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ORIGINAL ARTICLE

IS BEING IN THE GERIATRIC AGE GROUP AN ADDITIONAL RISK FACTOR OR CONTRAINDICATION FOR LIVING DONOR LIVER TRANSPLANTATION?

Abstract

Introduction: While advanced age was once a contraindication for liver transplantation, it is now routinely performed for individuals over (≥) 65. This study aimed to analyze preoperative findings, preoperative findings, perioperative graft-related and surgical factors, and postoperative complications in geriatric recipients (≥65 years) to assess the feasibility and outcomes of living-donor liver transplantation in this age group.

Materials and Method: Data regarding sex, model for end-stage liver disease score, Child score, body mass index, blood type, graft type (right or left lobe), ascites, esophageal variceal hemorrhage, hepatic encephalopathy, spontaneous bacterial peritonitis, preoperative INR, platelet, sodium, albumin, total bilirubin and creatinine, diabetes, hypertension, coronary artery disease, anhepatic phase, cold ischemia time, operation time, blood products transfusion rates, graft-to-recipient weight ratio, intensive care unit and hospital stay, biliary complications, hepatic vein thrombosis, portal vein thrombosis, postoperative hemorrhage, sepsis, and primary graft dysfunction were analyzed statistically in geriatric patients.

Results: The use of the right lobe was significantly higher in the ≥65 age group (p=0.036). Additionally, body mass index (p=0.039) and creatinine (p=0.018) were statistically higher in the group.

Conclusion: Living-donor liver transplantation can be safely performed in patients aged ≥65 years.

Keywords: Liver; Survival; Transplantation.

CORRESPONDANCE

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INTRODUCTION

Living-donor liver transplantation (LDLT), a procedure effectively practiced worldwide, offers a life-saving option for patients suffering from end-stage liver failure across all age groups. Once considered an obstacle, advanced age alone is no longer a barrier to successful LDLT, thanks to advancements in transplant techniques and patient care. This applies to individuals over (≥) 65 years old, provided that their respiratory and cardiovascular functions are adequately maintained (1).

In LDLT recipients, age has been extensively studied as a factor influencing surgical success. However, the presence and severity of pre-operative decompensation findings, such as ascites, esophageal variceal hemorrhage (EVH), hepatic encephalopathy (HE), and spontaneous bacterial peritonitis (SBP), play a crucial role alongside co-existing chronic diseases, perioperative graft-related and surgical factors, and post-operative complications. These factors impact hospital stays and recovery times in geriatric patients (those aged ≥65) compared to younger recipients (2,3).

This study aims to analyze demographic data, pre-operative decompensation findings, chronic disease presence, liver failure markers like the model for end-stage liver disease (MELD) and Child scores, perioperative graft-related and surgical factors, post-operative complications, and infection rates in geriatric patients undergoing LDLT, comparing them to data from younger recipients.

MATERIALS AND METHOD

Our study retrospectively examined the hospital computerized record system, patient follow-up files, files containing surgical findings, and operation notes, including the liver transplant database, and identified 276 patients who underwent LDLT for end-stage liver cirrhosis between July 2021 and October 2023. We analyzed the data by comparing two age groups: (≥65 years) and younger adult patients (18-64 years). Pediatric liver recipients under the age of 18 and cadaveric adult recipients have been excluded from the study. All LDLT patients included study were consecutive. The analysis compared these groups across various factors, including demographics, (sex, MELD score, Child score, weight, body mass index [BMI], and graft type [right or left]), decompensation findings (ascites, EVH, HE, and SBP), pre-operative laboratory values (blood INR, platelet count, sodium [Na], albumin total bilirubin, and creatinine), prevalence of chronic diseases (diabetes mellitus [DM], hypertension [HTN], and coronary artery disease [CAD]), perioperative findings (anhepatic phase, cold ischemia time, operation time, blood products transfused, and graft-to-recipient weight ratio [G.R.W.R.]), and post-operative outcomes (intensive care unit [ICU] stay, hospital stay, biliary complications, hepatic vein thrombosis [HVT], portal vein thrombosis [PVT], postoperative hemorrhage, sepsis, and primary graft dysfunction [PGD].

As the study was retrospective, written informed consent was not obtained from patients. All procedures were conducted in accordance with the ethical standards of the committees concerned with human experimentation (institutional and national) and the 1964 Declaration of Helsinki and its later editions. This study was approved by the İstanbul Aydın University Human Experiments Ethics Committee (approval numbered 2023/127, dated 10/18/2023).

