ANNALS OF TRANSPLANTATION

ORIGINAL PAPER

e-ISSN 2329-0358
© Ann Transplant, 2018; 23: 802-807
DOI: 10.12659/AOT.911550

Received: 2018.06.06
Accepted: 2018.08.17
Published: 2018.11.16

# Results of Adult Living Donor Liver Transplantation with Sixth-Decade Donors: A Propensity Score Matching Study in a High-Volume Institution

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**Source of support:** Departmental sources

**Background:** We assessed the prognostic impact of donor age on the outcome of adult living donor liver transplantation (LDLT).

**Material/Methods:** The study population comprised adult donor and recipients of right lobe grafts for LDLT performed from January 2005 to December 2016. There were 35 living donors aged ≥50 years (old-age donor group). As a control group, donors in their 20s (young-age donor group) were selected after one-to-one propensity score matching based on sex, model for end-stage liver disease (MELD) score, and primary diagnosis.

**Results:** Donor age was 52.5±1.5 years versus 25.4±3.1 years in the old- and young-age donor groups, respectively. Remnant volumes of the 2 groups were 38.9±3.0% versus 38.1±2.9%, respectively (p=0.98). One-month regeneration rate of the remnant liver was 101.1±10.6% versus 104.5±11.8%, respectively (p=0.08), and there was no significant difference in the incidences of donor complications. Mean MELD score was 15 versus 14, respectively (p=0.82). Graft-to-recipient weight ratio was 1.02±0.43 versus 0.91±0.63, respectively (p=0.28). In the recipients, biliary complication occurred in 11.4% versus 8.6%, respectively (p=0.12), and there was no difference in 5-year survival rates of both groups (p=0.15). The 1-week and 1-month regeneration rates of the remnant left liver were 71.6±9.9% and 100.1±10.6% in the old-age group, respectively, whereas those were 80.2±12.1% and 104.5±11.8% in the young-age group, respectively (p=0.08).

**Conclusions:** Right lobe grafts from donors aged ≥50 years showed the usual recovery of graft function but rather delayed liver regeneration. Thus, old-aged donors should be selected prudently after consideration of hepatic resection rate, graft size, and hepatic steatosis.

**MeSH Keywords:** **Donor Selection • Liver Cirrhosis • Living Donors**

**Abbreviations:** **ALD** – alcoholic liver disease; **ALT** – alanine aminotransferase; **AST** – aspartate aminotransferase; **DDLT** – deceased donor liver transplantation; **GRWR** – graft-to-recipient weight ratio; **HBV** – hepatitis B virus; **HCC** – hepatocellular carcinoma; **ICU** – Intensive Care Unit; **INR** – international normalized ratio; **LC** – liver cirrhosis; **LDLT** – living donor liver transplantation; **MELD** – model for end-stage liver disease

**Full-text PDF:** https://www.annalsoftransplantation.com/abstract/index/idArt/911550

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## Background

Liver transplantation (LT) has been regarded as an ultimate treatment option for patients with end-stage liver disease through refined operative techniques and availability of effective immunosuppressive agents. However, lack of organ donors is the most important problem. Accordingly, marginal grafts have been more frequently used recently in order to meet the demand for LT [1]. The factors considered in deciding on the use of marginal grafts include donor age, severity of fatty liver, severity of ischemic damage, duration of hypotension, and increase of liver enzymes. Among them, the results of LT with old-aged donor grafts have been shown to be favorable in a study based on deceased donor LT (DDLT) [2,3]. Recently, studies have also reported on DDLT with donors older than 80 years [4].

Unlike DDLT, the concept of marginal grafts in living donor LT (LDLT) is often limited to small-for-size graft or excessive hepatic fatty change because live donors are healthy and thoroughly evaluated before donor surgery [5–7]. Many LT centers have tried to limit the age of live donors from 55 to 60 years to secure donor safety [8,9]. However, some attempts have been made to properly clarify whether donor age has a negative effect on the recipient and donor outcomes after LDLT.

In the present study, we investigated the effect of donor age on LDLT by analyzing the sequences of donor recovery and recipient outcome.

