Liver Transplant for Hepatitis C Virus

Effect of Using Older Donor Grafts on Short- and Medium-Term Survival

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Hypothesis: Older donor grafts will provide suitable results of liver transplant, even in recipients with hepatitis C virus (HCV). Although HCV remains the leading indication for liver transplant in adults in the United States, it is associated with HCV recurrence, increased graft loss, and reduced survival. In addition, recent studies suggest that the use of older donors in recipients with HCV is associated with significantly worse short- and long-term survival.

Design: Prospective database analysis.

Setting: Washington University School of Medicine.

Patients: Between January 1, 1997, and June 30, 2006, a total of 579 liver transplants were performed. Ninety pediatric transplants were excluded. Of the remaining 489 adult patients (84.5%), 187 (38.2%) had HCV and 302 (61.8%) had other indications.

Main Outcome Measures: Patient and graft survival, recurrence of HCV, and need for and results of retransplant.

Results: At 1, 3, and 5 years, overall patient survival was 88.1%, 78.3%, and 69.2%, respectively, and graft survival was 85.6%, 75.6%, and 65.6%, respectively, in patients with HCV. There was no significant difference in patient or graft survival between patients with and those without HCV. Recurrent HCV with clinically significant disease was 20% at 1 year and 62% at 10 years. Seventy-two patients received transplants from donors 60 years or older (24 of 187 [12.8%] with HCV and 48 of 302 [15.9%] without HCV). No difference was demonstrated in short- or medium-term patient or graft survival in recipients of grafts from older donors.

Conclusion: The increasing use of marginal donors, including carefully selected older donors, does not seem to adversely affect short- or medium-term results and may be a source of additional organs for expanding liver transplant waiting lists.

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HCV infection in 5 to 10 years. Recurrent HCV cirrhosis is the major cause of the increased graft loss and reduced long-term survival often reported in this patient population. Complicating this matter is the poor efficacy of HCV treatment, with reports of 20% response rates and considerable associated morbidity.

Retransplant for recurrent HCV is widely debated and usually not recommended for recurrence within 1 year of initial transplant. Some researchers suggest that survival is significantly reduced in these patients. However, others maintain that in carefully selected recipients, retransplant for HCV is acceptable. The present study was undertaken to assess our experience with liver transplant for HCV during the past 10 years. We were especially interested in results with older donor graft use in the HCV-positive population.

**METHODS**

A prospectively maintained clinical transplant database that includes recipient and donor demographics, clinical details, and recipient outcomes was used for this study. All adult transplants performed between January 1, 1997, and June 30, 2006, were reviewed. Adult recipients with HCV were compared with patients with other causes of liver disease, including nonalcoholic steatohepatitis, cryptogenic cirrhosis, autoimmune hepatitis, primary biliary cirrhosis, hepatitis B virus, acute liver failure, metabolic disorders, and miscellaneous causes (Table 1).

Liver grafts from standard brain dead donors, ECDs, and donors after cardiac death donors were used. The HCV-positive recipients were considered for HCV-positive grafts. Patient and graft survival rates of HCV recurrence and retransplant were evaluated. We also compared outcomes among HCV-positive recipients who received grafts from older donors (≥60 and ≥65 years), HCV-positive recipients who received grafts from younger donors (<60 and <65 years), and HCV-negative recipients of older grafts.

At Washington University School of Medicine, we use a standard 3-drug immunosuppression regimen that includes tacrolimus (Prograf; Astellas Pharma US Inc, Deerfield, Illinois), corticosteroids (discontinued by 4-6 months), and an antimetabolite. Posttransplant bolus corticosteroid administration was used only for biopsy-proved severe rejection. Antibody induction therapy is not used at Washington University in liver transplant.

Cox multivariate analysis was performed to independently assess factors such as donor and recipient age, presence of HCV, warm and cold ischemia times, and Model for End-Stage Liver Disease (MELD) scores. Graft and patient survival rates were analyzed using Kaplan-Meier curves and log-rank analysis. Group homogeneity assessment was performed using the 2-tailed test or the χ² test as appropriate. Differences were judged to be statistically significant when P < .05.

