ORIGINAL SCIENTIFIC PAPER

Assessment of nutritional support in patients after liver and kidney transplantation

Maja Ćurić Delač[1,2], Zlata Flegar Meštrić[2], Sonja Perkov[2], Leda Borovac Štefanović[1,3], Željko Vidas[2], Branislav Kocman[2], Stipislav Jadrijević[2], Jasna Aladrović[4], Marina Mandelsamen Perica[1], Ivančica Delaš[1*]

[1]School of Medicine, University of Zagreb, Šalata 3, HR-10 000 Zagreb, Croatia
[2]University Hospital Merkur, Zajčeva 19, HR-10 000 Zagreb, Croatia
[3]Prolife, Marulićev trg 12, HR-10 000 Zagreb
[4]Faculty of Veterinary Medicine, University of Zagreb, Heinzelova 55, HR - 10 000 Zagreb, Croatia

**Corresponding author: ivancica.delas@mef.hr*

Abstract

During the last decades organ transplantation has evolved into a proven therapy for end-stage organ failure. However, the long-term success of organ transplantation depends significantly on the patients' ability to overcome possible postoperative complications and to recover from a severe metabolic imbalance. Therefore, in the present study we assessed the accuracy of the early post-operative nutritional intake in a vulnerable group of patients after organ transplantation and compared it with the calculated minimal nutritional requirements.

A number of 61 patients were included in the study, 48 with liver, 11 with kidney, and two patients with both, liver and kidney transplants. Mini nutritional assessment (MNA) was applied and total nutritional intake was recorded for fourteen consecutive post-transplant days. Serum concentrations of proteins, urea and creatinine, as well as catalytic concentrations of liver enzymes were measured. Urea to creatinine ratio was calculated. According to body mass index (BMI) only a few patients were malnourished, but low serum protein levels indicated a significant protein catabolism. Nutritional requirements were provided mainly by glucose, with low amounts of proteins, i.e. amino acids, and fats. It took more than seven days to reach the appropriate nutritional intake. Because of the intensive catabolism, especially of proteins, nutrition of organ transplant recipients requires permanent monitoring and better nutritional support through formulas for enteral and total parenteral nutrition.

Key words: *energy intake, protein intake, liver, kidney, organ transplantation*

Sažetak

Tijekom posljednjih desetljeća transplantacija organa razvila se u metodu odabira za terapiju pacijenata s terminalnim zatajenjem organa. Međutim, dugoročni uspjeh transplantacije organa ovisi o sposobnosti pacijenata da prevladaju moguće postoperativne komplikacije i da se oporave od teških poremećaja metaboličke ravnoteže. Stoga smo u ovoj studiji željeli procijeniti kvalitetu rane postoperativne prehrane u vrlo ranjivoj skupini bolesnika nakon transplantacije organa i usporediti nutritivni unos s međunarodnim preporukama kako bi se zadovoljili minimalni nutritivni zahtjevi. U istraživanje je uključen 61 pacijent, od kojih 48 s transplantiranom jetrom, 11 s transplantiranim bubregom i dva bolesnika kojima su transplantirana oba organa. Procjena rizika od malnutricije provedena je primjenom upitnika "Mini nutritional Assesment" i tijekom prvih četrnaest dana nakon transplantacije bilježen je ukupni dnevni nutritivni unos. U serumu pacijenata izmjerene su koncentracije proteina, uree i kreatinina, katalitičke koncentracije jetrenih enzima i određen je molarni omjer ureje i kreatinina. Prema vrijednostima indeksa tjelesne mase (BMI) samo je manji broj pacijenata pothranjen, ali smanjena koncentracija proteina u serumu ukazuje na značajan katabolizam proteina. Nutritivne potrebe pacijenata nakon operacije namiruju se uglavnom glukozom i manjim količinama proteina, tj. aminokiselina, dok je unos masti zanemariv. Odgovarajući postoperativni unos nutrijenata i energije postiže se nakon više od sedam dana. Zbog intenzivnog katabolizma, posebice proteina, prehrana pacijenata nakon transplantacije organa zahtijeva trajno praćenje i bolju nutritivnu potporu kroz pripravke za enteralnu i parenteralnu prehranu.

Ključne riječi*: energetski unos, unos proteina, jetra, bubreg, transplantacija organa*

Introduction

Organ transplantation (liver and kidney) is a procedure that significantly improves the prognosis in patients with chronic liver and kidney diseases, and clinical characteristics of organ function that were in decline are normalized with a successful organ replacement. A common complication of chronic liver disease is deterioration of nutritional status, whether it is primary or secondary malnutrition (Stickel et al., 2008; Campos et al., 2002).