Statistical analysis

Nominal and ordinal parameters were described using frequency analysis, while scale parameters were summarized with means and standard deviations. Differences between categorical parameters were assessed using Chi-Square or Chi-Square Likelihood tests, as appropriate. The Kolmogorov-Smirnov test was employed to assess the normality of scale parameters. Since the distributions were found to be non-normal, the Mann-Whitney U test was used for the analysis of

differences. All statistical analyses were conducted SPSS 17.0 (SPSS Inc., Chicago, 3., USA) for Windows with a 95% confidence interval.

RESULTS

Findings on Age

In this study, the age range spanned from 65 to 78 years for the group aged ≥65 years, while patients aged <65 fell within the range of 18 to 64 years. Of the total participants, 20% (n:55) belonged to the ≥65 group, while the remaining 80% (n:221) were in the <65 group.

Preoperative Demographic Findings (Table 1)

Among recipients aged ≥65 years, males represented 18.5%, while females constituted 23.1%. The mean MELD score was 14.7. Child scoring revealed 29.3% as Child A, 16.7% as Child B, and 18.1% as Child C. The average BMI was 28.4. Regarding etiologies, hepatocellular carcinoma (HCC) led with 33%, followed by hepatitis C virus (HCV) (28.6%), hepatitis B virus (HBV) (24.3%), nonalcoholic steatohepatitis (23.5%), and cryptogenic cirrhosis (23.2%). Additionally, the prevalence of chronic diseases in the ≥65 group was 19.7% for DM, 25.8% for HTN, and 10% for CAD. When it comes to decompensation findings, 20.5% had ascites, 20% exhibited HE, and 12.5% experienced EVH. Notably, SBP was not observed in this group. Preoperative laboratory values showed an average INR of 1.42, platelet count of 126 T/mm^3, Na level of 136 mm/L, creatinine level of 0.95 mg/dl, total bilirubin level of 4.1 mg/dL, and albumin level of 3.2 g/dL.

There were no statistically significant differences between recipients aged ≥65 years and younger recipients in terms of sex (p=0.404), blood type (p=0.226), MELD score (p=0. 276), Child score (p=142), etiology (p=0.681), comorbid conditions like DM (p=0.887), HTN (p=0.417), and CAD (p=406), decompensation findings like ascites (p=0.992), EVH (p=0.092), HE (p=926), and SBP (p=0.209), or laboratory parameters like INR (p=0.076), platelet (p=0.260), Na (p=0.965), albumin (p=0,473), and total bilirubin (p=0.501). BMI (p=0.039) and creatinine (p=0.018) were significantly higher in the ≥65 age group.

Perioperative Findings (Table 2)

In patients aged ≥65 years, the perioperative blood transfusion rate was 25.7%. The mean duration of the anhepatic phase was 83.5 minutes, and the mean cold ischemia time was 64.4 minutes. The mean operation time was 478.2 minutes. The G.R.W.R. was 1.06. The right lobe was used in 21% of cases, while the left lobe was not utilized in any patients. The average length of ICU stay was 2.8 days, and the average total hospital stay was 13.8 days.

There was no statistical difference between the age groups regarding perioperative parameters like blood transfusion (p=0.432), anhepatic phase duration (p=0.180), cold ischemia time (p=0.964), mean operation time (p=0.653), G.R.W.R. (p=0.373), length of ICU stay (p=0.650), and total hospital stay (p=0.662). However, the use of the right lobe was significantly higher in patients aged ≥65 years (p=0.036).

Postoperative complications (Table 3)

Among patients aged ≥65 years, the rate of PVT, HVT, and biliary complications were 20%, 25%, and 19.9%, respectively. Additionally, 16.7% experienced sepsis and 9.1% had intra-abdominal bleeding. Notably, PGD was not observed in this group. Hepatic artery thrombosis was not observed in any of the patients, regardless of age.

There were no statistically significant differences between the age groups in terms of the occurrence of PVT (p=0.680), HVT (p=0.754), biliary complications (p=0.103), sepsis (p=0.660), or intraabdominal bleeding (p=0.341). PGD also showed no statistically significant difference between the groups (p=0.470).

Table 1. Preoperative Demographic Findings, Comorbidities, Decompensation Findings, Laboratory Parameters and Statistical Results