**RESULTS**

During the 10-year study period, 579 liver transplants were performed. Ninety pediatric liver transplants (15.5%) were excluded from the study. Of the 489 remaining patients included in this analysis, 187 (38.2%) had HCV and 302 (61.8%) had other indications for transplant (Table 1). The median follow-up was 55 months. In the HCV and non-HCV groups, the median donor age was 40 and 44 years and the median recipient age was 49 and 53 years, respectively. The male to female ratio was 3:1 in the HCV group and 2.5:1 in the non-HCV group. The most common causes of non-HCV cirrhosis were alcoholic liver disease and cryptogenic cirrhosis. The donor organ cold ischemia times were not significantly different, averaging 6.3 and 6.2 hours for the HCV and non-HCV groups, respectively, and the median warm ischemia times were also similar, 40 and 39 minutes, respectively (Table 2). The number of recipients with hepatocellular carcinoma was 87 (55 [29.4%] in the HCV group and 32 [10.6%] in the non-HCV group). Twenty-three of these cancers were incidental findings in the explant (12 in the HCV group and 11 in the non-HCV group).

**Table 1. Indications for Liver Transplant in 489 Patients**

<table>
<thead>
<tr>
<th>Disease</th>
<th>Transplants, No. (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>HCV</td>
<td>187 (38.2)</td>
</tr>
<tr>
<td>Non-HCV</td>
<td>302 (61.8)</td>
</tr>
<tr>
<td>Alcoholic cirrhosis</td>
<td>59 (19.5)</td>
</tr>
<tr>
<td>Cryptogenic cirrhosis</td>
<td>37 (12.3)</td>
</tr>
<tr>
<td>PBC</td>
<td>36 (11.9)</td>
</tr>
<tr>
<td>PSC</td>
<td>26 (8.6)</td>
</tr>
<tr>
<td>Autoimmune hepatitis</td>
<td>24 (8.0)</td>
</tr>
<tr>
<td>Hepatitis B virus</td>
<td>23 (7.6)</td>
</tr>
<tr>
<td>Acute liver failure</td>
<td>18 (6.0)</td>
</tr>
<tr>
<td>Metabolic disorders</td>
<td>17 (5.6)</td>
</tr>
<tr>
<td>NASH</td>
<td>15 (5.0)</td>
</tr>
<tr>
<td>Miscellaneous</td>
<td>47 (15.6)</td>
</tr>
</tbody>
</table>

**Table 2. Comparison of Patients With vs Those Without HCV**

<table>
<thead>
<tr>
<th></th>
<th>HCV Group (n=187)</th>
<th>Non-HCV Group (n=302)</th>
<th>P Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Recipient age, mean (range), y</td>
<td>50.3 (30-75)</td>
<td>51.1 (18-75)</td>
<td>.39</td>
</tr>
<tr>
<td>Donor age, mean (range), y</td>
<td>38.3 (7-75)</td>
<td>41.2 (8-78)</td>
<td>.07</td>
</tr>
<tr>
<td>Warm ischemia time, median (range), min</td>
<td>40 (25-59)</td>
<td>39 (33-59)</td>
<td>.25</td>
</tr>
<tr>
<td>Cold ischemia time, median (range), h</td>
<td>6.3 (0:44-11:16)</td>
<td>6.2 (0:27-11:54)</td>
<td>.52</td>
</tr>
<tr>
<td>MELD score, mean (range)</td>
<td>21 (6-37)</td>
<td>24 (7-43)</td>
<td>&lt;.001</td>
</tr>
<tr>
<td>MELD score without exception points, mean (range)</td>
<td>17.2 (6-40)</td>
<td>21.8 (5-50)</td>
<td>.001</td>
</tr>
<tr>
<td>Split liver transplants, No. (%)</td>
<td>5 (2.7)</td>
<td>7 (2.3)</td>
<td>.06</td>
</tr>
<tr>
<td>Living donors, No. (%)</td>
<td>3 (1.6)</td>
<td>10 (3.3)</td>
<td>.42</td>
</tr>
<tr>
<td>DCD donors, No. (%)</td>
<td>6 (3.2)</td>
<td>5 (1.7)</td>
<td>.40</td>
</tr>
<tr>
<td>HCV-positive donors, No. (%)</td>
<td>7 (3.7)</td>
<td>NA</td>
<td>NA</td>
</tr>
</tbody>
</table>

**Abbreviations:** HCV, hepatitis C virus; NASH, nonalcoholic steatohepatitis; PBC, primary biliary cirrhosis; PSC, primary sclerosing cholangitis.

