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**How transplant patients are fed in the intensive care unit:
A one-year retrospective study**

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Running title: Transplant patients' nutrition in the ICU

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ABSTRACT

Background and Objectives: Even though the nutritional status of patients following organ transplant has a significant effect on outcomes, the energy intake of transplant patients hospitalized in the intensive care department is not well reported. The present study aims to examine the medical nutritional therapy of transplant patients in a large transplant center.

Methods and Study Design: Data were collected retrospectively. All patients after perioperative transplant surgery or with late complications after organ transplants were included. The study included 78 patients who underwent liver (n=36), kidney (n=21), lung (n=14), pancreas (n=3) or both pancreas and kidney (n=4) transplants in 2017. Energy requirements were predicted using the Faisy-Fagon predictive equations calculated daily for 14 days. Energy intake was assessed, and daily energy balance was calculated. Complications and mortality were noted.

Results: The mean energy intake was 1150 kcal/day. Most patients were in a negative energy balance (NEB; range -5735 to 3437 kcal/day). A greater NEB was associated with longer length of ventilation (LOV) and length of stay (LOS). The observed mortality rate was 42.3%. The correlation between energy balance (14 days) and LOS was $r=-0.549$; for LOV, it was $r=-0.569$. Patients who underwent lung transplant had the highest negative energy balance and the highest mortality ($p<0.01$).

Conclusions: Most of the transplant patients were underfed, and there was a significant correlation between energy balance and mortality ($r = -0.324$). Optimal energy intake should be assessed prospectively.

Key Words: transplant patients, enteral nutrition, parenteral nutrition, mortality, negative energy balance

INTRODUCTION

Malnutrition is a common diagnosis in patients who have had an organ transplant.¹ Insufficient nutritional status has been associated with complications such as morbidity and mortality and is associated with an extended hospital stay.² Studies clearly show that early identification of nutritional deficiencies and initiation of appropriate treatment can prevent complications in transplant patients. Nutritional treatment is, therefore, an essential factor in the standard of care after transplantation surgery.¹⁻⁴ Specifically, according to a study by inadequate intake of protein and calories leads to changes in body composition and reduces biological function.

If the patient has a functioning gastrointestinal tract, the recommendations are to initiate early enteral nutrition.⁵⁻⁷ Although the nutritional status of transplant patients has a significant

effect on outcomes, the energy intake of the intensive care unit (ICU) transplant patients is not always well reported. The objective of the present study was to audit the nutritional intake from enteral and parenteral nutrition administered to organ transplant patients in a large transplant center.

MATERIALS AND METHODS

The study population included all transplant patients (N=78) admitted to the ICU of Rabin Medical Center (Israel), a 16-bed multidisciplinary unit in a university-affiliated tertiary-care medical center, in 2017. The study was conducted for 1 year and included all patients admitted after elective transplant surgery or complications from transplant surgery. The Rabin Medical Center institutional ethical review board approved the study. The IRB waived the requirement to obtain informed consent from the patients, because of the retrospective design, which analyzed the data from the ICU computerized system patient confidentiality that maintained by encoding patient identification information in a manner that prevents identification of individual patients. During 2017, 36 liver transplant patients, 21 kidney transplant patients, 14 lung transplant patients, 3 pancreas transplant patients and 4 pancreas-kidney transplant patients were admitted. Heart and lung perioperative transplant patients were excluded because they were not accepted in the general intensive care department but in the open-heart surgery intensive care unit immediately after transplantation. Therefore, only the liver and kidney-pancreas transplants were admitted directly from the operating room or after complications; the others were admitted only after complications and far from the transplant surgery.

Data were taken from a computerized system (iMDsoft, Israel) used in the ICU and included demographics, the Acute Physiology and Chronic Health Evaluation (APACHE II) score, the Sequential Organ Failure Assessment (SOFA) score, body mass index (BMI), LOV, LOS in the ICU and mortality after 60 days. In addition, the daily average of parenteral and enteral energy intake was recorded over a period of 14 days of ICU hospitalization. Faisy-Fagon predictive equations for energy expenditure⁸ from day 1 to day 14 following admission were retrieved from the computerized information system, enteral and parenteral nutrition were reported. Energy balance was calculated every day by subtracting energy requirements obtained by the Faisy-Fagon equation from energy intake (enteral and/or parenteral nutrition).