Preoperative malnutrition, operative stress, postoperative protein catabolism, postintervention complications and the period of fasting all have a significant influence on the success of transplantation (Stickel et al., 2008). Immediately after tran-

splantation, the basic aim of nutrition is to ensure the appropriate diet, sufficient for recuperation and refill of the exhausted nutrients' supplies (Qiu et al., 2009). In addition, having in mind that ischemia-reperfusion injury is, at least partially, attributable to reactive oxygen species (ROS), supplements with antioxidative capacity are desirable (Codoñer-Franch et al., 2008). The appropriate enteral and parenteral nutrition have multiple positive effects on postoperative course of the patient's recovery, such as shorter stay in the intensive care unit, and consequently lower medical expenses (Hasse et al., 1995; Wicks et al., 1994). According to recommendations the early enteral nutrition begins within 24 hours after the transplantation of liver or pancreas, if necessary even in combination with parenteral nutrition (Weimann et al., 2009).

Plank et al. (2005) concluded that in the patients at the advanced stage of liver disease, protein and energy malnutrition are very often a common condition. In patients with cirrhosis the increased ratio of proteins is catabolised and the protein deficiency is worsened with the deterioration of the disease.

The care about a patient's diet before and after the organ transplantation is an important segment in the process of medical treatment. In spite of the knowledge that malnutrition is a significant risk factor for a successful transplantation and postoperative recovery of the patient, there is still a large number of open questions about the selection of food and its application at the early postoperative phase. So far, the nutritional status of patients and the risk of malnutrition were assessed on admittance, and followed up through the application of different questionarries. To the best of our knowledge, there is no data about the recorded nutritional intake during early postoperative period for patients with liver or kidney transplant. Therefore, the aim of this investigation was to estimate total nutritional intake during the first two postoperative weeks in patients with liver or kidney transplant in order to assess whether minimal nutritional requirements are met. Some biochemical parameters were analysed as possible biomarkers of nutritional recovery.

Subjects and Methods

The present study was a prospective cochort singlecenter trial that was conducted in Merkur University Hospital in Zagreb, Croatia. Sixty-one adult (≥ 18 years) patients who were admitted for liver or kidney transplantation were included. Of the total number of patients, 48 received liver transplants, 11 received kidney transplants and 2 patients received both, liver and kidney transplants.

Among 48 liver transplant patients, 46 were diagnosed with cirrhosis, one patient suffered from Wilson's disease, and one suffered trauma in car accident. In 19 patients cirrhosis developed as a consequence of the alcohol related liver disease (ARLD), while in others it was mainly the result of hepatitis B (HBV) or hepatitis C (HCV) virus infection. Besides cirrhosis, 15 patients were diagnosed with hepatocellular carcinoma (mainly as a consequence of HBV and HCV infections). Among 11 kidney transplant patients, 10 of them had diagnosys of renal failure (4 of them also had diabetes). One patient was diagnosed with necrosis of pancreas with hepatitis B and diabetes. Of the two patients with both liver and kidney transplants, one suffered from hepatocellular carcinoma, and the other from cirrhosis, both with kidney failure. Therefore these two patients were considered as liver transplants for statistical analysis. Among the patients involved in this study, three died within 1 month, while the others were released home with precise recommendations about their diet.

This experiment was performed in accordance with the principles of the Declaration of Helsinki of the World Medical Association and was approved by the Ethics Committee of Merkur University Hospital, Zagreb, and School of Medicine, University of Zagreb, Croatia. At the beginning of the study all patients gave their written consent.

Blood samples were collected before transplantation (day 0), and then on the 1st, the 3rd and the 7th day after the transplantation. Venous blood was collected under controlled pre-analytical conditions into vacutainer tubes (Becton Dickinson, Franklin Lakes, NJ, USA) without additives. Serum was separated within 1 hour after blood collection by centrifugation at 1800×*g* for 10 min. All biochemical measurements were performed at the Department of Clinical Chemistry and Laboratory Medicine at the Department of Clinical Chemistry and Laboratory Medicine at the Merkur University Hospital, Zagreb, Croatia. Catalytic concentrations of serum enzymes alanine aminotransferase (ALT; EC 2.6.1.2), aspartate aminotransferase (AST; EC 2.6.1.1), gamma-glutamyltransferase (GGT; EC 2.3.2.2) and alkaline phosphatase (AP; EC 3.1.3.1) and concentrations of serum proteins, creatinine and urea, were determined by commercially available reagents (Olympus, Ireland). All measurements were performed on an Olympus AU 600 analyzer (Olympus Mishima Co., Ltd., Shizuoka, Japan) according to instructions from the manufacturer. Urea to creatinine molar ratio was calculated.