**Abbreviations:** DCD, donation after cardiac death; HCV, hepatitis C virus; MELD, Model for End-Stage Liver Disease; NA, not applicable.

**a The range is given as hours:minutes.**
Model for End-Stage Liver Disease.

Figure 1
Overall patient (P=.45) (A) and graft (P=.22) (B) survival comparing recipients with and without hepatitis C virus (HCV).

Table 3. Multivariate Analysis

<table>
<thead>
<tr>
<th>Variable</th>
<th>Hazard Ratio (95% CI)</th>
<th>P Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>HCV</td>
<td>1.39 (0.50-4.70)</td>
<td>.55</td>
</tr>
<tr>
<td>Donor age =60 y</td>
<td>3.03 (0.70-12.20)</td>
<td>.12</td>
</tr>
<tr>
<td>Donor age =65 y</td>
<td>2.89 (0.50-16.20)</td>
<td>.23</td>
</tr>
<tr>
<td>Age of recipient</td>
<td>1.02 (0.96-1.08)</td>
<td>.51</td>
</tr>
<tr>
<td>Cold ischemia</td>
<td>1.00 (1.00-1.01)</td>
<td>.05</td>
</tr>
<tr>
<td>Warm ischemia</td>
<td>1.01 (0.94-1.08)</td>
<td>.74</td>
</tr>
<tr>
<td>MELD score</td>
<td>1.16 (1.03-1.30)</td>
<td>&lt;.001</td>
</tr>
<tr>
<td>MELD score, laboratorya</td>
<td>0.98 (0.87-1.03)</td>
<td>.24</td>
</tr>
</tbody>
</table>

Abbreviations: CI, confidence interval; HCV, hepatitis C virus; MELD, Model for End-Stage Liver Disease.
aThe laboratory MELD score is the score without exception points.

There was no significant difference in patient survival at 1, 3, and 5 years in patients with hepatitis C infection compared with the non-HCV group (P=.45). This continued for 8 years, with survival rates of 63.0% in HCV-positive recipients vs 75.5% in HCV-negative recipients (P=.40), although there seemed to be a divergence in survival at 5 years (Figure 1A). Twenty-four HCV-positive recipients received grafts from donors 60 years or older, and 11 of these were from donors 65 years or older. Forty-eight recipients without HCV received grafts from donors 60 years or older, and 27 of these were from donors 65 years or older. Recipients with HCV and older donor grafts had survival similar to recipients without HCV with older donor grafts, and this was true for all donor graft age groups. The 1-, 3-, and 5-year patient survival of 91.0%, 71.6%, and 71.6%, respectively, was seen in HCV-positive recipients receiving grafts from donors 60 years or older and of 85.0%, 76.3%, and 64.6% in HCV-negative recipients receiving similar-aged grafts. There was no difference in HCV-positive recipients who received grafts from donors younger than 60 years (P=.90) (Figure 2A). Furthermore, there was no difference between recipients with and without HCV receiving grafts from donors 65 years or older (P=.93).