Statistical analysis

Continuous, normally distributed variables are presented as the mean \pm standard deviation (SD). A comparison of measurements was performed using the t-test.

The mean differences were calculated by comparing the sum of the enteral and parenteral energy intake from day 1 to day 14 to the target energy intake.

The energy balance was obtained by applying the Faisy-Fagon equation to descriptive statistics and was compared between nutritional methods by the one-way ANOVA test (SPSS 25 software, USA). Statistical significance for a two-sided test required $p < 0.05$.

The survival rate was obtained using the chi-square test. In addition, the Pearson test was administered to calculate the correlation between negative energy balance (NEB), LOV and hospitalization LOS.

RESULTS

The study population included a total of 78 transplant patients admitted to the ICU after elective surgery (n=43) or after postsurgical complications (n=35). The participants comprised patients who had undergone transplants involving the kidney (n=21), lung (n=14), liver (n=36), pancreas (n=3) or both pancreas and kidney (n=4). The average age was 53 ± 15 years. The mean APACHE II score was 28.8 ± 3.4 , and the mean SOFA score was 9.9 ± 4.2 (Table 1), showing the severity of illness of the patients.

The mean energy requirement, based on the Faisy-Fagon predictive equation, was 1867 ± 178 kcal/day. On the 3rd day after admission, results indicated that the patients received an average of 629 ± 493 kcal/day through enteral, parenteral or supplemental parenteral nutrition. On the 8th day after admission, the average energy intake of the patients increased to 1252 ± 695 kcal/day and stabilized to give an average nutritional intake of 1238 ± 913 kcal/day on the 14th day of hospitalization (Fig. 1). Most patients were in an NEB by the second day after admission (-1178 ± 599 kcal/day). When calculating the energy intake of the patients, during the first 7 days after ICU hospitalization, enteral nutrition and parenteral nutrition together reached 40% of the energy target (705 kcal out of an energy target of 1783 kcal). Forty-eight patients received enteral nutrition and 16 patients received parenteral nutrition. Fourteen patients received enteral and supplemental parenteral nutrition.

The mean LOS in the ICU was 7.6 ± 11 days, with a mean LOV during that time of 5.2 ± 8.3 days. The mortality rate was 42.3% (33/78) in patients with an APACHE II score of 28.8 ± 3.4 . The lung transplant patients admitted with postsurgical complications had the highest NEB (-912 ± 589 kcal/day) and the highest mortality rate (93%, $X^2 = 21.83$, $p < 0.01$). All these patients

were suffering from septic shock and required high doses of vasopressors. The results show a significant correlation between higher energy deficit and LOS ($r=-0.549$, $p<0.01$) as well as LOV ($r=-0.569$, $p<0.05$).

DISCUSSION

Our audit suggests that transplant patients received a hypo energetic intake during their ICU stay. Negative energy balance has been shown to increase post-surgical complications and mortality.⁹ After transplant surgery, the patients are treated with inotropic medications and usually require mechanical ventilation.¹⁰ According to the European Society for Clinical Nutrition and Metabolism (ESPEN) guidelines for clinical nutrition in the ICU,⁷ patients whose energy needs are estimated using predictive equations should be treated with hypo energetic nutrition (70% of the energy target) for the first week rather than iso energy nutrition that can supply 85% to 100% of the energy target. However, it now appears that the treating medical team may underestimate the patients' nutritional needs despite the critical role of nutrition. The present study results stress the fact that the energy nutritional intake by enteral and/or parenteral nutrition in the first 7 days of ICU hospitalization amounted to only 40% of the nutritional target. Other research has also shown a hypo energetic intake in ICU populations.¹¹ Our group showed that a too- hypo energetic intake might be associated with an increased risk of mortality.⁹

According to the Faisy-Fagon equation calculation of the target kcal/day, all the transplanted patients in the present study received from 192 to 1252 kcal/day on average, much less than required. This deficit was shown to have a significant effect on outcome after transplantation surgery. showed that a cumulative NEB overtime was closely associated with postsurgery complications such as sepsis, adult respiratory distress syndrome (ARDS), renal failure, renal replacement therapy, and overall total complication rate.¹⁰ According to the present study, underfeeding with less than 70% of the nutritional target was associated with increased LOS and LOV.

