



Transplantation of Liver Grafts From Older Donors: Impact on Recipients With Hepatitis C Virus Infection

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ABSTRACT

Introduction. Older donor allografts are being accepted for liver transplantation (LTx) due to shortage of organs. Hepatitis C virus (HCV) infection-related disease is presently the most common indication of LT in the United States. We studied the impact of donor age on patient and graft survivals in patients with HCV infection.

Patients and methods. One hundred fifty four consecutive HCV(+) LTx recipients (117 men, 37 women) were studied. The mean follow-up period was 41.0 ± 30.2 months. The population was divided into four groups according to donor age: group I (≤ 20 years); group II (21 to 40 years); group III (41 to 60 years); group IV (> 60 years).

Results. Thirty-two (20.8%) patients died during follow-up and 16 patients (10.4%) required retransplantation. The actuarial 7-year patient survivals for groups I, II, III, and IV were 87.1%, 73.7%, 69.3%, and 68.5%, respectively ($P = .4$). Patient survivals for donor age groups III + IV ($n = 95$) and groups I + II ($n = 59$) were 68.9% and 77.2%, respectively ($P = .19$). The 7-year graft survivals for groups I, II, III, and IV were 82.7%, 71.8%, 65.8%, and 62.5%, respectively ($P = .17$). Graft survivals for groups III + IV and groups I + II were 58.4% and 76.2%, respectively ($P = .03$).

Conclusion. Patient and graft survivals for HCV-positive liver transplant recipients in this study decreased progressively as the donor age increased. Patient and graft survivals were best for group I recipients. There were significant differences in graft survivals when recipients were grouped with a cutoff donor age of 40 years.

IMPROVEMENT IN LIVER TRANSPLANTATION (LTx) outcomes over the last two decades has increased its demand. However, during this period, the donor supply has remained relatively static. As a result, grafts from older donors are being used more frequently for LTx.¹ The long-term patient and graft survivals reported for LTx involving older donors are generally inferior to the overall results of LTx.

In the past decade, there has been a rise in the number of LTx being performed in patients with hepatitis C virus (HCV) infection.^{2,3} Posttransplant HCV recurrence in recipients is almost universal. The treatment currently available for HCV infection causes significant side effects, and less than 25% of patients show a sustained viral response. Thus, long-term patient and graft survivals for recipients with HCV infection are lesser than those without HCV. Some reports suggest that for HCV-positive recipients, liver transplants from older donors result in lower patient and graft survivals than those from younger donors.^{4,5}

The aim of this study was to compare patient and graft survivals for LTx recipients with HCV infection among different donor age groups.

PATIENTS AND METHODS

From February 1997 through November 2003, 154 patients with HCV infection received a deceased donor liver allograft at our institution. The recipients were 117 men and 37 women with mean age of 49.2 ± 7.6 years. After our institutional review board approved the study protocol, we retrospectively reviewed patient and graft survival data for these cases.

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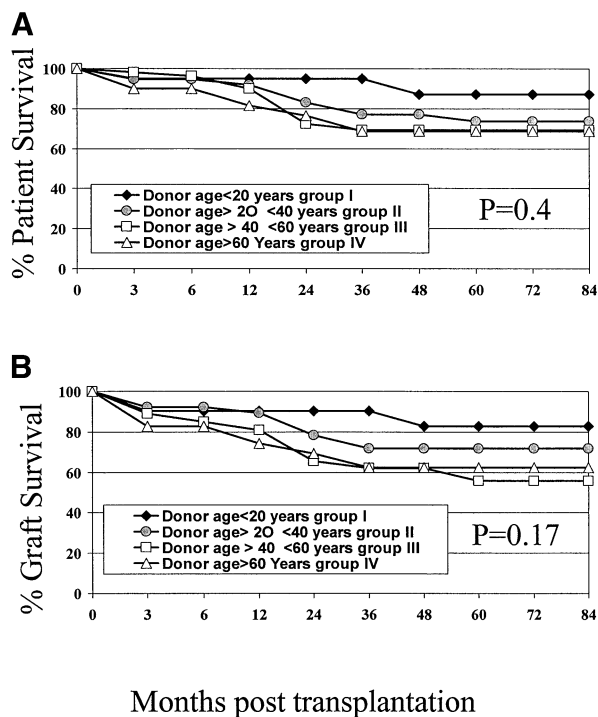


Fig 1. Recipient statistics for all groups studied individually. **(A)** Patient survival for the four donor age groups investigated. **(B)** Graft survival for the four donor age groups investigated.