## Material and Methods

### Study design

The study population comprised adult recipients of right lobe grafts for LDLT from January 2005 to December 2016. A total of 3391 patients underwent adult LDLT at the Asan Medical Center. Of these, 35 living liver donors in their 50s (old-age donor group) were analyzed in this study. We excluded the living donors of left lobe grafts and donors of right lobe grafts used for dual-graft LDLT. Their medical records were analyzed retrospectively. This study was approved by the Institutional Review Board of Asan Medical Center (IRB No. 2014-0831).

The criteria for donor selection were limited to cases when the graft volume-to-recipient standard liver volume was ≥40% or the graft-to-recipient weight ratio (GRWR) was ≥0.8%. The sixth-decade group was strictly selected, especially in terms of the proportion of future liver remnant volume (>35% of the total liver volume) and minimal fatty change (<15%) [10–12]. Our guidelines for safe donor selection are as follows: For age ≤35 years and no fatty change, remnant liver volume (RLV) should be at least 30% of total liver volume (TLV); For age ≤35 years and <15% fatty change, RLV should be at least 30–35% of TLV; For age ≤35 years and ≤30% fatty change, RLV should be at least 35% of TLV; and for age of 35–55 years and ≤15% fatty change, RLV should be at least 35% of TLV.

After donor right hepatectomy, the total bilirubin, prothrombin time, and liver enzyme levels were measured 1 week, 2 weeks, and 1 month postoperatively to estimate the functional recovery time to normalization. The liver regeneration rate was calculated using 5-mm interval computed tomography (CT) volumetry (Petavision 2 software, Seoul, Korea), with the initial liver graft weight and the transplanted liver graft volume [13,14]. After donor hepatectomy, we performed CT scans with volumetry at 1 week and 1 month postoperatively.

### Propensity score matching

Patients in the old-age donor group were matched 1: 1 through propensity score matching to patients in their 20s (young-age donor group). Propensity scores were calculated from the recipients' demographic and clinical characteristics, including sex, model for end-stage liver disease (MELD) score, GRWR, body mass index, and primary diagnosis. Propensity scores were generated for 35 patients in the old-age donor group by using the R program (R Core Team 2015; The R Foundation), and individually matched to patients in the young-age donor group at a 1: 1 ratio. The propensity-matched groups were subsequently compared statistically. After confirming that the propensity score matching was appropriate, the perioperative and surgical outcomes were compared in the 35 pairs of patients.

### Statistical analysis

Survival data were analyzed using the Kaplan-Meier method and compared using the log-rank test. Continuous variables were compared using the *t* test, whereas categorical variables were analyzed using the chi-square test. A p-value of <0.05 was considered statistically significant. Statistical analyses were performed using SPSS (version 22; IBM, New York, NY).

## Results

### Preoperative profiles of donors and recipients

The characteristics of donors and recipients in the old-age and young-age groups are summarized in Table 1. The mean donor age was 52.5±1.5 years in the old-age group (range, 50–57 years). The size of the left lobe liver and the degree of hepatic steatosis were 3.9±3.0% and 3.0±0.6%, respectively. There was no significant difference compared with the young-age group. The future liver remnant proportion of donors were





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**Table 1.** Preoperative characteristics of the living donors and recipients.

| | Old-age group (n=35) | Young-age group (n=35) | p-Value |
|---|---|---|---|
| **Donor** | | | |
| Age (years) | 52 (50–58) | 24 (20–29) | <0.01 |
| Sex (Male, %) | 27 (77.1) | 24 (68.6) | 0.19 |
| Future liver remnant proportion (%) | 38.9±3.0 | 38.1±2.9 | 0.98 |
| Hepatic steatosis (%) | 3.0±0.62 | 3.9±0.40 | 0.48 |
| BMI | 23.2±3.1 | 23.4±0.5 | 0.51 |
| **Recipient** | | | |
| Age (years) | 47±2.53 | 49±1.94 | 0.75 |
| Sex (Male, %) | 21 (60) | 19 (55.6) | 0.82 |
| Primary diagnosis | | | |
| HBV | 20 (57.1) | 18 (51.4) | 0.85 |
| HCC | 15 (42.9) | 17 (48.6) | 0.63 |
| MELD score | 15 (6–42) | 14 (6–41) | 0.82 |
| ICU-bound (%) | 3 (8.6) | 4 (11.4) | 0.56 |

BMI – body mass index; HBV – hepatitis B virus; HCC – hepatocellular carcinoma; MELD – model for end-stage liver disease; ICU – Intensive Care Unit.