PATIENT SURVIVAL

There was no significant difference in patient survival at 1, 3, and 5 years in patients with hepatitis C infection compared with the non-HCV group (P=.45). This continued for 8 years, with survival rates of 63.0% in HCV-positive recipients vs 75.5% in HCV-negative recipients (P=.40), although there seemed to be a divergence in survival at 5 years (Figure 1A). Twenty-four HCV-positive recipients received grafts from donors 60 years or older, and 11 of these were from donors 65 years or older. Forty-eight recipients without HCV received grafts from donors 60 years or older, and 27 of these were from donors 65 years or older. Recipients with HCV and older donor grafts had survival similar to recipients without HCV with older donor grafts, and this was true for all donor graft age groups. The 1-, 3-, and 5-year patient survival of 91.0%, 71.6%, and 71.6%, respectively, was seen in HCV-positive recipients receiving grafts from donors 60 years or older and of 85.0%, 76.3%, and 64.6% in HCV-negative recipients receiving similar-aged grafts. There was no difference in HCV-positive recipients who received grafts from donors younger than 60 years (P=.90) (Figure 2A). Furthermore, there was no difference between recipients with and without HCV receiving grafts from donors 65 years or older (P=.93).

Graft survival

The 1-, 3-, and 5-year graft survival rates were not significantly different in the HCV group compared with the non-HCV group (Figure 1B). There was also no difference in 1-, 3-, and 5-year graft survival in recipients with HCV who received grafts from donors 60 years or older (87.0%, 60.2%, and 60.2%, respectively) compared with recipients without HCV who received grafts from donors 60 years or older, (79.0%, 64.1%, and 57.7%, respectively) (P=.23) (Figure 2B). Comparing recipients who received grafts from donors 65 years or older, there was no significant survival difference between recipients with and those without HCV. We also did not observe any difference comparing these recipients with HCV-positive recipients receiving grafts from donors younger than 60 years (Figure 2B) or younger than 65 years.

HCV recurrence

Clinically significant HCV reinfection after transplant was defined as biopsy-proved grade 2, stage 2 or a higher level of recurrent hepatitis (Table 4). There were no differences in HCV recurrence between recipients with and those without HCV. We also did not observe any difference comparing these recipients with HCV-positive recipients receiving grafts from donors younger than 60 years (Figure 2B) or younger than 65 years.

HCV recurrence

Clinically significant HCV reinfection after transplant was defined as biopsy-proved grade 2, stage 2 or a higher level of recurrent hepatitis (Table 4). All recipients were followed up at Washington University School of Medicine after transplant, and at 1 year, a protocol liver biopsy was performed, unless one had been done recently for clinical reasons. Any other biopsies (eg, from 0 to 12 months and then from 1 year on) are dictated by clinical indications. Once a histologic diagnosis of recurrent HCV is made, follow-up biopsies are performed based on clinical variables.
In the first year after transplant, we demonstrated a 20.0% incidence of biopsy-proved HCV recurrence. However, by 5 years, 51.3% of patients had recurrence of HCV, and by 10 years, 62.0% had clinically significant HCV recurrence (Figure 3). Of 187 recipients with HCV, 48 (25.7%) have died. Three of these recipients had undergone retransplant. Fifteen (31.3%) of these recipients died of graft failure secondary to recurrent HCV.

Of the 89 patients who developed recurrent HCV, 51 had at least 1 episode of rejection. Twenty-six of these recipients received pulse corticosteroids to treat the rejection, and the remaining 25 were managed by adjustment of their standard immunosuppression dose. There was no difference in the number of patients who developed recurrence based on management of the rejection (13 of the 26 patients who received pulse corticosteroids [50.0%] and 12 of the 25 patients who were managed with immunosuppression readjustment [48.0%] eventually developed recurrent HCV). Fifty-five patients who developed recurrent HCV never had an episode of rejection. Of the HCV-positive recipients who received donor grafts 60 years or older, 50.0% (12 of 24 recipients) developed recurrence vs 41.7% (68 of 163 recipients) who received donor grafts younger than 60 years (P = .38); therefore, donor age seemed to have no significant effect on the recurrence of HCV. The median transplant-to-recurrence interval in the older donor group (aged ≥60 years) was 17 months (range, 4-23 months), whereas the median interval in the younger donor group (aged <60 years) was 14 months (range, 3 months to 8 years) (P = .10).