Each recipient was placed on a tacrolimus-based regimen that included steroid and mycophenolate mofetil, as described earlier.⁶ Antibody induction was not used. All the patients were followed until January 2004, and the mean follow-up period was 41.0 ± 30.2 months. For analysis, the population was divided into four groups according to donor age: group I (≤ 20 years); group II (21 to 40 years); group III (41 to 60 years); group IV (> 60 years).

Data are expressed as mean \pm standard deviation. Actuarial survival was determined using the Kaplan-Meier formula, and differences among group survival rates were analyzed using the log-rank formula. The software package SPSS for Windows version 11.5 was used for all calculations.

RESULTS

Of the 154 donors, 21 (13.6%) belonged to group I, 38 (24.7%) to group II, 54 (35.1%) to group III, and 41 (26.6%) to group IV.

Patient Survival

Thirty-two (20.8%) of the 154 patients died during follow-up. The actuarial 7-year patient survivals for groups I, II, III, and IV were 87.1%, 73.7%, 69.3%, and 68.5%, respectively. The survival decreased with increasing donor age, but these differences were not statistically significant ($P = .4$; Fig 1A).

Analysis was also done between donors in group IV ($n = 41$) and groups I + II + III together ($n = 113$). The 7-year patient survivals for recipients in these two categories were 68.5% and 73.5%, respectively. This difference was not statistically significant ($P = .44$; Fig 2, top left). Also, there

was no significant difference between the corresponding patient survivals for the donor-age groups III + IV together ($n = 95$) and groups I + II together ($n = 59$). The patient survivals in these groups were 68.9% and 77.2%, respectively ($P = .19$; Fig 2, top right).

Graft Survival

Sixteen patients (10.4%) required retransplantation during the follow-up period. Seven of these 16 recipients died. The 7-year graft survivals for groups I, II, III, and IV were 82.7%, 71.8%, 65.8%, and 62.5%, respectively ($P = .17$). The 7-year graft survivals for the recipients in group IV and groups I + II + III together were 61.7% and 66.8%, respectively ($P = .32$). This difference was not statistically different. However, there was a statistically significant difference between the 7-year graft survival rates for the recipients among groups III + IV together and groups I + II together, 58.4% versus 76.2%, respectively ($P = .03$).

DISCUSSION

Liver grafts from older donors are known to be associated with poor outcome irrespective of the recipient's HCV infection status.^{7,8} Our analysis of 7-year patient and graft survivals for HCV-positive liver recipients revealed that both patient and graft survivals decreased as the donor age increased, although this observation was not statistically significant among all four groups ($P = .4$; Fig 1A). Analysis of distribution of donor ages in our study revealed that only 38.2% of donors were below 40 years of age, and only 13.6% younger than 20 years. The recipients with the youngest donors (group I: 20 years or younger) had the highest 7-year patient and graft survivals.

We also examined differences with donors grouped in larger age categories. We observed significant differences only in graft survival when the cutoff donor age for groups was 40 years. This difference needs to be examined in more detail by accounting for various other factors that lead to retransplantation or death.