38.9±3.0% and 38.1±2.9% in the old- and young-age donor groups, respectively (p=0.98). The ages of recipients in the old- and young-age donor groups were 47.3±2.5 and 47.3±2.5 years, respectively. The median values of MELD score were 15 (6–42) and 14 (6–41) in the old- and young-age donor groups, respectively. As primary diseases for LT, there were 20 cases of hepatitis B virus-associated liver cirrhosis (57.1%), 15 cases of hepatocellular carcinoma (42.9%), 7 cases of alcoholic liver cirrhosis (20%), 1 case of hepatitis C virus-associated liver cirrhosis, and 1 case of autoimmune hepatitis in the old-age donor group. The proportion of primary disease was similar comparing with the young-age group (p≥0.63).

**Postoperative profiles of donors**

The length of hospital stay of donors in the old-age group was 13.1±3.0 days. The length of normalization of liver enzyme levels after right hepatectomy was 10.8±2.3 days, and it took 7.2±3.1 days for normalization of the total bilirubin level. In the control young-age group, the lengths of hospital stay and length of liver enzyme normalization were 9.6±3.5 days and 6.7±2.4 days, respectively, showing no significant difference (p=0.25 and p=0.43 respectively).

Concerning postoperative complications in the donors, pleural effusion occurred in 3 cases (8.6%) in the old-age donor group and in 2 cases (5.7%) in the young-age donor group. None of the donors required any therapeutic intervention for postoperative complications.

The 1-week and 1-month regeneration rates of the remnant left liver were 71.6±9.9% and 100.1±10.6%, respectively, in the old-age donor group, whereas the rates were 80.2±12.1% and 104.5±11.8%, respectively, in the young-age donor group. There was a slightly lower rate of the remnant liver regeneration in the old-age donor group (p=0.08), although it was not significantly different.

**Postoperative profiles of recipients**

In the recipients, both donor groups had similar levels of peak aspartate aminotransferase (AST) and alanine aminotransferase (ALT) within the first 48 h after transplantation. The levels of AST and ALT decreased within the first week after LDLT. The values of the international normalized ratio and bilirubin, which represents liver function, decreased within the first week after LT. GRWR was 1.02±0.43 and 0.91±0.63 in the old- and young-age groups, respectively. The overall rate of acute rejection was similar between the old- and young-age donor groups (14.3% and 20.0%; p=0.42) (Table 2). Overall, the hepatitis C virus recurrence rate during the entire follow-up period was similar in both groups (11.4% and 14.3%; p=0.62).





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**Table 2.** Operative and postoperative outcomes of the living donors and recipients.

| | Old-age group (n=35) | Young-age group (n=35) | p-value |
|---|---|---|---|
| **Donor** | | | |
| Operation time (min) | 413±20.6 | 442±40.6 | 0.38 |
| Postoperative complications | | | |
| Pleural effusion (n, %) | 3 (8.6) | 2 (5.7) | 0.72 |
| Dindo-Clavien complication ≥3b (n, %) | 0 (0) | 0 (0) | |
| Hospital stay (days) | 13.1±3.0 | 13.6±3.5 | 0.31 |
| In-hospital mortality (n, %) | 0 (0) | 0 (0) | 1.0 |
| **Recipient** | | | |
| AST peak (IU/L) | 215±25.2 | 421±317 | 0.31 |
| ALT peak (IU/L) | 721±820 | 501±587 | 0.29 |
| INR peak | 1.42±0.03 | 1.40±0.10 | 0.52 |
| Bilirubin peak (mg/dL) | 2.3±0.26 | 2.1±0.20 | 0.69 |
| Operation time (min) | 798±130 | 815±78 | 0.42 |
| Biliary complication (n, %) | 4 (11.4) | 3 (8.6) | 0.12 |
| Vascular complication (n, %) | 5 (14.3) | 3 (8.6) | 0.46 |
| Hospital stay (days) | 27.6±13.3 | 28.6±14.1 | 0.45 |
| In-hospital mortality (n, %) | 2 (5.7) | 1 (2.8) | 0.12 |
| HCC recurrence (n, %) | 4 (11.4) | 5 (14.3) | 0.62 |
| Follow-up period (months) | 51.0 (1–133) | 57 (5–131) | 0.52 |
| **Graft** | | | |
| Cold ischemic time (min) | 45.1±9.6 | 40.2±11.0 | 0.21 |
| Warm ischemic time (min) | 44.5±2.1 | 42.9±1.1 | 0.32 |
| Weight (g) | 644±102 | 701±136 | 0.43 |
| GRWR | 1.02±0.43 | 0.91±0.63 | 0.28 |
| Acute rejection (n, %) | 5 (14.3%) | 7 (20.0) | 0.42 |