Of 187 HCV-positive patients, 13 (7.0%) underwent retransplant, 7 (53.8%) for transplant-related complications (4 for hepatic artery thrombosis and 3 for primary nonfunction). The remaining 6 recipients underwent retransplant for HCV recurrence. Of these 6 patients, 3 have died (1 within 30 days, 1 at 4 months of sepsis, and 1 at 4 years of recurrent HCV cirrhosis). In the 7 HCV-positive recipients who underwent retransplant for other indications, there was 1 intraoperative death and no cirrhosis from recurrent HCV to date.

The median interval between the primary and second transplants was 30 months (range, 8.5-78 months). Of 302 recipients in the non-HCV group, 28 (9.3%) required retransplant during follow-up. Overall survival in recipients with vs those without HCV at 1, 3, and 5 years was 77.8%, 66.7%, and 44.4% vs 89.3%, 89.3%, and 81.6%, respectively. When this was subdivided into retransplant for cirrhosis secondary to HCV recurrence and retransplant for reasons other than HCV in HCV-positive recipients, there is an apparent divergence because the 1- and 3-year survival rates are 66.7% and 66.7% vs 85.7% and 85.7%, respectively. Three of these recipients have
died, but only 1 of recurrent HCV, and this death was 4 years after the second liver transplant.

**COMMENT**

In the present study, we reviewed our single-center experience with transplant for HCV during the past 10 years and compared 187 recipients with HCV with 302 recipients without HCV. Demographic, donor, operative, and recipient factors between groups were similar except for the presence or absence of HCV infection. We found no difference in patient or graft survival between the 2 groups, and the 1-, 3-, and 5-year survival rates are similar to those from other studies. Twenty-four recipients with HCV and 48 without HCV received grafts from donors 60 years or older, and no significant difference was seen in patient and graft survival (Figure 2). In addition, we examined results from donors 65 years or older and did not observe a negative effect on short- or medium-term survival. However, similar to other large transplant centers, we observed a negative effect from recurrent HCV with a trend toward worsened long-term survival between years 5 and 10. We defined clinically significant HCV recurrence as stage 2, grade 2 fibrosis, and we found that the 1-, 5-, and 10-year HCV recurrence rates were 20.0%, 51.3%, and 62.0%, respectively. We did not see a difference in recurrence based on donor age.

A recent study examining United Network for Organ Sharing data suggests an improvement in 1-year graft survival from 81% to 85% comparing transplantation from the early 1990s with transplantation from 1997 to 2002. However, 5-year graft survival remains similar (67%), with no change in outcome when comparing the early with the more recent transplantation period. The researchers suggest that lack of long-term survival improvement may be related to the increase in recipients with HCV in the later period. Reduced survival in HCV-positive recipients has been reported by many researchers, and at least half of the failures are related to HCV recurrence. In this study of 187 HCV-positive recipients, we did not observe a significant decrease in overall 1-, 3-, and 5-year survival. However, it seems that at 5 years, patient and graft survival curves begin to diverge, and by 8 years a trend toward decreased survival is evident. Of those who died during long-term follow-up, 30.0% of the deaths were from HCV-related graft failure. Of the HCV-positive recipients, 50.0% developed clinically significant recurrent HCV infection within 5 years (Figure 3). In the present series, graft survival mirrored patient survival, including the divergence in the curves noted at the 5-year mark.

