Nutritional Support Team Approach Decreases the In-Hospital Mortality Rate after Deceased Donor Liver Transplantation

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Purpose: This study compared the mortality rates between a period of time without employing a nutritional support team (NST) and a period of time with an NST.

Materials and Methods: Forty-six patients underwent adult deceased donor liver transplantation (DDLT) in 2016, and their medical records were prospectively collected. All the donor recipients underwent routine enteral feeding after liver transplantation. An NST cared for twenty-one patients after September 2016. The NST consisted of transplant surgeons, hepatologists, a critical care team, a rehabilitation team, dietitians, pharmacists, and nurses. We defined the patients within the time period without an NST as the control group and those patients within the time period with an NST as the case group.

Results: There were no statistically significant differences in baseline or perioperative characteristics between the two groups. The median model for the end-stage liver disease (MELD) score was 36 (range: 21~40) for the control group and 36 (range: 23~40) for the case group ($P=0.596$). The 30-day mortality rate was 24.0% (6/25) for the control group, but it was 4.8% (1/20) for the case group. The patient survival rates at 1-year and 2-year were 68.0% and 64.0% in the control group and 85.7% and 81.0% in the case group, respectively. However, there were no statistically significant differences of the 30-day mortality rate and 1~2 year patient survival rate between the two groups.

Conclusion: The present study suggests that an NST should be required to prevent 30-day mortality and increase patient survival of adult DDLT patients with a high MELD score. (*Surg Metab Nutr* 2020;11:7-11)

Key Words: Nutritional support, Multidisciplinary approach, Liver transplantation, Malnutrition, Mortality

INTRODUCTION

Malnutrition is common among patients with chronic liver disease and patients awaiting liver transplantation (LT), because the liver is a central organ for metabolism. [1] Over 90% of patients with end-stage liver disease

(ESLD) experience protein malnutrition due to reduced protein intake, metabolic changes, long hospitalization periods, and nutritional deficiencies. In cirrhotic patients, malnourishment is associated with increased rates of complications and mortality. Inadequate protein intake in such patients also has deleterious effects such as

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hepatic encephalopathy and poor clinical outcomes.[2-5]

LT has become the treatment of choice for patients with chronic liver disease such as liver cirrhosis and hepatocellular carcinoma. Advances in surgical techniques, perioperative management and post-transplant care have greatly improved the outcomes of patients after LT; however, malnutrition significantly worsens the outcomes of LT.[6] A malnourished status prior to LT increases the rates of complications and mortality after LT [2,7,8], and many patients die after adult deceased donor liver transplantation (DDLT) because of severe malnutrition. The median model for end-stage liver disease (MELD) score was higher for DDLT patients than for living donor liver transplantation (LDLT) patients in Korea. Thus, proper nutritional status assessment and support are essential for perioperative nutritional treatment and patient survival.

Multidisciplinary approaches have proven to be highly effective for treating and managing severe disease cases. Thus, our transplantation team created a nutritional support team (NST) to manage liver transplant patients. The purpose of the present study was to compare the mortality rates between a period without an NST and a period with an NST.

MATERIALS AND METHODS

1. Patients

Forty-six patients underwent deceased donor liver transplantation (DDLT) at Samsung Medical Center from January to December of 2016, and their medical records were prospectively collected. We excluded LDLT patients and pediatric transplantation patients (recipients under the age of 18). The patients were divided into two groups, with the control group being defined as patients from the period without an NST (n=25), and the case group being defined as patients from the period with an NST (n=21). This study was approved by the Institutional Review Board (IRB) at Samsung Medical Center (SMC-2018-06-066), and all patients provided written informed consent prior to study enrollment.

2. NST approach

The NST consisted of transplant surgeons, hepatologists, a critical care team, a rehabilitation team, dietitians, pharmacists, and nurses. When a candidate patient for DDLT was admitted, a dietician would evaluate his or her nutritional status with a patient-generated subjective global assessment (SGA). Candidates for DDLT who scored over 9 points were directed to the NST, because such patients were thought to require intensive nutritional support. Patients received enteral nutrition (EN) or parenteral nutrition (PN) support during the waiting period for DDLT. Additionally, all patients consulted with the rehabilitation team to receive exercises to maintain performance and prevent muscle weakness.

3. Enteral nutrition support

We routinely provided EN to almost every patient via a nasogastric tube placed in the stomach for several days after DDLT. Enteral feeding was started within 12 hours after DDLT. The starting enteral nutritional amounts was 20 mL/hour for 12 hours. If this was well-tolerated, the infusion rate was increased to 60 to 80 mL/hour by post-operative day 5. A low-residual enteral liquid diet was administered. Enteral feeding was discontinued once a patient could eat more than 50% of the provided regular diet.

