



Results of Liver Transplantation With Donors Older than 75 Years: A Case-Control Study

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ABSTRACT

Background. The inclusion of elderly donors can increase the pool of organs available for transplantation. The objective of this study was to compare clinical outcomes and survival rates of patients who received livers from donors aged ≥ 75 years versus younger donors.

Methods. We considered all liver transplantations performed in our unit from January 2006 to January 2015. Thirty-two patients received a liver from a cadaveric donor aged ≥ 75 years (study group), and their outcomes were compared with those of patients who received a liver from a younger donor (control group) immediately before and after each transplantation in the study group. This is a descriptive, retrospective, case-control study carried out to analyze the characteristics of donors and recipients as well as the clinical course and survival of recipients of older and younger donors.

Results. Statistically significant differences were observed according to donors' age (53.3 ± 13.6 vs 79 ± 3.4 years; $P < .001$). In total, 6.2% of the recipients of a liver from a donor aged < 75 years required retransplantation versus 15.6% of recipients of donors ≥ 75 years. Patient survivals at 1, 3, and 5 years, respectively, were 89%, 78.6%, and 74.5% for recipients of donors < 75 years versus 83.4%, 79.4%, and 59.6% for the study group.

Conclusions. Livers from older donors can be safely used for transplantation with acceptable survival rates. However, survival rates are lower for recipients of livers from older donors compared with younger donors, and survival only increased with retransplantation.

MORTALITY in candidates waiting for liver transplants increases by 10% per year in Spain. This is due to the large number of candidates on the waiting list for an orthotopic liver transplantation and the limited number of liver donors [1]. Therefore, to expand the pool of donors, the selection criteria were broadened to include older donors, although there is no general consensus on the safety of this practice [2]. On the one hand, some studies associate the use of organs from older donors with higher rates of dysfunction and primary graft failure [3,4]. On the other hand, other studies confirm the safety and optimal outcomes of transplants from older donors if patients are appropriately selected [5,6]. The objective of the present study was to compare the clinical outcomes and survival rates of patients who received a liver from a donor aged ≥ 75 years versus younger donors.

METHODS

We considered all liver transplantations performed in our unit from January 2006 to January 2015 and identified a total of 32 cadaveric donors aged ≥ 75 years. A retrospective case-control study design was selected with the use of a 1:2 ratio. Donor and recipient variables were matched to a control group of 64 patients, who were transplanted from younger donors immediately before and after each index case. During the procurement phase, liver biopsies were obtained at the discretion of the surgeon. Exclusion criteria were the presence of steatosis $\geq 30\%$, bridging fibrosis, or hepatitis. Post-transplantation biopsy was considered to be positive for steatosis if $\geq 30\%$.

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We analyzed both donor characteristics of age, sex, body mass index (BMI), aspartate aminotransferase (AST)/alanine aminotransferase (ALT), bilirubin, presence of steatosis, and ischemia time and recipient variables of age, sex, BMI, etiology of liver disease, Model for End-Stage Liver Disease (MELD) score, time on the waiting list, liver function parameters, pre- and post-transplantation intensive care unit (ICU) stay, hospital stay, presence of primary graft nonfunction, initial poor graft dysfunction, need for retransplantation, reoperation, rejection, infection, vascular and biliary complications, hospital re-stay, and graft survival. IPGD was defined as the presence of ≥ 1 of the following previously defined post-operative laboratory results suggestive of liver injury and dysfunction: bilirubin >10 mg/dL on day 7, international normalized ratio >1.6 on day 7, and ALT or AST $>2,000$ IU/L within the 1st 7 days [7]. All patients who were selected for liver transplantation for hepatocellular carcinoma (HCC) met the Milan criteria: a single tumor ≤ 5 cm in diameter or ≤ 3 nodules ≤ 3 cm.

Statistical Analysis

Differences between mean values were evaluated with the use of Student *t* test or Mann-Whitney *U* test. Differences in categorical variables between the 2 groups were evaluated with the use of the chi-square test. Postoperative graft survival was computed from the day of transplantation to the last follow-up visit or death or retransplantation. Survival rates were estimated by means of the life table method with differences compared with the use of log-rank test. Data were processed with the use of SPSS 15.0 software (SPSS, Chigaco, Illinois, USA). A *P* value of $\leq .05$ was considered to be statistically significant.

