causality. For any ICU specialist, it is evident that as the patients stay prolongs the probability of encountering complications and administering antibiotics increases. The most severe patients are also the most difficult to feed by the enteral route. The fact that this negative correlation was already present at the end of the first week is another argument supporting the role of the negative balances in favoring complications; finally the strong relationship between the complications and the initiation time of feeding also supports the hypothesis.

It has recently been shown that evidence-based nutritional support promoting the use of early EN is able to improve clinical outcome and even to reduce death risk in critically ill patients. [22] But there is yet no answer to the question ' 'how long can an ICU patient be starved without deleterious consequences". Considering the results of the present study, which show that the initial energy deficits cannot be compensated, this time appears to be limited.

CONCLUSION:

The present study confirms that negative energy balances are very frequent during severe critical illness admitted in ICU despite nutrition protocols. It shows that underfeeding is correlated with increasing number of complications, and particularly with infections and loss of body mass. Future research is required to identify the optimal energy intake targets that could result in significant reductions of complications, mortality and costs.

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