Previous studies have suggested that end-organ damage in recipients with HCV may be accelerated when older donor grafts are used. However, because “ideal” donors are increasingly less common, many medical centers have increased the use of ECDs, including older donor grafts, to accomplish transplant. Recurrent HCV after transplant is probably multifactorial, and numerous studies suggest different contributing factors. The role of the immunosuppression used is contentious, including suggestions that the choice of calcineurin inhibitor may or may not be significant. In addition, the risk of accelerated fibrosis when using induction agents is controversial. Pulse corticosteroid therapy for acute cellular rejection can induce recurrence and should be avoided in recipients with HCV without definitive proof of rejection. A high viral load before transplant and viral genotype 1B are also associated with a more aggressive recurrence risk. Many researchers have suggested that recipients with HCV should not receive grafts from donors older than 50 years because there may be an increased risk of HCV recurrence, accelerated disease progression to fibrosis, and reduced patient and graft survival. On the other hand, 1 study suggests that the use of ECDs has significantly reduced waiting list numbers without affecting results, but it does suggest that donor age older than 60 years is associated with reduced patient and graft survival. Because of donor shortages and lack of younger donors, having an exclusive allocation for recipients with HCV is probably impractical and has not been implemented by the United Network for Organ Sharing. Bahra and colleagues suggested that donor liver histologic features are an important risk factor in the progression of HCV-positive recipients to clinically significant HCV recurrence and inferior outcome. They suggest that portal inflammation on donor biopsy, which is more commonly encountered in older donor grafts, is associated with worse outcome. However, Briceño and colleagues looked at their 120 HCV-positive recipients and found that steatosis greater than 30% and a prolonged cold ischemia time of more than 12 hours were independent risk factors for poor outcome and that donor age older than 70 years was not a risk factor. A 10-year review from the UK national transplant database suggested that although donor age has increased by a mean of 6.1 years, there has been no detrimental effect on results.

At Washington University School of Medicine, we have used older donors in recipients with and without HCV in recent years. We do not use older donors with severe steatosis. If the donor graft is HCV positive, a normal biopsy finding is a prerequisite. The donor artery must be normal (good pulse with no plaque), and cold ischemia time is kept to a minimum. Although we cannot prove that this selectivity has affected the results, we advocate for the continued use of selective older donors in adult liver transplant. These data do not suggest that the use of older donors for HCV-positive recipients has led to increased short- or medium-term graft loss or recipient mortality. Because our increased use of older donors has primarily occurred in the past 5 years, it is not yet possible to comment on the effect on long-term outcome. It remains possible that longer follow-up will demonstrate a difference in graft or patient survival. However, we have not observed the accelerated graft loss due to recurrent HCV in recipients of older donor grafts that has been previously suggested, leading us to believe that this practice is safe.

Six patients who developed end-stage liver disease from recurrent HCV underwent retransplant along with 7 HCV-positive patients who underwent retransplant for other indications. We compared this group with 28 recipients without HCV requiring retransplant. There was a trend
toward a worse outcome in HCV-positive recipients compared with HCV-negative recipients, but statistical significance was not achieved, likely because of the few retransplants performed in patients with recurrent HCV. Survival after retransplant for indications other than HCV was similar to survival after an initial liver transplant. Re-transplant in HCV-positive patients who have end-stage liver disease from recurrent HCV infection or from other causes is controversial. Hepatitis C virus is an independent risk factor for decreased survival after retransplant \textsuperscript{10,17,38} Some researchers advocate that HCV-positive patients should at least be considered for retransplantation\textsuperscript{13} and preferably before decompensation. In a review encompassing 11 US medical centers,\textsuperscript{39} 1- and 3-year survival was 69% and 49%, respectively, in recipients with retransplant for recurrent HCV (n = 43) and 73% and 55%, respectively, in those with transplant for non-HCV etiologies (n = 73). Many patients with HCV (30%) are not considered for reevaluation, fewer are waitlisted, and most (79%) die while on the waiting list. Overall, less than 1% of patients with recurrent HCV cirrhosis actually undergo retransplant according to these authors. Poor predictors of survival are a high MELD score, recipient age older than 60 years, and cirrhosis within 2 years of initial transplant.\textsuperscript{60,61}

In conclusion, overall patient and graft survival in HCV-positive recipients is comparable with that in HCV-negative patients, and there seems to be little, if any, adverse effect on short- and medium-term follow-up with the use of carefully selected older donor grafts in recipients with HCV. Data from this series suggest that the continued use of selected older donors is a safe method of expanding the liver donor pool, even for HCV-positive recipients.

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Additional Contributions: Yan Yan, MD, PhD, helped with the statistical analysis for this work.

REFERENCES

29. Machicado VI, Bonatti H, Krishna M, et al. Donor age affects fibrosis progression with the statistical analysis for this work.