4. Outcomes

The primary endpoints were 30-day mortality rate and patient survival. The secondary endpoints were complications such as infections and acute rejection. Cytomegalovirus infection was diagnosed based on a CMV pp65 antigen-positive cell number greater than one positive cell per 200,000 white blood cells in whom the CMV antigen was not previously detectable.

5. Statistical analysis

All data for continuous variables are presented as median and range, while the data for categorical variables are expressed as frequency and proportion. The patient survival was estimated by the Pearson's chi-squared test

(χ^2), and the groups were compared by the log-rank test. Continuous variables were compared by the Mann-Whitney U Test, and categorical variables were compared by Fisher's exact test. All statistical analyses were performed with SPSS 21.0 software. Differences were considered statistically significant at $P < 0.05$.

RESULTS

1. Patient characteristics

The patient characteristics are summarized in Table 1. All patients were Child-Pugh class C. The median MELD score was 36 points in both the control group and the case group. The percentage of re-transplantation was higher in the case group than in the control group (23.8% vs. 4.0%), as was the proportion of patients receiving continuous renal replacement therapy (CRRT) prior to DDLT (42.9% vs. 20.0%); however, these differences were not statistically significant. Age, sex, body mass index, HCC co-existence, pretransplant ICU care, pretransplant

ventilatory care, and hepatic encephalopathy incidence did not differ between the two groups.

The perioperative characteristics are outlined in Table 2. Recipient operation time, cold ischemic time, warm ischemic time, post-transplant intensive care unit (ICU) stay duration, and length of hospitalization did not differ between the two groups.

1) Target calorie achievement days

We estimated the target caloric intake for all patients. All patients received EN after DDLT. The control group achieved their target caloric intake in 6.4 days, while the case group achieved it in 6.7 days. There was no statistically significant difference between the two groups ($P=0.377$).

2) Outcomes

The 30-day mortality rate was 24.0% (6/25) in the control group but was 4.8% (1/20) in the case group; however, this difference was not statistically significant ($P=0.070$) (Fig. 1). The proportion of patients who contracted pneumonia within three months after DDLT was

Table 1. Patient characteristics (median and range)

Variables	Control group (n=25)	Case group (n=21)	P value
Age (years)	53 (20~69)	56 (32~73)	0.480
Sex			0.363
Male	14 (56.0%)	15 (71.4%)	
Female	11 (44.0%)	6 (28.6%)	
Body mass index	24.3 (19.2~33.5)	25.2 (14.9~33.1)	0.938
Reason for liver transplantation			0.512
NBNC	2 (8.0%)	1 (4.8%)	
Alcohol	7 (28.0%)	5 (23.8%)	
HBV	8 (32.0%)	5 (23.8%)	
HCV	3 (12.0%)	1 (4.8%)	
Retransplantation	1 (4.0%)	5 (23.8%)	
Toxic	3 (12.0%)	2 (9.5%)	
Autoimmune	1 (4.0%)	2 (9.5%)	
HCC co-existence	5 (20.0%)	2 (9.5%)	0.428
Pretransplant ICU care	9 (36.0%)	9 (42.9%)	0.764
Pretransplant ventilator	4 (16.0%)	6 (28.6%)	0.475
Hepatic encephalopathy			0.837
None	10 (40.0%)	11 (52.4%)	
Grade 1 and 2	11 (44.0%)	3 (14.3%)	
Grade 3 and 4	4 (16.0%)	7 (33.3%)	
MELD score	36 (21~40)	36 (23~40)	0.596
Hepatorenal syndrome			0.198
None	12 (48.0%)	8 (38.1%)	
HR without CRRT	8 (32.0%)	4 (19.0%)	
HR with CRRT	5 (20.0%)	9 (42.9%)	

NBNC = non-B non-C; HBV = hepatitis B virus; HCV = hepatitis C virus; HCC = hepatocellular carcinoma; ICU = intensive care unit; MELD = model for end-stage liver disease; HR = hepatorenal syndrome; CRRT = continuous renal replacement therapy.

Table 2. Perioperative characteristics

Variables	Control group (n=25)	Case group (n=21)	P value
Recipient operative time (min)	347 (199~490)	335 (186~735)	0.755
Cold ischemic time	309 (203~452)	265 (40~468)	0.155
Warm ischemic time	29 (14~68)	24 (13~41)	0.166
Posttransplant ICU stay	6 (1~22)	7 (2~37)	0.596
Hospitalization	22 (1~106)	30 (13~136)	0.164

ICU = intensive care unit.