During their stay in the intensive care unit, the following formulas were used for the enteral and parenteral nutrition of patients: glucose solutions 5 and 10 % (Pliva Hrvatska plc, Zagreb, Croatia), glucose solution 40 %, and Aminoplasmal® Hepa-10 % (B. Braun Melsungen AG, Melsungen, Germany), albumin (human) 5 and 20 % (Institute of immunology, Zagreb, Croatia), Nephrotect, Kabiven, Dipeptiven, Intralipid 10 % and Intralipid 20 % (Fresenius Kabi, Graz, Austria), OliChlinomel N7-1000E (Baxter, Lessines, Belgium).

The Mini-nutritional assessment (MNA) test was applied to all participants by the same researcher. The version used in this study includes 6 items for dietetic assessment (concerning number of meals, food and fluid intakes, and autonomy of feeding), with the maximal score of 14 points (Kondrup et al., 2003; Kaiser et al., 2009). Screening score classifies patients in two categories: 1) ≥ 12 points - normal, not at risk; 2) ≤ 11 points - possible malnutrition.

The complete nutritional intake was monitored by a qualified nutritionist during the patients' stay in the intensive care unit and through first fourteen postoperative days. Total energy and nutrients intake was calculated based on the volume and composition of the applied solutions. After oral feeding was introduced, the type and the amount of consumed food was recorded and the nutritive composition calculated (Kaić-Rak and Antonić, 1990). For resting energy expenditure (REE) calculation the Harris-Benedict equation was used (Roza and Shizgal, 1984). The estimation of protein requirements was based on

the recommended value of 1.2 g/kg body mass (Plauth et al., 1997).

Data were analyzed with statistical package Statistica 8.0 (StatSoft Inc., Tulsa, USA). Depending on the results of distribution normality testing, results are presented as mean ± SD, or as median and quartile range. Wilcoxon Matched Pairs Test was used to analyze differences between two variables, while Spearman's correlation (*r*, *P*) was calculated for associations between parameters. *P* values ≤ 0.05 were considered statistically significant.

Results and discussion

General data on patients involved in the study, along with the body mass index (BMI), are given in Table 1. For patients with kidney transplant, the median value (24.4 kg/m^2) for BMI was within the recommended values (18.5 - 24.9 kg/m^2). However, in patients with liver transplant the increased average BMI was detected (26.9 kg/m^2). In the group with liver transplant 18 patients (36 %) were overweight, while in the group with kidney transplant 3 overweight patients (27.3 %) were identified. Only for 3 patients (6 %) from the liver group and for 3 patients (27.3 %) from the kidney group the calculated BMI was below 18.5 kg/m^2.

At the admission, the mean MNA score was 10.48 and 9.27 points in liver and kidney transplant group, respectively.

Table 1. *Baseline characteristics of patients with organ transplants*

Parameter	Organ	
	Liver (n = 50)	**Kidney (n = 11)**
Age (years), mean (SD)	52.3 (11.3)	44.0 (12.4)
Gender, n (%)		
Male Female	36 (72.0) 14 (28.0)	5 (45.5) 6 (54.5)
MNA score, mean (SD)	10.48 (1.83)	9.27 (2.76)
at risk (MNA<11), n (%)	27 (54.0)	7 (63.6)
not at risk (MNA≥ 11), n (%)	23 (46.0)	4(36.4)
Body mass (kg), mean (SD)	79.1 (13.7)	66.8 (16.0)
Body mass index (kg/m^2), mean (SD)	26.2 (3.9)	24.4 (6.0)
low (BMI < 18.5), n (%)	3 (6.0)	3 (27.3)
normal (18.5 ≤ BMI ≤ 24.9), n (%)	29 (58.0)	5 (45.5)
overweight (BMI ≥ 25), n (%)	18 (36.0)	3 (27.3)
Education, n (%)*		
Elementary school (≤ 8 years)	6 (19.3)	0 (0.0)
Secondary school (9 - 12 years)	19 (61.4)	2 (33.3)
High school (> 12 years)	6 (19.3)	4 (66.7)
Smoking, n (%)*		
no	25 (80.6)	5 (83.3)
≤ 10 cigarettes/day	3 (9.7)	1 (16.7)
> 10 cigarettes/day	3 (9.7)	0 (0.00)

MNA - Mini Nutritional Assessment

* The sum does not add up to total because of missing values

Metabolic status of the organ transplant recipients is characterized by a significant malnutrition. When evaluating the nutritive status of a patient, we often rely on the values of body mass index (BMI), the recommended values of which are 20 to 25 kg/m^2. The mean BMI values for the patients involved in this study were within the recommended values or slightly increased, which can mislead to a conclusion that malnutrition is not present. However, severe liver damage resulted in protein malnutrition, which is confirmed by the low serum protein levels (Table 1).