A study conducted by Wilcox 2 concluded that malnutrition after transplant surgery represents an independent variable for mortality. In accordance with this observation, lung transplant patients in our study, whose NEB was lower than that of other study participants, had a significantly higher rate of mortality (93%) than the overall rate of 42.3%. Although the causes of more morbidity and mortality in transplant patients are multifactorial as results from other explanation categories related like elective transplant patients, the primary pathology, degree of the illness type of solid organ transplant, etc., However, the purpose of the current

study indicate a significant hypo energetic intake in these patients which may have reason for higher morbidity and mortality.

The reason for not reaching the energy target despite an appreciation of the dangerous consequences of underfeeding is not clear. A number of reports in the literature¹²⁻¹⁴ have discussed the possibility that reliance on measurements of gastric residual volume (GRV) in the ICU can result in insufficient energy intake in transplant patients because of the fear of an increase in GRV.¹⁵ In addition, the amount of time during which the patient is outside the ICU, possibly in the operating theatre or undergoing computed tomography, a magnetic resonance imaging scan, etc., can reduce the time the patient receives enteral (EN) or parenteral nutrition (PN), especially if the medical staff delays the resumption of supply.¹⁶ These issues may contribute to the development of an NEB.

In practice, the first 7 days of hospitalization in the ICU can be divided into 2 main phases: the early acute phase and the late acute phase. The early phase, which typically occurs during the 1st and 2nd days in the ICU, is characterized by a highly catabolic state. The late phase, from the 3rd up to the 7th day, is characterized by a high level of muscle deterioration and metabolic disturbances.⁷ There is currently no validated specific ICU nutrition assessment that can reliably satisfy the requirements of critically ill patients. Consequently, all patients admitted to the ICU should be considered at risk for malnutrition.⁷ Patients in the present study were hospitalized in the ICU for at least 48 hours, so all were considered to be at high risk for malnutrition. Considering the energy requirement for the first 7 days of ICU hospitalization compared to the inadequate energy intake recorded in the present study, the high mortality rate (42.3%) may be explained by previous studies that reported an association between NEB and mortality in the ICU.^{16,17}

The present study data show that when the enteral energy intake of the patient was insufficient to achieve the target nutrition, the patient did not receive the recommended amounts of parenteral supplements. According to the ESPEN guidelines,⁷ there is a complete consensus that oral diet is preferable over all other options if the patient is able to eat.⁷ If not, EN should be initiated within the first 48 hours, followed by PN or supplemental PN within 3 to 7 days if the patient is unable to obtain the full amount of nutritional calories through EN. A major concern is a risk of overfeeding when using PN, and there is also a risk of increased infectious morbidity.¹⁷ However, recent studies seem to agree that the amount of nutrients provided is more significant than the possibility of complications due to the route of nutritional support.^{18,19}

Our study has limitations. First, this study was a retrospective mono center study. A different type of center perhaps would give results that are easier to generalize to other populations. Second, protein intake was not accessible and is not shown in this study, we concentrate just on energy balance. Nitrogen deficit may also have affected outcomes. We chose to use the Faisy-Fagon equation mainly because it was developed using a population of very ill patients with APACHE II and SOFA scores very similar to those of our patients. However, it would have been preferable to use indirect calorimetry to accurately evaluate the energy balance estimated in our study. Finally, the observed mortality may be associated with factors other than undernutrition, since lung transplant patients with severe septic shock have a high mortality rate.

Conclusion

Our study shows that most of the transplant patients admitted in our ICU were underfed. NEB was associated with higher mortality, most notably in patients who had undergone a lung transplant. Enteral and supplemental parenteral nutrition may be effective if a calorie target can be précised, and this could minimize the NEB. Finally, energy intake and calorie balance should be assessed daily to prevent the occurrence of severe NEB and complications.