Fig. 1. In hospital mortality.

higher in the control group than in the case group (28.0% vs. 4.8%; $P=0.055$). However, the rates of infection, cytomegalovirus (CMV) infection, and acute rejection did not differ between the two groups (Table 3).

The 1-year and 2-year patient survival rates were 68.0% and 64.0%, respectively, in the control group and were 85.7% and 81.0% in the case group. The patient survival curve was worse in the control group than in the case group, but there was no statistically significant difference between the groups ($P=0.189$).

DISCUSSION

In the present study, we observed better survival in adult DDLT patients who received NST support. There

Table 3. Complications within 3 months after adult DDLT

	Control group (n=25)	Case group (n=21)	P value
Infection	17 (68.0%)	13 (61.9%)	0.760
Pneumonia	7 (28.0%)	1 (4.8%)	0.055
Cytomegalovirus infection	12 (48.0%)	12 (57.1%)	0.568
Acute rejection	2 (8.0%)	2 (9.5%)	0.855

are several plausible explanations for this improvement. An NST can alter the direction of patient care by improving the patient's nutritional status in the perioperative period and changing their treatment recommendations.

Those who received NST support had different baseline characteristics than those who did not. The proportions of patients requiring re-transplantation due to graft failure or CCRT due to severe hepatorenal syndrome in the pre-transplant period were greater in the NST support (case) group than in the control group. The 30-day mortality and patient survival rates were better in the case group than in the control group. In addition, the incidence of pneumonia was lower in the case group than in the control group. However, the differences in 30-day mortality, patient survival, and pneumonia incidence were not statistically significant. Our study suggests that NST support is more beneficial when DDLT patients have high MELD score and many complications.

A multidisciplinary approach with coordinated surgical, medical and nutritional management is needed to improve the outcomes of LT. A previous study indicated that managing the nutritional status of patients undergoing transplantation is complex and requires specialized knowledge. Nutritional counselling and support are now recognized as necessary to reduce the severity of nutritional impairment in such patients; however, physicians have minimal training and experience in the area of nutritional support. A multidisciplinary team focused on nutritional support is the best way to solve the complex problems arising in patients undergoing transplantation. Such teams generally consist of health care professionals specializing in each area of patient care, such as dietitians, nurses, physicians, and pharmacists.[9] Merli et al. [6] reported that dietary counseling may only benefit clin-

ically stable patients who are followed for an adequate period of time while on the waiting list. Our approach to improving liver transplantation outcomes included assessing the admitted patients awaiting transplantation; selecting the patients who needed nutritional support pre-, peri- and post-operatively; calculating the exact caloric requirement of each patient; and following up to assess compliance. This approach improved outcomes in the NST period.

However, our study had several limitations. First, because the sample size was small, its statistical power of the study was limited and statistical outcomes including survival rates and target calorie achievement days between two groups were not different although death rate in the group without NST was higher. Second, improvement in protein supply or managing EN intolerance might be needed to measure the effect of NST approach meaning NST had an effect on survival rates, but we had difficulty in analyzing quantitatively in those variables. Furthermore, in assessing patient nutritional state, we did not assess specific variables within the subjective global assessment (SGA) or measure parameters such as midarm muscle circumference (MAMC); only BMI was recorded. Only 7 patients recorded PG-SGA and the others did not because most of the patients were nutritionally healthy (n=28), one patient denied to do PG-SGA, and 10 patients were unable to answer the form due to their medical condition (e.g. hepatic encephalopathy). However, the complications have been lowered, which is clearly possible because of the NST effect. Third, we did not evaluate performance status, which is an important variable for estimating the postoperative recovery of patients.

In conclusion, the present study suggests that an NST prevents 30-day mortality and increases patient survival in adult DDLT patients with high MELD score. Therefore, NST consultation should be implemented to increase the survival of such patients or patients with many complications, through accurate assessment and management of nutritional status.

CONFLICTS OF INTEREST

The authors of this manuscript have no conflicts of interest to disclose.

AUTHOR'S CONTRIBUTION

Sang-Oh Yun: literature search, data interpretation, and writing.

Jong Man Kim: design, data acquisition, analysis, interpretation.

Hyung Joo Kim, Soo Hyun Park, and Hyo Jung Park: data acquisition and interpretation.

Sangjin Kim, Jinsoo Rhu, and Eunmi Gil: data acquisition and interpretation.

Wonseok Kang, Gyu-Seong Choi, and Won Hyuck Chang: data interpretation and writing.

Jeong-Meen Seo and Jae-Won Joh: design, data interpretation, and writing.

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