Care about the patient's appropriate nutrition should start already during the treatment of the primary disease. At admittance, according to MNA, the increased risk of malnutrition was detected in 54 % of patients in the liver, and 63.6 % in the kidney transplant group. According to recently published data, malnutrition was found in 25 % to 54 % of hospitalized patients in the United States (Malone, 2015). Statistical data for the year 2012 revealed the prevalence of undernutrition in 10 % to 70 % of Croatian patients, depending on diagnosis (Benković et al., 2014).

Nutrition of the patients involved in this study was followed in detail during their stay in the intensive care unit and the postoperative care, fourteen days in total. Diet included parenteral nutrition, ready-made formulas for enteral use and, when appropriate, oral feeding was introduced. The average daily energy intakes for patients with liver and kidney transplant are given in Fig. 1.

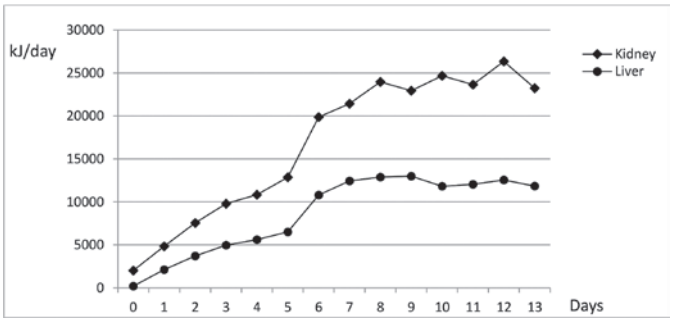

Figure 1. *The average daily energy intake for patients with liver and kidney transplant.*

Carbohydrates remain the leading energy source during the follow-up period, with proteins introduced later, mainly through enteral protein-rich shakes. However, significantly low fat intake was noticed. Glucose represents a core nutrient for all patients and its application begins already during the operative procedure. However, during the first three days

in more than 90 % of patients the total energy intake was below REE as calculated by Harris-Benedict formula (Table 2). During the first week total energy intake was improved, but in approximately 50 % of the patients it was still below the requirements.

During the first three days protein requirements were covered in nearly 50 % of the patients, and during the first seven days the protein intake was satisfying in more than 70 % of patients (Table 2).

Planning the appropriate diet after the organ transplantation represents a special challenge. There is increasingly more evidence of the advantages of enteral nutrition, compared to a total parenteral nutrition (TPN), although selection depends on the conditions of each individual patient. Research papers show that by using enteral nutrition the metabolic response to stress is improved, there are fewer technical and metabolic complications, lower rate of infections, and improved synthesis in visceral muscles. Reduced expenses compared to TPN are not negligible (Bower et al., 1986; Moore et al., 1992). However, a positive effect of TPN with the addition of somatostatin in the treatment of patients with ascites was observed (Baran et al., 2008). Furthermore, a synthetic function, as well as the reduction of a damage to the liver transplant using alanyl-glutamine dipeptide in a TPN were reported (Qiu et al., 2009).

Table 2. *The average energy and macronutrients intake during the first three and seven post-transplant days*

Organ	Liver (n = 50)	Kidney (n = 11)	Liver (n = 50)	Kidney (n = 11)
	3 days average		7 days average	
Protein intake (g/day), median (min-max)	88.75 (37.5 -156.7)	79.2 (16.7 – 130.0)	120.7 (85.7 – 184.9)	96.3 (66.5 – 137.1)
< Recommendation, n (%)	26 (52.0)	6 (54.5)	11 (22.0)	3 (27.3)
≥ Recommendation, n (%)	24 (48.0)	5 (45.5)	39 (78.0)	8 (72.7)
CHO intake (g/day), median (min-max)	118.3 (69.5 – 230.6)	132.0 (66.7 – 290.8)	207.2 (103.8 – 557.3)	215.3 (94.2 – 290.3)
Fat intake (g/day), median (min-max)	0.0 (0.0 – 51.3)	0.0 (0.0 – 37.44)	30.0 (0.0 – 91.0)	31.2 (0.0 – 59.3)
Energy intake (kJ/day), median (min-max)	3728 (2238 – 7966)	3326 (1393 – 7990)	6736 (3260 – 12200)	6464 (3100 – 7980)
< Recommendation, n (%)	47 (94.0)	10 (90.9)	25 (50)	5 (45.5)
≥ Recommendation, n (%)	3 (6.0)	1 (9.1)	25 (50)	6 (54.5)
Total serum proteins (g/L), mean (min-max)	49.9 (34.0 – 80.1)	44.2 (25.0 – 48.7)	48.4 (34.4 – 91.6)	nd

CHO = carbohydrates
nd = not detected

Data for patients' nutritional intake during the first two post-operative weeks are given in Fig. 2.