	>65 years (n:55)	<65 years (n:221)	p value
Gender			
Male	18.5%	81.5%	0.404
Female	23.1%	76.9%	
MELD score	14.7 (+5.8)/(12.9-16.4)	15.9 (+6.6)/(14.9-16.9)	0.276
Child			
A	29.3%	70.7%	
B	16.7%	83.3%	0.142
C	18.1%	81.9%	
BMI	28.4 (+4.3)/(27.1-29.7)	26.9 (+5.3)/(26.1-27.7)	**0.039**
Etiology			
HBV	24.3%	75.7%	0.681
NASH	23.5%	76.5%	
Cryptogenic	23.2%	76.8%	
HCC	32.4%	68.6%	
Ethanol	0%	100%	
Autoimmune	6.7%	93.3%	
HBV+HDV	0%	100%	
Budd Chiari Syndrome	0%	100%	
HCV	28.6%	71.4%	
Biliary Cirrhosis	16.7%	83.3%	
Primary Sclerosing Cholangitis	25%	75%	
Wilson Disease	0%	100%	
Hemochromatosis	0%	100%	
Hyperoxaluria	0%	100%	
Alagille Syndrome	0%	100%	
Caroli Disease	0%	100%	
Sjogren's syndrome	0%	100%	
Sarcoidosis	0%	100%	
Comorbidities			
DM	19.7%	80.3%	0.887
HTN	25.8%	74.2%	0.417
CAD	10%	90%	0.406
Decompensation findings			
Ascites	20.5%	79.5%	0.922
EVB	12.5%	87.5%	0.092
HE	20%	80%	0.926
SBP	0%	100%	0.209
Laboratory parameters			
Platelet (T/mm^3)	126 (+87.5)/(100-152)	113 (+87.5)/(100-126)	0.260
INR	1.42 (+0.3)/(1.3-1.5)	1.52 (+0.5)/(1.4-1.6)	0.076
Sodium (mmol/L)	136.2 (+4.1)/(134-137)	136.1 (+4.6)/(135-136)	0.965
Creatinine (mg/dl)	0.95 (+0.54)/(0.7-1.1)	0.86 (+0.7)/(0.7-0.9)	**0.018**
Total Bilirubin (mg/dl)	4.1 (+7.2)/(2-6.3)	4.5 (+6.3)/(3.6-5.5)	0.501
Albumin (g/dl)	3.2 (+0.7)/(3-3.4)	3.1 (+0.7)/(3-3.2)	0.473

BMİ: Body Mass Index, CAD: Coronary Artery Disease, DM: Diabetes Mellitus, HBV: Hepatitis B virus, HCV: Hepatitis C virus, HDV: Hepatitis D virus, HE: hepatic encephalopathy, HTN: Hypertension, INR: International Normalized Ratio, NASH: Nonalcoholic steatohepatitis, OVB: Esophageal Variceal Bleeding, SBP: Spontaneous Bacterial Peritonitis

Table 2. Perioperative Blood Transfusion, Graft And Operation Time Findings And İCU/Hospital Stay

	>65 years (n:55)	<65 years (n:221)	P value
Blood Transfusion			
Yes	25.7%	74.3%	0.432
No	19.8%	80.2%	
Anhepatic phase (min)	83.5 (+28.5)/(73.2-93.8)	93.1 (+36.2)/(87.2-99)	0.180
Cold ischemia time (min)	64.4 (+31.2)/(53.3-75.5)	65.7 (+35.2)/(59.9-71.5)	0.964
Operation time (min)	478.2 (+84.9)/(445-511)	462.3 (+78.8)/(446-477)	0.653
G.R.W.R.	1.06 (+0.18)/(1-1.12)	1.04 (+0.24)/(1-1.08)	0.373
Graft Side			
Right Lobe	21%	78.1%	**0.036**
Left Lobe	0%	100%	
ICU stay (day)	2.88 (+2.7)/(2-3.7)	2.46 (+1.9)/(2.1-2.7)	0.650
Hospital Stay (day)	13.8 (+4.6)/(12.4-15.3)	14.8 (+7.5)/(13.7-15.9)	0.662

G.R.W.R.: Graft-To-Recipient Weight Ratio, ICU: Intensive Care Unit, Min: minute

Table 3. Postoperative Complications and Statistical Results

	>65 years (n:55)	<65 years (n:221)	P value
PVT			
Yes	20%	80%	0.680
No	23.8%	76.2%	
HVT			
Yes	25%	75%	0.754
No	20.5%	79.5%	
Bile complication (leakage and stricture)			
Yes	19.9%	80.1%	0.103
No	50%	50%	
Sepsis			
Yes	16.7%	83.3%	0.660
No	20.1%	79.9%	
Intraabdominal Hemorrhage			
Yes	9.1%	90.9%	0.341
No	20.9%	79.1%	
PGD			
Yes	0%	100%	0.470
No	20.7%	79.3%	

HVT: Hepatic Vein Thrombosis, PGD: Primary Graft Dysfunction, PVT: Portal vein Thrombosis.