At present, close to 50% of all LTx performed in the United States are for HCV-related liver disease. With such large numbers, it is not possible for all HCV-positive patients to receive allografts from younger donors. It is still not clear if the effect on poorer survival is because the presence of HCV infection alone or due to other factors. There has been a suggestion in the literature to study the impact of older donor grafts and fibrosis on chronic rejection.^{5,9}

In conclusion, the data from this study indicate that both patient and graft survivals for HCV-positive liver transplant recipients decrease as donor age increases, although this observation was not statistically significant among all groups. The patients who received grafts from donors 20 years or younger had the best patient and graft survivals. We only detected significant differences in graft survivals when recipients were grouped with a cutoff donor age of 40 years. More prospective multicenter trials with long-term

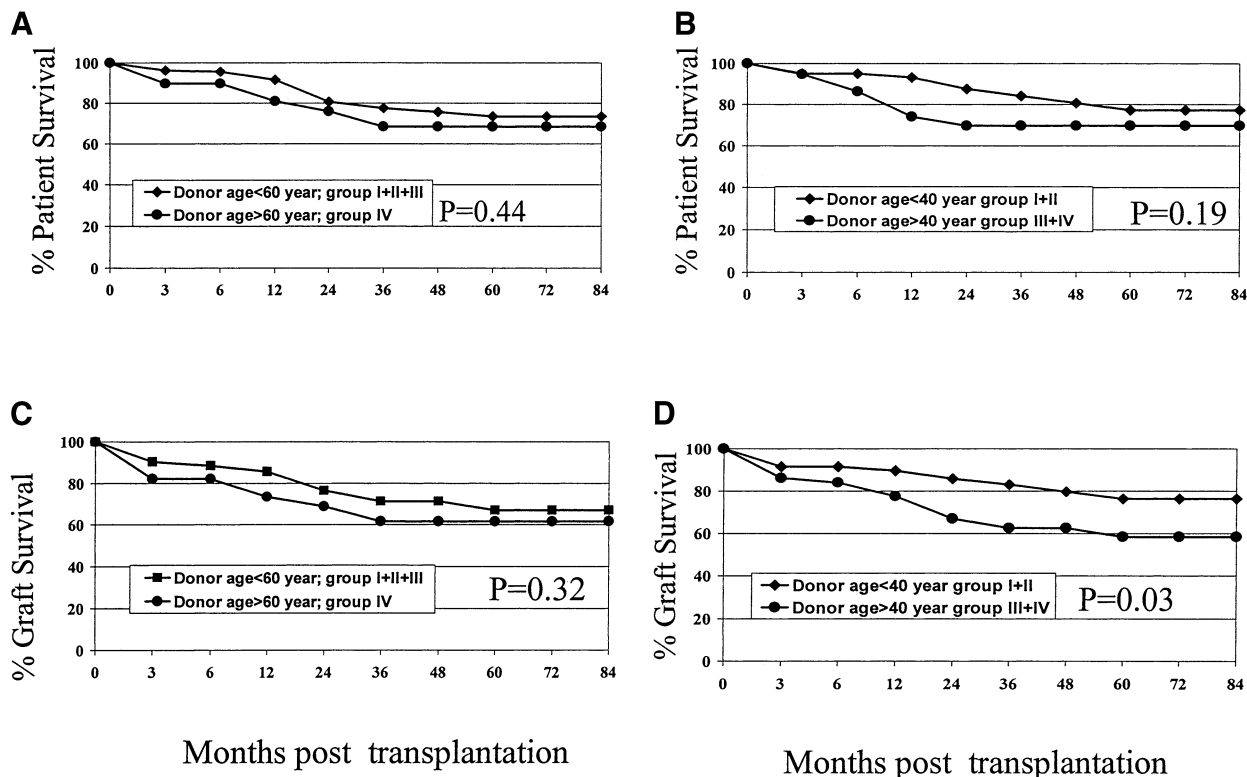


Fig 2. Recipient statistics for larger groups studied. Patient survival: **(A)** age \leq 60 years (groups I + II + III) and $>$ 60 years (group IV); **(B)** age \leq 40 years (groups I + II) and age $>$ 40 years (groups III + IV). Graft survival: **(C)** age \leq 60 years (groups I + II + III) and $>$ 60 years (group IV); **(D)** age \leq 40 years (groups I + II) and age $>$ 40 years (groups III + IV).

follow-up are needed to determine the full impact that grafts from older donors have on HCV-positive liver recipients.

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