**How are transplanted patients fed in the ICU: a one-year retrospective study**

Running Title: **Transplant Patients’ Nutrition in the ICU**

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**Background**: Even though the nutritional status of transplanted patients has a significant effect on outcomes, the caloric intake of transplant patients hospitalized in the intensive care department is not well reported. The present study examines the medical nutritional therapy of transplanted patients in a large transplant center*.*

**Methods:** Data were collected retrospectively. All patients after perioperative transplant surgery or late complications after organ transplant 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 every day for 14 days. Energy intake was assessed and daily energy balance was calculated. Complications and mortality were noted.

**Results:** Mean energy intake was 1150 Kcal/day. Most patients were in a negative energy balance (NEB) of (range -5735 to 3437 kcal). A higher negative energy balance was associated with longer Length of Ventilation (LOV) and Length of Stay (LOS). The observed mortality rate was 42.3%.The correlation between Caloric Balance (14 days) and Length of Stay was r=-0.549 and for Length of Ventilation of r=-0.569. Patients who underwent lung transplant had the highest negative energy balance and the highest mortality (p < 0.02).

**Conclusion:** Most of the transplant patients were underfed and there was a significant correlation between Caloric Balance and mortality (r=-.324). Optimal calorie intake should be assessed prospectively.

**Key words:** Transplanted patients, Enteral Nutrition, Parenteral Nutrition, Mortality, Negative Energy Balance

**Background**:

Malnutrition is a common diagnosis in transplanted patients.1 Insufficient nutritional status has been shown to be a risk factor independent of postoperative 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 transplanted patients. Nutritional treatment is therefore an essential factor in the standard of care after transplantation surgery.1-4 Specifically, according to the study by de Luis et al.,5 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.6-7 Despite the fact that the nutritional status of transplanted patients has a significant effect on outcomes, the caloric intake of ICU transplant patients is not always well reported. The objective of the present study was to audit the nutritional intake of enteral and parenteral nutrition administered to organ transplantation patients in a large transplant center.

**Methods**

The study population included all the transplanted patients admitted to the Intensive Care Unit (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 a period of one year, and included patients admitted after elective surgery or complications of transplant surgery. The Rabin Medical Center institutional review board approved the study. During 2017, 36 liver patients, 21 kidney patients, 14 lung patients, 3 pancreas and 4 pancreas-kidney patients were performed. The heart and the lung perioperative transplant patients were excluded since not being accepted in the general intensive care department but in the open heart surgery intensive care unit immediately after transplantation. Therefore, only the liver, the kidney-pancreas transplants were admitted directly from the operative room or after complications, and the other only after complications and far from the transplant surgery.

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

 *Statistical analysis*

Continuous normally distributed variables are presented as the mean ± standard deviation (SD). Comparison of measurements was performed using the *t*-test.

The mean differences were calculated by taking the sum of the enteral and parenteral calorie intake from day 1 to day 14 compared to the target caloric intake.

The energy balance was obtained by applying the Faisy equation to descriptive statistics and 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, Person test was administered to obtain correlation between the NEB to the Length of Ventilation (LOV) and hospitalization Length of Stay (LOS).

**Results**

The study population included a total of 78 transplanted patients admitted to the ICU after elective surgery (n = 43) or post-surgical 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 old. The mean APACHE II score was 28.8 ± 3.4, SOFA score was 9.9 ± 4.2 (Table 1), showing the severity illness of our patients.

 Mean Faisy predictive equation energy requirement was 1867 ± 178 kcal/day. By the 3rd day, our results indicated that the patients received an average enteral, parenteral or supplemental parenteral nutrition of 629 ± 493 kcal/day. On the 8th day after admission, the average calorie intake of the patients increased to 1252 ± 695 kcal/day and stabilized to give an average nutritional intake of 1238 ± 913 kcal/d on the 14th day of hospitalization (Fig. 1). Most patients were in a negative energy balance (NEB) by the second day after admission (‑1178 ± 599 kcal/day). Mean daily negative balance was When calculating the percentage of caloric intake of the patients, during the first seven days after the ICU hospitalization, the EN and PN together reached 40% of the caloric target (705± kcal out of 1783± kcal of the caloric target). Four patients received oral feeding, 44 patients enteral feeding and 16 patients parenteral nutrition. Fourteen patients received enteral and supplemental parenteral nutrition.

The mean hospitalization LOS at 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) and was in relation to high APACHE II score. The lung transplant patients admitted with post-surgery complications had the highest NEB (-912 ± 589 kcal/day) and the highest mortality rate (93%, X2=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 caloric deficit and LOS (r=-0.549 p <0.001), as well as with LOV (r=-0.569 p <0.05).

**Discussion**

Our audit suggests that transplant patients received a low caloric intake during their ICU stay. Negative energy balance has been proven 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 ESPEN guidelines for clinical nutrition in the ICU,7 patients whose energy needs were estimated using predictive equations, should be treated with hypocaloric nutrition (70% of the caloric target), for the first week rather than isocaloric nutrition that can supply 85%-100% of the caloric 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 calorie nutritional intake by EN and/or PN in the first seven days of ICU hospitalization amounted to only 40% of the nutritional target. Others (Heyland, Elke) has aslo showed a low calorie intake in ICU populations. Our group showed that too low calorie intake might be associated with an increased risk of mortality.9

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

A study conducted by Wilcox et al.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%.

The reason for not reaching calorie 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 a reliance on measurements of Gastric Residual Volume (GRV) in the ICU can result in insufficient caloric 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 (CT) or Magnetic Resonance Imaging (MRI) scan, etc., can reduce the time the patient receives enteral or parenteral nutrition, especially if the medical staff delay the resumption of supply.16 These issues may all contribute to the development of a NEB.

In practice, the first seven days of hospitalization in the ICU can be divided into two main phases, the early acute phase and the late acute phase (7). The early phase, which typically occurs during the first and second days in the ICU, is characterized by a highly catabolic state. The late phase from the third up to the seventh day is characterized by a high level of muscle deterioration and metabolic disturbances. 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, and so, all are considered to be at high risk for malnutrition. Considering the caloric requirement for the first seven days of ICU hospitalization compared to the inadequate caloric intake recorded in the present study results, the high mortality rate (43.6%) may be explained by previous studies that reported an association between NEB and mortality in the ICU.17-18

The present study data shows that when the enteral caloric 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 guidelines7, 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 SPN or PN, within 3-7 days if the patient unable to obtain the full amount of nutritional calories through EN. A major concern is the risk of overfeeding when using PN and there is also a fear of increased infectious morbidity.18 However, recent studies seem to agree that the amount of nutrients provided is more significant than the possibilities of complications due to the route of nutritional support.19-20

Our study has limitations. First, this study was a retrospective mono center study. Second, protein intake was not available and are not shown in this study. Nitrogen deficit may be even more affecting outcome.. We chose to use the Faisy-Fagon equation mainly because it has been developed in a population of very sick patients with APACHE II and SOFA scores very similar to ours. However, it would have been preferable to use indirect calorimetry to evaluate accurately the energy balance which is estimated in our study. Finally the observed mortality may be associated with other factors than undernutrition since lung transplant patients with severe septic shock have a high mortality.

In conclusion, our study shows that most of transplanted patients admitted in our ICU were underfed. NEB was associated with higher mortality, most notably in patients after lung transplantation. Enteral and supplemental parenteral nutrition may be effective if a calorie target can be précised, and this could minimize the NEB. Finally, calorie intake and calorie balance should be assessed daily to prevent the occurance of severe NEB and complications.

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