Mortality and Survival

The mortality rate was 18% in patients aged ≥65 years and 20% in those aged <65 years. No statistically significant difference in mortality was observed between the age groups (p=0.540). Mean survival for patients aged ≥65 years was 19.8 months (range: 16.4-23.1 months), while for those aged <65 years, it was 20.8 months (range: 19.1-22.1 months). Analysis revealed no statistically significant difference in patient survival between the age groups (p=0.554).

DISCUSSION

The destructive impact of liver cirrhosis and the outcomes of liver transplantation can vary between elderly and young populations. While the research landscape presents diverse findings, objectively evaluating and understanding these discrepancies is crucial. Although some studies suggest male sex is less frequent among recipients aged ≥65 years (2,4,5) and BMI remains stable (6,7) or low (8), our study found no difference between sexes and a statistically higher BMI in the ≥65 group. With respect to other preoperative variables, while etiological factors may vary with age, MELD and Child scores tend to increase, leading to a shortened survival (7,9). However, other studies report lower MELD and Child scores in the elderly (4,5,8,10). While several studies show no significant difference in etiology between younger and older recipients (5,7,9), some suggested a higher prevalence of HBV or HCC in the elderly (4,8,10,11). Our study found no statistical differences in MELD and Child scores, or etiologic factors between the age groups.

The results pertaining to perioperative factors related to the graft suggest a potential worsening with advancing age (8). While some studies associate shorter anhepatic phase and cold ischemia time, increased blood transfusion needs, and unchanged operation times in patients aged over 65 years (4), it is essential to consider results that show no age-related differences in these parameters (5). In our study, no statistically significant differences were observed in terms of the anhepatic phase, cold ischemia time, operation time, or perioperative blood transfusion requirements.

In LDLT, the right lobe is generally preferred; however, evidence indicates no difference in complication rates between the right and left lobes in elderly recipients. In fact, some studies even suggest a preference for the left lobe in this age group. Furthermore, no disparity was noted across age groups with respect to G.R.W.R. (4,12). Interestingly, in our study, it was observed that the right lobe was statistically more utilized in patients aged ≥65 years; however, there was no difference in G.R.W.R.

Postoperative ICU and hospital stays might increase with additional comorbidities and treatment needs. While some studies suggest longer stays in elderly recipients, others report no age-related differences (4,5,11). Our findings align with the latter, showing no statistically significant differences in ICU or total hospital stay between the age groups.

While SBP, a decompensation finding, is often reported more frequently in elderly patients (2), studies have not consistently shown differences in the prevalence of EVH, HE, ascites, or SBP between older and younger recipients (5). Consistent with this, our study found no statistically significant differences in these decompensation findings between the age groups.

Meta-analyses have shown that comorbidities like DM, HTN, and CAD are more prevalent in recipients aged ≥65 years (2,5,6). However, it is important to acknowledge studies that report no age-related differences in these comorbidities (9). Additionally, higher mortality rates from cardiovascular diseases have been observed in the elderly (13,14). In our study, no statistically significant differences were found in DM, HTN, or CAD between the age groups.

Studies investigating complications have observed no statistically significant differences in biliary leakage or stenosis, portal vein, hepatic vein,

or hepatic artery thrombosis between recipients aged ≥65 and younger groups (4,5,7,15,16). Similarly, no significant difference was found in bleeding or PGD (4). While some studies report no difference in sepsis and infections between age groups (4-6), others suggest a lower prevalence in the ≥65 group (10). These literature findings are consistent with our study, demonstrating no statistically significant difference in vascular and biliary complications, PGD, or sepsis among age groups.

Mortality rates in the literature have been mixed, with some studies reporting higher rates in the elderly group (6,17,18) while others find no difference (7,12,15,19). Some studies even report shorter survival in older recipients (2,10,20). However, others find no age-related differences in mortality or survival (5,17). Our findings echo the latter, revealing no statistically significant differences in mortality or survival between recipients aged ≥65 and the younger group. Mortality rates and patient survival also remained similar between the two groups, in our study.

When analyzing preoperative laboratory parameters, we found no difference in platelet, albumin, INR, or total bilirubin between the groups. However, creatinine was statistically higher in patients aged ≥65 years (5,7). In our study, no statistically significant differences were observed in preoperative albumin, INR, total bilirubin, and platelet values; however, it was noted that only creatinine levels were elevated in the group aged ≥65 years. This finding underscores the importance of closely monitoring renal function after transplantation in elderly recipients, particularly for creatinine elevation.

The limitations of the study in terms of survival research may include the relatively low number of patients aged ≥65, lack of information about patients requiring preoperative hospitalization, and unspecified details about the administered treatment.

Given these findings on preoperative demographic, laboratory values, perioperative characteristics, and postoperative complication rates LDLT can be safely performed in patients aged ≥65 years. High creatinine and BMI-related issues also require careful attention in this population.

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