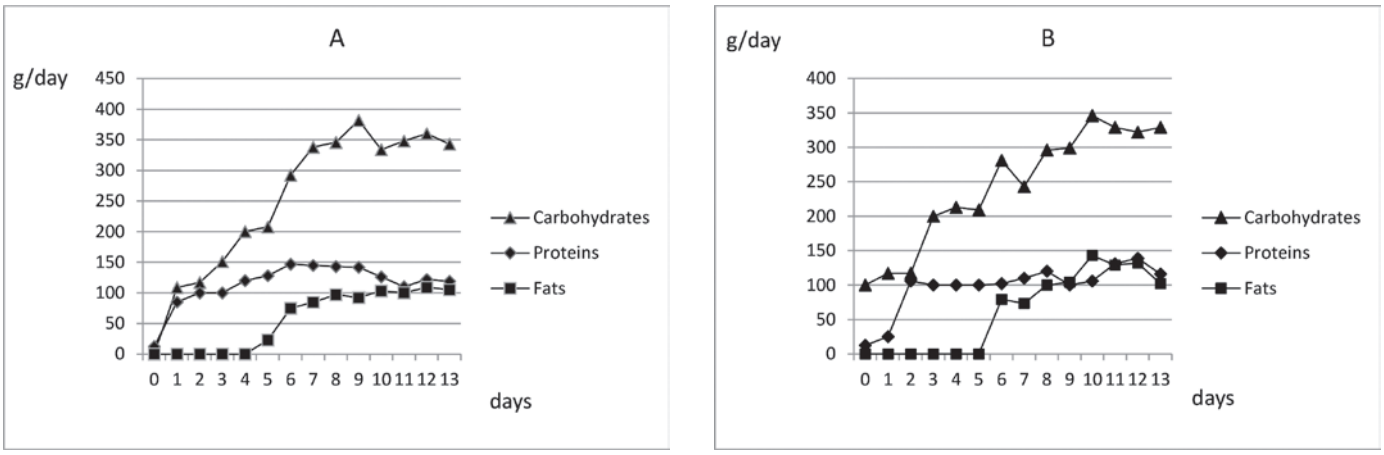

Figure 2. *Average daily macronutrients intake for patients with liver (A) and kidney (B) transplant.*

Regarding the proteins intake, they are mostly introduced with formulas for enteral use, which is why their average intake during the first three days after the transplantation is rather low and covers the requirements in less than 50 % of the patients. After implementation of protein shakes the intake was improved, and after a week the average protein intake was sufficient in more than 70 % of patients (Fig. 2). Comparing the total protein intake and the concentration of proteins in blood of the patients we did not find any significant correlation. However, one should keep in mind that serum protein levels are affected by many variables, including inflammation, and do not correspond proportionally to a nutritional intake (Banh, 2006). Since patients were followed up for fourteen days it can be assumed that further improvement will be reached with time.

In accordance with the statement that the diet of patients with a chronic liver disease must contain appropriate proteins to avoid a severe protein deficiency (Sanchez and Aranda-Michel, 2006), branched chain amino acids which enable fast recovery of muscle tissue are frequently applied. However, Hansen et al. (2015) have recently shown that the diet with complex proteins stimulates proteolytic activity of enterocytes and results in improved growth.

It is important to point out that only one of our patients received the fat containing formula in the first three days, although it is a well-known fact that fats contain twice the amount of energy per unit of mass compared to carbohydrates. The application of lipid formulas offers a possibility to ensure in a smaller volume the sufficient amount of energy that is so much needed for convalescens, as well as the essential fatty acids necessary for membrane structure and cell recovery (Delaš, 2011). The lack of long chain polyunsaturated fatty acids might be a contributing factor in chronic liver damage (Cabré et al., 1993; Cabre and Gassull, 1996), and the possibility to improve hepatic function and perhaps the outcome of liver transplantation by supplementation of arachidonic and/or docosahexaenoic acid in cirrhotic patients was shown (Pazirandeh et al., 2007). A direct protective effect of eicosapentaenoic acid on rat hepatocytes was refered (Shoma et al., 2007), which indicates the possibility that the use of essential polyunsaturated fatty acids in the organ perfusion solution after the explantation might have a positive effect on the protective role, in order to reduce the damage, and preserve the function of the organ until the transplantation. In randomized, controlled clinical trial with patients undergoing liver transplantation it was shown that n-3 polyunsaturated fatty acid-supplemented parenteral nutrition significantly reduces injury of the transplanted liver and improves postoperative recovery (Zhu et al., 2013).