AST – aspartate aminotransferase; ALT – alanine aminotransferase; INR – international normalized ratio; HCC – hepatocellular carcinoma; GRWR – graft-recipient weight ratio.

**Table 3.** Profiles of the in-hospital mortality recipients who received a right lobe graft.

| Recipient sex/age (years) | Primary disease | MELD score | GRWR | Graft steatosis | Donor age (years) | Cause of death |
|---|---|---|---|---|---|---|
| Male/43 | HBV-LC | 16 | 1.12 | No | 54 | Pneumonia |
| Male/41 | ALD-LC | 26 | 0.97 | 1% | 54 | Sepsis |
| Male/61 | ALD-LC | 12 | 0.83 | 2% | 25 | Sepsis |

MELD – model for end-stage liver disease; GRWR – graft-recipient weight ratio; HBV – hepatitis B virus; LC – liver cirrhosis; ALD – alcoholic liver disease.





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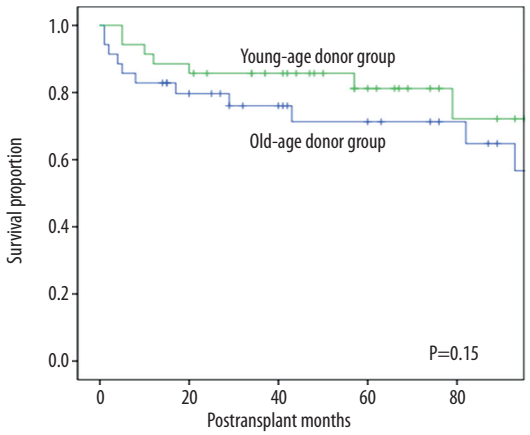


**Figure 1.** Comparison of the recipient survival curves in old- and young-age donor groups.

There were 5 cases of vascular complications (14.3%), 4 cases of biliary stricture (11.4%), 1 case of pneumonia (2.8%), and 1 case of ileus (2.8%) as postoperative complications in the old-age group. Among the vascular complications, the most frequent complication was occlusion of the reconstructed middle hepatic vein conduit because of anastomosis site stricture (n=4). There were 3 cases of vascular complication (8.6%) and 3 cases of biliary stricture (8.6%) as postoperative recipient complications in the young-age group. All vascular complications were similar in both groups (p=0.46). The mean lengths of hospital stay in recipients were 27.6±13.3 days and 28.6±13.3 days in the old- and young-age groups, respectively (Table 2).

There were 2 cases of hospital mortality within 3 months after LT operation (5.7%) in the old-age group due to pneumonia (n=1, 2.8%) and sepsis (n=1, 2.8%) (Table 3). In the old-age donor group, the 1-, 3-, and 5-year recipient survival rates were 82.9%, 79%, and 71.3% respectively, which were not significantly different from those in the young-age control group (p=0.15, Figure 1).