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AUTHOR DISCLOSURE

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Table 1. Patient characteristics

Transplant organ	Elective, No. (%)	Complication admission, No. (%)
Kidney	12 (15.4)	9 (11.5)
Lung	0 (0)	14 (17.9)
Pancreas	0 (0)	3 (3.9)
Liver	27 (34.6)	9 (11.5)
Kidney + pancreas	4 (5.1)	0 (0)
Criteria	Mean±SD	
Age	52.70±14.75	
BMI	25.49±6.18	
APACHE II	28.8±3.4	
Total SOFA score	9.9±4.2	
LOV (days)	5.23±8.3	
LOS (days)	7.6±11	
Gender	N (%)	
Male	48 (61.5)	
Female	30 (38.5)	

BMI: body mass index; APACHE II: acute physiology and chronic health evaluation; SOFA: sequential organ failure assessment; LOV: length of ventilation; LOS: length of stay.

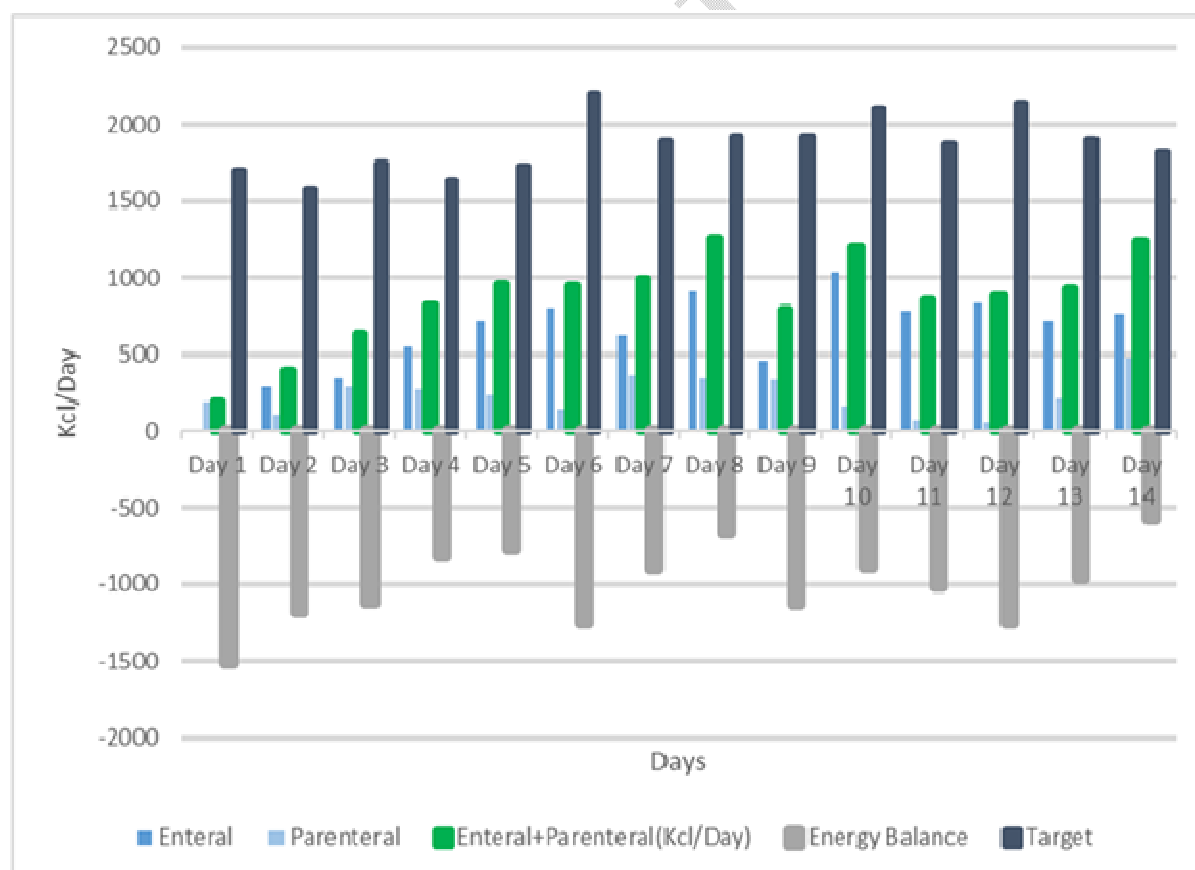


Figure 1. Difference between mean target energetic intake and mean enteral and parenteral nutrition of transplanted patients from the first day to 14th day after ICU admission. The difference presented as negative energy balance (NEB).