From the clinical laboratory results (Table 3), a severe organ damage in patients involved in the study can be seen, followed by a serious catabolism and loss of proteins. Enzymes alanine aminotranferase (ALT) and aspartate aminotransferase (AST) are considered to be indicators of the liver activity, so the increase of catalytic concentration of these enzymes in the blood is an indicator of the liver damage, that can be of various etiologies. By catalyzing the transamination reaction, which initiates the amino acid catabolism, these enzymes are involved directly in the decomposition of proteins. Their ratio in serum of healthy humans is about 1, with ALT only slightly higher. Since ALT is a cytosolic enzyme, and AST is, apart from cytosol, also present in mitochondria, the increased activity of these enzymes almost certainly indicates a severe liver disease such as cirrhosis. After transplantation, with the organ function reestablished, the level of these enzymes in blood is reduced. In that process, a greater decrease in the value of mitochondrial enzyme, AST, is especially encouraging. In patients with kidney transplants, the activity of ALT retained its tendency to increase, which is not surprising if it is kept in mind that in this case liver suffers only the secondary strain due to a kidney failure, and some time is needed for the kidney to take over its function.

After organ transplantation patients are at a high risk from the post-transplant acute renal failure. In the evaluation of kidney function, urea and creatinine levels in blood play a key role. Due to inability to eliminate metabolites and toxins, including urea and creatinine, through ineffective kidneys, these concentrations were almost five to ten times above reference intervals in patients waiting for kidney transplantation. After transplantation, creatinine concentration significantly decreased, indicating the recovery of kidney function. In patients with the liver disease, these changes are much less intense. Urea to creatinine ratio can be useful in a differential diagnosis and is commonly used to distinguish between acute and chronic renal disease. However, changes in the ratio can also be caused by other disorders, including congestive heart failure, dehydration, severe catabolic state, severe liver dysfunction and malnutrition

Table 3. *Biochemical assessment of patients with organ transplants (Fridman Anova and post hoc Wilcoxon test, Mann Whitney U test; $P \leq 0.05$). Results are expressed as median (lower and upper quartile).*

Parameter (reference values)	**Organ**	**Day 0**	**Day 1**	**Day 3**	**Day 7**
Urea (2.8-8.3 mmol/L)	Liver	6.00 (4.50-8.50)	7.45Δ (5.40-9.50)	12.9Δ (9.70-18.3)	10.4Δ (7.90-15.1)
	Kidney	16.4* (15.1-29.2)	13.9Δ* (12.2-18.5)	15.4 (8.7-20.5)	24.6* (10.8-34.9)
Creatinine (M 79-125 µmol/L F 63-107 µmol/L)	Liver	95.0 (75.0-118)	91.5 (78.0-115)	94.0 (74.0-150)	76.5Δ (66.0-101)
	Kidney	644* (553-942)	562* (389-673)	363 Δ* (128-510)	251Δ* (118-506)

Urea/Creatinine (40-100:1 mol/mol)	Liver	61.0 (52.6-73.5)	72.7Δ (58.6-88.0)	132 Δ (104-155)	132Δ (101-160)
	Kidney	27.9* (23.5-32.2)	27.9* (24.5-35.7)	43.6* (31.9-75.2)	91.5* (53.2-108)
AST (M 11-38 U/L F 8-30 U/L)	Liver	196 (73.0-786)	447 Δ (249-1152)	123 (76.0-249)	48,0Δ (32.0-73.0)
	Kidney	26.0* (13.0-58.0)	27.0* (23.0-31.0)	34.0* (31.0-38.0)	45.5 (42.5-58.0)
ALT (M 12-48 U/L F 10-36 U/L)	Liver	136 (46.0-496)	345 (152-798)	218 (139-654)	142 (86.0-268)
	Kidney	33.0* (13.0-49.0)	21.0* (16.0-37.0)	40.0* (25.0-48.0)	112Δ (96.0-127.5)
AP (M 60-142 U/L F 64-153 U/L)	Liver	91.5 (68.0-126)	65.0 (53.0-84.0)	72.0 (54.0-94.0)	108 (76.0-141)
	Kidney	127 (72.5-118)	45.0 (30.0-133)	52.0* (41.0-55.0)	49.0* (41.0-71.0)
GGT (M 11-55 U/L F 9-35 U/L)	Liver	60.0 (36.0-85.0)	55.0 (36.0-87.0)	116 (66.0-210)	195Δ (137-378)
	Kidney	29.5* (18.0-38.0)	15.0* (10.0-39.0)	33.0* (20.0-68.0)	113 Δ* (83.0-175)

AST, aspartate aminotransferase; ALT, alanine aminotransferase; AP – alkaline phosphatase; GGT, gamma-glutamyl transferase; Δ - statistically significant difference compared to day 0; * - statistically significant difference liver vs. kidney

In our patients with kidney transplant the initial values of urea to cretinine ratio were lower compared to reference range (40 - 100:1 mol/mol). After three days the mean value reached lower limit indicating improvement in protein metabolism and kidney function. In patients with liver transplant, initial values were not significantly below the reference limit, but the obtained successive increase might also be a result of repaired protein metabolism.