RESULTS

Donor characteristics, biochemical parameters, and ischemia time are presented in Table 1. Obviously, significant differences were found in the age of donors between the study group and the control group (79.03 ± 3.41 y vs 53.27 ± 17.8 y; *P* < .001). No statistically significant differences were observed in sex, biochemical parameters (except for ALT levels [*P* = .01]), and steatosis. No statistically significant differences were found in ischemia time either.

Recipient characteristics and postoperative data are presented in Tables 2 and 3. The age of recipients was

Table 1. Donor Characteristics

Characteristic	Donor <75 y	Donor ≥ 75 y	<i>P</i> Value
<i>n</i>	64	32	
Age (y)	53.27 ± 13.58	79.03 ± 3.41	<.001
Sex			
Male	29 (45.3%)	16 (50%)	NS
Female	35 (54.7%)	16 (50%)	NS
BMI	27.42 ± 5.31	26.21 ± 4.17	NS
AST (U/L)	54.54 ± 53.71	43.06 ± 42.34	NS
ALT (U/L)	47.10 ± 50.65	26.06 ± 14.56	.01
Bilirubin (mg/dL)	0.56 ± 0.55	0.81 ± 0.45	NS
Steatosis (biopsy data)	5 (7.8%)	0 (0%)	NS
Warm ischemia (min)	54.53 ± 32.43	54.28 ± 16.61	NS
Cold ischemia (min)	368.53 ± 106.77	338.22 ± 71.41	NS

Abbreviations: NS, not significant; BMI, body mass index; AST, aspartate transaminase; ALT, alanine transaminase.

similar in both groups, as well as time on the waiting list, MELD score, and type of transplant. Of note is that the prevalent etiology of liver disease in the study group was liver cancer, hepatitis C virus, and alcohol abuse, whereas the prevalent causes of liver disease in the control group were liver cancer and alcohol abuse. There were statistically significant differences regarding indication of transplantation for hepatitis C virus (25% for the control group vs 3.1% for the study group; *P* = .05).

No statistically significant differences were found regarding the type of postoperative complications, apart from acute cellular rejection (26.6% for the control group vs 3.12% for the study group; *P* = .006). In total, 6.2% of the recipients of donors <75 years required retransplantation versus 15.6% of recipients of donors ≥ 75 years. The median follow-up time was 2 months (range, 6–108). Patient survivals (Fig 1) for the control group at 1, 3, and 5 years were 89%, 78.6%, and 74.5%, respectively, versus 83.4%, 79.4%, and 59.6% for the study group. If positive hepatitis C virus recipients are excluded, the survival rate was 37.5% for the control group versus 12.5% for the study group. Differences in survival rates at 5 years increased and reached 79.8% for the control group versus 60.2% for the study group.

DISCUSSION

Although there is evidence that the use of organs from older donors is associated with liver dysfunction and lower survival rates, the available evidence is not conclusive. If older donors are appropriately selected by eliminating extra risk factors, there is no strong evidence to discourage the use of grafts from older donors [8,9]. According to our experience, there are no statistically significant differences between recipients of older donors and those of younger donors. The results obtained here show that the incidence of

Table 2. Recipient Characteristics

Characteristic	Donor <75 y	Donor ≥ 75 y	<i>P</i> Value
Age	52.94 ± 10.79	57.97 ± 9.27	NS
Sex			
Male	45 (62.5%)	27 (37.5%)	NS
Female	19 (79.2%)	5 (20.8%)	NS
BMI	26.69 ± 4.40	27.24 ± 5.18	NS
Time in list for OLT (d)	274.64 ± 369.56	206.84 ± 174.63	NS
MELD score	14 ± 6	15 ± 8	NS
Etiology of liver disease			
HCC	15 (23.4%)	11 (34.4%)	NS
Hepatitis C virus	16 (25%)	1 (3.1%)	.05
Hepatitis B virus	1 (1.6%)	0 (0%)	NS
Alcohol	15 (23.4%)	14 (43.8%)	NS
Other	17 (26.6%)	6 (8.17%)	NS
Type of transplantation			
Standard	64 (67.4%)	31 (96.9%)	NS
Retransplantation	0 (0%)	1 (3.1%)	NS

Abbreviations: OLT, orthotopic liver transplantation; MELD, Model for End-Stage Liver Disease; HCC, hepatocellular carcinoma; other abbreviations as in Table 1.

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