## Discussion

Outcomes of LT related to donor age are often reported in DDLT cases. In some studies, donor age was associated with negative outcomes after LT [15–17], although others found that the initial function of the transplanted livers was favorable after LT using old-aged donor livers [7,8]. Researchers have defined the old-aged donors as those in their 50s to 70s. In the field of LDLT, there have been only a few reports on the effect of donor age on the transplantation outcomes. In this study, based on extensive data, we performed an analysis of the prognostic impact of donor age on the outcome of LDLT.

Liver grafts from old-aged donors are more vulnerable to cold ischemic damage, especially in DDLT [16]. However, in LDLT, the duration of cold preservation is relatively short; thus, the impact of ischemic damage on the results of LT would be less. In fact, the cold ischemic time was <60 min in all cases in our present study. Therefore, in LDLT, there is less concern about cold ischemic damage with old-aged donors.

Among the significant prognostic factors in old-aged donors at the time of DDLT, the degree of fatty liver and atherosclerosis are believed to influence the outcome of transplantation in LDLT [1]. Therefore, in LDLT, it could be important to select a donor showing low fatty change in the histological examination. At our center, hepatic fatty change <15% is defined as one of the essential selection criteria for old-aged living donors.

One of the potential problems with old-aged donors is that the ability of the transplanted liver to recover its normal function may be decreased. Previous studies reported that reduced protein synthesis and prolonged cholestasis last longer in the old-aged donors of DDLT and LDLT [6,18]. In contrast, Borchert et al. reported no difference between the cholestasis period and liver synthesis ability when comparing the livers of older (age >70 years) and younger donors [3]. In this study, there was no difference in the ability to recover liver function between the old- and young-age donor groups who received LDLT.

The regeneration ability of old-aged donor livers should be considered as a matter of special attention in LDLT. Feng et al. reported that reduced liver graft transplantation is an independent risk factor of hepatic failure after DDLT [17]. Because a partial liver graft has the limitation compatible to small-for-size graft, a thorough understanding on liver regeneration is necessary because the old-aged donor liver may have a relatively low rate of regeneration. Although the age of old-age donors is relatively young (from age 50 years) in our present study, the outcome showed that the regeneration rate of the remnant liver after LDLT is rather lower. Therefore, it is important to carefully choose an appropriate elderly donor considering the liver volume, especially when the condition of the recipient is poor. Concerning the transplanted liver graft size, the GRWR should be >1.0, considering the general status of the recipient before LT. Moreover, complete surgical techniques of outflow vein reconstruction, including the inferior right hepatic vein and middle hepatic vein, are required to make the transplanted liver graft function well. In the present study, none of the recipients with middle hepatic vein anastomotic stenosis showed laboratory liver function test abnormality, but a wall stent was inserted prophylactically after early detection with bedside Doppler sonography.

Delayed recovery of recipients who received an old-aged donor liver also implies a negative impact on the donor's recovery.





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In fact, clinicians apply strict selection criteria for donors in their 50s if right lobe liver donation is needed. The most important factor is the future remnant liver volume, which must be >35% of TLV [19]. In this study, we selected elderly donor who had a sufficiently large remaining left lobe. The average resection rate of the right liver was 61.1%. The oldest donor in this study was 57 years. We have sometimes chosen living donors older than 60 years for donation of the left lobe or left lateral segment when their general condition is excellent. However, so far, we have restricted the donor age to <60 years for right liver donation [19].

The outcome of LDLT in the old-age donor group was similar to that in the young-age donor group in terms of liver function recovery; however, the liver regeneration ability tended to be lower in the old-age donor group. For donors over the age of 50 years, we suggest that prudent selection criteria should be applied to provide fully qualified partial liver grafts as well as to ensure donor safety. First, for the safety of the donor, there should be little fatty change of the liver and the proportion of the future liver remnant should be ≥35% of the whole liver volume. Second, the GRWR should be nearly 1.0 or greater. Third, the inferior right hepatic vein and middle hepatic vein should be completely reconstructed to make the liver graft function well.

## Conclusions

Right lobe grafts from donors aged ≥50 years showed the usual recovery of graft function but rather delayed liver regeneration. Thus, old-aged donors should be selected prudently after consideration of hepatic resection rate, graft size, and hepatic steatosis.

### Conflict of interest

None.

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