However, besides very well established correlations of biochemical parameters, i. e. AST to ALT, or urea to creatinine, no significant correlations between biochemical parameters and nutritional intake were found.

The results of this preliminary study reassert the problem of (in)adequacy of perioperative nutrition in patients with liver and/or kidney transplantation. By the analysis of total costs from disease-related undernutrition in Croatian patients, it was shown that only 7.1 % came from expenses for parenteral and enteral nutrition (Benković et al., 2014). In contrast to that, it was estimated that malnutrition increases total hospitalization costs for more than 20 % (Amaral et al., 2007).

Strengths of this study include its prospective design with detailed nutritional record, and focus on the patients with organ transplantation. Limitations of the study include the lack of some important potential confounding information, such as medications and preoperative nutritional habits. More transplantation centers should be included as well.

Further interventional studies are necessary, in order to provide the answer how to reduce the organ damage during explantation by changing the composition of perfusion solutions and how supplemental nutrition can accelerate the postoperative recovery. BMI and serum protein levels are not reliable indicators of malnutrition; therefore it is necessary to search for new protocols and additional methods with the aim to clearly assess nutritional status. Urea to creatinine ratio might be of further interest in kidney transplant patients.

Conclusions

Severe damage to the liver and kidney inevitably causes increased catabolism and loss of body proteins. Organ transplantation is a complex therapeutic procedure which enables better prospects of recovery from the illness, but its success and recovery of a patient largely depend on the appropriate diet. Special attention should be paid to the quantity and the quality of proteins. Insufficient application of lipid-containing formulas has been observed.

Acknowledgments

We thank all the volunteers for taking part in this study. We also thank Mr. Goran Kapustić for his skilful assistance, and Mrs. Zrinka Pongrac Habdija for her careful reading of the manuscript. The research was supported by the University Hospital Merkur Zagreb, and the grant No. 0108068 from Croatian Ministry of Science, Education and Sports.

Conflict of interest

The authors declare no conflicts of interest.

References

Amaral T.F., Matos L.C., Tavares M.M., Subtil A., Martins R., Nazaré M., Sousa Pereira N. (2007) The economic impact of disease-related malnutrition at hospital admission. *Clinical Nutrition,* 26 778-784.

Banh L. (2006) Serum proteins as markers of nutrition: what are we treating? *Practical Gastroenterology* [serial online]. 46-64. Available at: http://www.medicine.virginia.edu/clinical/departments/medicine/divisions/digestive-health/nutrition-support-team/nutrition-articles/BanhArticle.pdf/. Accessed November 20, 2013.

Baran M., *Çakır* M., Yüksekkaya H.A., Arıkan Ç., Aydın U., Aydogdu S., Kilic M. (2008) Chylous ascites after living related liver transplantation treated with somatostatin analog and parenteral nutrition. *Transplantation Proceedings,* 40 320-321.

Benković V., Kolčić I., Ivičević Uhernik A., Vranešić Bender D., Oreb I., Stevanović R., Krznarić Ž. (2014) The economic burden of disease-related undernutrition in selected chronic diseases. *Clinical Nutrition,* 33 689-693.

Bower R.H., Talamini M.A., Sax H.C., Hamilton F., Fischer J.E. (1986) Postoperative enteral versus parenteral nutrition: a randomized controlled trial. *Archives of Surgery*, 12 1040-1045.

Cabré E., Abad-Lacruz A., Núñez M.C., González-Huix F., Fernández-Bañares F., Gïl A., Esteve-Comas M., Moreno J., Planas R., Guilera M. (1993) The relationship of plasma polyunsaturated fatty acid deficiency with survival in advanced liver cirrhosis: multivariate analysis. *The American Journal of Gastroenterology,* 88(5) 718-722.

Cabre E., Gassull M.A. (1996) Polyunsaturated fatty acid deficiency in liver disease: pathophysiological and clinical significance. *Nutrition* 12 542-548.

Campos A.C.L., Matias J.E.F, Coelho J.C.U. (2002) Nutritional aspects of liver transplantation. *Current Opinion in Clinical Nutrition and Metabolic Care,* 5 297-307.

Codoñer-Franch P., Muñiz P., Gasco E., Domingo J.V., Valls-Belles V. (2008) Effect of a diet supplemented with α-tocopherol and β-carotene on ATP and antioxidant levels after hepatic ischemia-reperfusion. *Journal of Clinical Biochemistry and Nutrition,* 43 13-18.

Delaš I. (2011) Benefits and hazards of fat-free diets. *Trends in Food Science and Technology*, 22 576-582.