DISCUSSION

C. Wright Pinson, MD, Nashville, Tennessee: Because HCV is the leading indication for liver transplantation, close scrutiny of our results in these patients is important. Furthermore, an investigation of the results with the use of “marginal donors” in this population is important as it is commonly practiced at many centers, given the exigencies of the donor liver availability circumstances.

As a first topic of discussion, the data presented in the manuscript and here today show no statistical difference in the long-term patient or graft survival after liver transplantation for the diagnosis of HCV than for other diagnoses. However, the concluding paragraph of the manuscript reads, “In conclusion, overall patient and graft survival in HCV-positive recipients is comparable with that in HCV-negative patients,” and this seems to be more reflective of the data. One question is, however, why is there not a difference in this data set for survival after HCV than non-HCV diagnosis? Is it a combination of the difference in donor age, recipient age, the difference in male to female ratio of 3:1 vs 1:2:1, and the difference in the median MELD score of 21 vs 24—all these risk factors favoring your HCV group—so perhaps a selection bias? Another thought is perhaps the distribution of HCV subtypes is favorable in your patient population, although we don’t have those data. I wonder if your fine record with short cold ischemia times in both groups isn’t what overrides all the other risk factors. Finally, I would suggest that if we just wait long enough, the diversion of the curves probably would become significant.

As a second topic of discussion, the data indicate there was no difference in outcome of older donors vs younger donors for either the HCV or non-HCV group. A second question is why is there not a difference for this data set? Is it that there is an extremely careful donor selection for the HCV recipients? For example, only 6% of the donors for the HCV group were from older donors as opposed to 13.5% for the non-HCV group. So I wonder if the reason for the equally good results is that you are very selective in your choice of older donors, as you mention in your discussion, coupled again with the point about short cold ischemia times. I am not ready to accept that a general broadening to marginal donors, including all older donors, those with steatosis, and those with longer ischemia times, will continue to give equally good results for patients receiving liver transplantation for HCV. In other words, I would agree with the concluding paragraph in your manuscript emphasizing very careful selection of older donors, and I would agree with the wording stated today, but I was somewhat uneasy about the wording in the concluding paragraph of your abstract.

Dr Chapman: Dr Pinson has made a number of excellent points regarding the issues surrounding liver transplantation for patients with HCV. This is a big problem, and it’s probably the major problem that we face in liver transplantation today. We are transplanting our largest group of patients who have a disease that we know has a 100% chance of recurrence in the new graft. And when those patients have a recurrence, a rescue therapy for an additional transplant has particularly poor results. So this is a difficult challenge that we face and likely will be continuing to face for many years to come.

The first question related to the issue of whether or not there’s a difference in long-term outcome for patients who have liver transplantation for HCV compared with patients who did not have HCV. In our initial analysis, which was if you look at these divergent curves at specific time points and follow-up using, for example, χ² analysis, there is a difference once you get out to 8 years in survival. However, in this data set, when we look at these results with Kaplan-Meier survival curves and log-rank analysis, which is in our opinion the more appropriate way to analyze the long-term survival outcomes, we do not demonstrate a statistical difference in our data set.

This is not a small series. This is almost 500 patients. But I think, as Dr Pinson pointed out, with additional time, with these curves beginning to diverge at 5 years, and with a rate of at least 60% clinically significant HCV that exists by 8 years, there almost certainly would be a statistical difference if these patients were followed for a longer period of time.

A second major point that Dr Pinson brought up was the issue of donor age and does donor age matter. In our experience, we looked at donor age as a variable, an important consideration, but used in context with the other donor variables that are important in patients who are transplanted. So I would agree with Dr Pinson that based on our data we would not say that a 65-year-old or a 70-year-old donor is going to be the same as a 40-year-old donor with other variables and can be used equally. Donor age has to be considered just like other important variables, including cold ischemia, graft steatosis, hepatitis in the graft, etc. So I think it’s a variable that’s important, but I think certainly based on our data we feel that in properly selected donors who otherwise appear to be suitable that donor age alone should not be an exclusion criteria even in patients who have HCV. And this is a different finding than some groups who have recommended that an older donor should never be used in a patient with HCV because of the risk of early and severe recurrence of HCV leading to graft loss.

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