Hansen S.A., Ashley A., Chung B.M. (2015) Complex dietary protein improves growth through a complex mechanism of intestinal peptide absorption and protein digestion. *JPEN Journal of Parenteral and Enteral Nutrition,* 39 95-103.

Hasse J.M., Blue L.S., Liepa G.U., Goldstein R.M., Jennings L.W., Mor E., Husberg B.S., Levy M.F., Gonwa T.A., Klintmalm G.B. (1995) Early enteral nutrition support in patients undergoing liver transplantation. *JPEN Journal of Parenteral and Enteral Nutrition,* 19 437-443.

Kaić-Rak A., Antonić K. (1990) Tablice o sastavu namirnica i pića (Tables of food and drinks composition, *in Croatian*). Zavod za zaštitu zdravlja R Hrvatske, Zagreb, Croatia.

Kaiser M.J., Bauer J.M., Ramsch C., Uter W., Guigoz Y., Cederholm T., Thomas D.R., Anthony P., Charlton K.E., Maggio M., Tsai A.C., Grathwohl D., Vellas B., Sieber C.C.; MNA-International Group. (2009) Validation of the Mini Nutritional Assessment short form (MNA®-SF): a practical tool for identification of nutritional status. *The Journal of Nutrition, Health and Aging,* 13(9) 782-788.

Kondrup J., Allison S.P., Elia M., Vellas B., Plauth M. (2003) ESPEN Guidelines for Nutrition Screening. *Clinical Nutrition,* 22 415-421.

Malone A. (2015) Malnutrition: Our time is now! *The Journal of Parenteral and Enteral Nutrition,* 39 63-72.

Moore F.A., Feliciano D.V., Andrassy R.J., McArdle A.H., Booth F.V., Morgenstein-Wagner T.B., Kellum J.M. Jr, Welling R.E., Moore E.E. (1992) Early enteral feeding, compared with parenteral, reduces postoperative septic complications. The results of a meta-analysis. *Annals of Surgery,* 216 172-183.

Pazirandeh S., Ling P.-R., Ollero M., Gordon F., Burns D.L., Bistrian B.R. (2007) Supplementation of arachidonic plus docosahexaenoic acid in cirrhotic patients awaiting liver transplantation: a preliminary study. *The Journal of Parenteral and Enteral Nutrition,* 3 511-516.

Plank L.D., McCall J.L., Gane E.J., Rafique M., Gillanders L.K., McIlroy K., Munn S.R. (2005) Pre-and postoperative immunonutrition in patients undergoing liver transplantation: a pilot study of safety and efficacy. *Clinical Nutrition*, 24(2) 288-296.

Plauth M., Merli M., Kondrup J., Weimann A., Ferenci P., Muller M.J. (1997) ESPEN guidelines for nutrition in liver disease and transplantation. *Clinical Nutrition,* 16 43-55.

Qiu Y., Zhu X., Wang W., Xu Q., Ding Y. (2009) Nutrition support with glutamine dipeptide in patients undergoing liver transplantation. *Transplantation Proceedings,* 41 4232-4237.

Roza A.M., Shizgal H.M. (1984)The Harris Benedict equation reevaluated: resting energy requirements and the body cell mass. *American Journal of Clinical Nutrition,* 40 168-182.

Sanchez A.J., Aranda-Michel J. (2006) Nutrition for the liver transplant patient. *Liver Transplantation,* 12 1310-1316.

Shoma R., Takahashi M., Takada H., Takada H., Kuwayama H. (2007) Protective effect of n-3 polyunsaturated fatty acid on primary culture of rat hepatocytes. *Journal of Gastroenterology and Hepatology,* 22 1965-1970.

Stickel F., Inderbitzin D., Candinas D. (2008) Role of nutrition in liver transplantation for end-stage chronic liver disease. *Nutrition Reviews*, 66 47-54.

Weimann A., Ebener Ch., Holland-Cunz S., Jauchk K.W., L. Hausser L., M. Kemen M., L. Kraehenbuehl L., E. R. Kuse E.R., Laengle F. (2009) Surgery and transplantation-Guidelines on parenteral nutrition Chapter 18. *GMS German Medical Science* 7:ISSN 1612-3174:1-15.

Wicks C., Somasundaram S., Bjarnason I., Menzies I.S., Routley D., Potter D., Tan K.C., Williams R. (1994) Comparison of enteral feeding and total parenteral nutrition after liver transplantation. *Lancet*, 344 837-840.

Zhu X., Wu Y., Qiu Y., Jiang C., Ding Y. (2013) Effects of ω-3 fish oil lipid emulsion combined with parenteral nutrition on patients undergoing liver transplantation. *Journal of Parenteral and Enteral Nutrition*, 37 68-74.